CHARACTERIZATION OF PARTICIPANTS TREATED WITH ULTOMIRIS® AND LONG-TERM SAFETY OUTCOMES: AN IPIG PNH REGISTRY-BASED STUDY

Protocol M07-001 and ALX-PNH-501

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ABBREVIATIONS

Abbreviation	Definition
AE	adverse event
AIHA	autoimmune hemolytic anemia
APS	antiphospholipid syndrome
AT	anti-thymocyte globulin
ATG	anti-thymocyte globulin
BMD	bone marrow disorder
C5	complement component 5
C5a	complement component 5a
C5b	complement component 5b
BMT	bone marrow transplant
COVID-19	coronavirus disease 2019
CI	confidence interval
DLP	data lock point
eGFR	estimated glomerular filtration rate
EMA	European Medicines Agency
EU	European Union
GPI	glycosylphosphatidylinositol
IHF	impaired hepatic function
IPIG	International PNH Interest Group
IRF	impaired renal function
ITP	idiopathic thrombocytopenic purpura
LDH	lactate dehydrogenase
MAA	Marketing Authorisation Application
MAH	marketing authorization holder
MAVE	major adverse vascular event
MDS	myelodysplastic syndrome
Non-TE MAVE	non-thrombotic major adverse vascular event
NMSC	non-malignant skin cancer
PNH	paroxysmal nocturnal hemoglobinuria
PSUR	Periodic Safety Update Report
Q1	first quartile

Abbreviation	Definition
Q3	third quartile
RBC	red blood cell
SAE	serious adverse event
SAP	Statistical Analysis Plan
$t_{½}$	half-life
TE	thrombotic event
TTP	thrombotic thrombocytopenic purpura
ULN	upper limit of normal
WBC	white blood cell

1. INTRODUCTION

Paroxysmal nocturnal hemoglobinuria (PNH) is an ultra-rare and life-threatening acquired hematologic disorder caused by uncontrolled activation of the terminal complement pathway (Bektas, 2020; DeZern, 2015; Kulasekararaj, 2023). The prevalence is estimated to be between 10 to 38 cases per million (Hansen, 2020; Jalbert, 2019; Richards, 2021). The disease has a roughly equal sex distribution and can occur at any age though is diagnosed most often in the fourth or fifth decade of life (Schrezenmeier, 2020). Patients with PNH are at risk of substantial morbidity and mortality. Thromboembolic events are the leading cause of death in patients with PNH and pulmonary hypertension and end-organ damage of vital organs, such as the liver, kidneys, brain, and intestines are sequelae of thromboembolic events (Hillmen, 2010; Nishimura, 2004). Prior to the availability of Soliris® (eculizumab), the estimated survival of patients with PNH 15 years after diagnosis was approximately 50% (Socie, 1996).

Soliris (first approval, 2007) and Ultomiris® (ravulizumab [first approval, 2018]) are structurally related and are both indicated for the treatment of patients with PNH. Soliris is a humanized monoclonal antibody that binds to complement component 5 (C5) and blocks its activation by complement pathway convertases, thereby preventing the release of the proinflammatory anaphylatoxin complement component 5a (C5a) and the formation of the terminal complement complex via complement component 5b (C5b). Soliris is administered every 2 weeks during the maintenance phase. Ultomiris is the first long-acting complement inhibitor that provides immediate, complete, and sustained inhibition of C5 with an 8-week dosing interval. Ultomiris is structurally related to Soliris. Ultomiris was designed to have a longer serum half-life ($t_{½}$) and corresponding duration of pharmacologic activity relative to Soliris, thus extending the dosing interval and providing patients and physicians with additional options for effective treatment.

Alexion Pharmaceuticals, Inc. has been the Sponsor of a global PNH Registry (M07-001) since Aug 2004 enrolling participants with PNH worldwide, including participants treated with Soliris since its first approval in 2007. Following the approval of Ultomiris in 2018, the PNH Registry was subsequently amended (Protocol Amendment 7, 18 Jan 2019) to permit patients who were receiving Ultomiris (including those who completed participation in sponsored clinical studies of Ultomiris) to be included in the Registry.

The primary aim of the Alexion PNH Registry was to record the natural progression of PNH and collect and evaluate safety data specific to the use of Soliris or Ultomiris in patients with PNH. The data collected from the Alexion PNH Registry are intended for health care providers to optimize clinical decision making by enhancing their understanding of the natural history of PNH, ultimately improving the guidance and assessment of therapeutic interventions. Methods of PNH diagnosis, treatment data, clinical outcomes, and quality of life assessments are also collected. An additional objective is to increase PNH knowledge within both the medical and patient communities.

In 2023, the Alexion PNH Registry began transitioning to the International PNH Interest Group (IPIG) PNH Registry with the objective to move from an industry-sponsored registry to an academic-led registry database. The IPIG PNH Registry aims to enroll patients with PNH, regardless of the type of PNH-specific therapy they are receiving, to capture data on clinical outcomes on all enrolled patients, as well as long-term safety data of PNH-specific treatments. In addition, the registry collects information on disease progression within the PNH population. The

IPIG PNH Registry is intended to increase knowledge about PNH in the medical community and patient population.

The IPIG PNH Registry is composed of the Core PNH disease Registry (Core Registry) and several product-specific silo protocols initiated by IPIG on request by the respective marketing authorization holders (MAHs). Core variables are collected in the Core Registry at enrollment and during follow-up, while specific data (eg, postauthorization safety data) for participants treated with PNH-specific therapies are collected in the silos to address specific objectives or requests from regulatory authorities and MAHs. Retrospective data from the Alexion PNH registry are transferred to the IPIG PNH Registry for consenting participants. This analysis utilizes data from the Alexion PNH Registry (Protocol M07-001) and the newly established IPIG PNH Registry to characterize the long-term safety of Ultomiris as specified in the postauthorization safety Study ALX-PNH-501. Please find more details of this study in Appendix 1 of the Statistical Analysis Plan (SAP), version 1.0 dated 15 Apr 2025 (Appendix B).

This 2025 Interim Report of the Alexion PNH Registry and IPIG PNH Registry (Protocols M07-001 and ALX-PNH-501, respectively) is specific for Ultomiris and is part of the additional pharmacovigilance activities associated with Ultomiris Marketing Authorisation Application (MAA) in the European Union (EU; Category 3 study in the EU Risk Management Plan, Version 9.0, dated 04 Sep 2024). This is the third and proposed final interim analysis report for Ultomiris. The most recent interim report was submitted in Jun 2023, European Medicines Agency (EMA) reference EMEA/H/C/004954/MEA 008 and was the last report submitted using data solely from the Alexion PNH Registry. This report presents data from the Alexion PNH Registry as well as data from participants who have enrolled into the Alexion Products Silo (referred to as Alexion Silo) of the IPIG PNH Registry (referred to as IPIG PNH Registry).

2. ANALYSIS OBJECTIVES

The objectives and endpoints of this third and proposed final interim analysis of Alexion PNH Registry and IPIG PNH Registry data specific to Ultomiris are as follows:

Objectives	Endpoints
Primary	**Primary Endpoints**
To characterize the safety of Ultomiris in participants with PNH	Incidence of reported SAEs and special events
To characterize the incidence of targeted clinical outcomes among participants with PNH	Incidence rate of MAVE, TE, malignancy, serious infection, impaired renal function, impaired hepatic function, hemolysis[a], mortality, and bone marrow transplant. Incidence of pregnancy outcome (both maternal and fetal events)
Secondary	**Secondary Endpoints**
Describe the demographic and clinical profile at treatment initiation for Ultomiris-treated participants with PNH	Frequency and univariate assessment of demographic characteristics, medical history, co-medications, and laboratory measures
Assess Ultomiris treatment patterns among participants with PNH	Initiation dose and average dose patterns Number of participants who discontinue Ultomiris and reasons for discontinuation

[a] Hemolysis data specific to potential breakthrough hemolysis were only collected in the IPIG PNH Registry and were thus described in Appendix 1 of the SAP version 1.0 dated 15 Apr 2025 (Appendix B).
Abbreviations: IPIG = International PNH Interest Group; MAVE = major adverse vascular event; PNH = paroxysmal nocturnal hemoglobinuria; SAE = serious adverse event; SAP = Statistical Analysis Plan; TE = thrombotic event

3. METHODS

The methods used to produce the results for this report are described in the SAP (Appendix B). Selected methods are summarized below.

3.1. Eligibility Criteria

The following inclusion and exclusion criteria were used to identify participants for enrollment into the Alexion and IPIG PNH Registry (Table 1):

Table 1: Eligibility Criteria for Alexion PNH Registry and for IPIG PNH Registry

	Alexion PNH Registry	IPIG PNH Registry
Inclusion Criteria	Participants of any age with PNH, with a detected proportion of PNH cells (PNH clone) of at least 1%, whether treated or not with Soliris or Ultomiris, or previously treated with Soliris or Ultomiris and withdrawn from treatment.	Participants with PNH confirmed by flow cytometry.
	Ability to comprehend and sign consent or able to give assent to have data entered in the PNH Registry. Participants who were minors were to have parent/legal guardian consent. Participants who were minors were to be willing and able to give assent, if applicable as determined by the ECs/IRBs. Upon attaining adulthood, these participants were to be re-consented.	Participants and/or legally authorized representative were to provide written informed consent/assent to participate in the core IPIG PNH Registry in a manner approved by the IRB/IEC and local regulations.
Exclusion Criteria	Participants currently enrolled in an interventional clinical study for treatment of PNH could not be enrolled in the PNH Registry while enrolled/participating in the clinical study for PNH therapy[a].	

[a] For the IPIG PNH Registry: A participant included in the registry, who enrolled in an interventional PNH clinical study during the course of the registry, was to be kept in the registry but data collection was to be paused in the registry during their involvement in the clinical study/extension study. Data collection in the registry was to continue after participant involvement in the clinical study/extension study ended or study protocol mandated data collection ceases. The data were to be included within the relevant MAH silo if the pharmaceutical partner sponsoring the study preferred.
Abbreviations: EC = Ethics Committees; IEC = Independent Ethics Committee; IPIG = International PNH Interest Group; IRB = Institutional Review Board; MAH = marketing authorization holder; PNH = paroxysmal nocturnal hemoglobinuria

3.1.1. Study Population

The study population for this analysis included participants enrolled in the Alexion PNH Registry and the Alexion Silo of the IPIG PNH Registry who met the following eligibility criteria:

- Participants with a valid Patient ID enrolled in the:
  - Alexion PNH Registry as of the data cutoff date of 06 Jan 2025 or
  - IPIG PNH Registry (Alexion Silo) as of the data cutoff date of 13 Jan 2025.
- Participants with known date of birth, sex, enrollment date, and Ultomiris treatment status.
- Only participants who initiated Ultomiris on or after enrollment in either of the registries were included in the Ultomiris study population, and specifically for IPIG PNH Registry participants (Figure 2 of Appendix 1 of the SAP [Appendix B]):
  - Participants previously enrolled in the Alexion PNH Registry who initiated Ultomiris during their participation in the Alexion PNH Registry and did not have a record of treatment.
  - Participants not previously enrolled in the Alexion PNH Registry, or who did not initiate Ultomiris while enrolled in the Alexion PNH Registry, but who initiated Ultomiris on or after enrollment in the IPIG PNH Registry.
- Only participants who initiated Soliris on/after enrollment in the Alexion PNH Registry analysis were included in the Soliris analysis population for the Alexion PNH Registry study population.

Frequent treatment switchers, defined as participants who switched their treatment with Soliris or Ultomiris more than once, were excluded from the analysis.

The listings (Listing 15 and Listing 16 of the Alexion PNH Registry [Analysis: Ravuema202501]) and (Listing 15 and Listing 16 of the IPIG PNH Registry [Analysis: IPIG]) of frequent treatment switchers were generated to provide details on demographics, disposition at last Registry follow-up, treatment information characteristics, and serious adverse events (SAEs).

3.2. Analysis Set, Treatment Group, and Exposure Period Definitions

3.2.1. Analysis Set

3.2.1.1. Alexion PNH Registry

Participants who met the eligibility criteria for the Alexion PNH Registry analysis and who initiated Ultomiris during their participation in the Alexion PNH Registry.

3.2.1.2. IPIG PNH Registry

Participants who met the eligibility criteria for the IPIG PNH Registry analysis were classified into 2 groups based on the time of Ultomiris initiation:

1. Alexion PNH Registry Study Population: Participants previously enrolled in the Alexion PNH Registry and who initiated Ultomiris during their participation in the Alexion PNH Registry.

2. IPIG PNH Registry Study Population: Participants who initiated Ultomiris on or after enrollment in the IPIG PNH Registry irrespective of their participation in the Alexion PNH Registry.

This combined population is referred to as the Ultomiris study population (Figure 2 of Appendix 1 of the SAP [Appendix B]).

All analysis outputs are presented separately for each analysis set.

3.2.2. Treatment Groups

Participants were classified into the following treatment groups according to their treatment status as follows, where "registry enrollment" referred to enrollment in either Alexion PNH Registry or IPIG PNH Registry:

- **Treated with Ultomiris:** participants with a known date of Ultomiris initiation on or after registry enrollment.
- **Prior Soliris treatment:** participants treated with Soliris, who discontinued Soliris within less than 28 days of Ultomiris initiation and switched treatment to Ultomiris once, on or after registry enrollment.
- **Without prior Soliris treatment:** participants who initiated Ultomiris on or after registry enrollment and never treated with Soliris before Ultomiris initiation, or Soliris was discontinued at least 28 days prior to Ultomiris initiation.
- **Prior Soliris treatment unknown:** participants who initiated Ultomiris on or after registry enrollment and with Soliris treatment status uncertain based on the data reported in the registry (eg, missing Soliris treatment end date).

For further details, see Section 1.2.1 of the SAP (Appendix B).

3.2.3. Exposure Period Definitions

The summary of participant demographics, participant disposition, vital status at last registry follow-up, and the registry follow-up duration were presented by treatment groups (as defined in Section 3.2.2). Information collected at Ultomiris initiation, such as medical history, concomitant medication, and laboratory values were also summarized by treatment groups.

3.2.3.1. Definitions of Exposure Periods in Alexion PNH Registry

- Untreated period: This period included the time from enrollment to last untreated follow-up date (as defined in Section 1.2.2 of the SAP [Appendix B]).
- Treated with Soliris (prior to Ultomiris switch) (Soliris exposure period): This period was from registry enrollment, if Soliris was initiated prior to enrollment, or Soliris initiation date to last Soliris treated follow-up date (as defined in Section 1.2.2 of the SAP [Appendix B])
- Treated with Ultomiris (Ultomiris exposure period): This period was from Ultomiris initiation date to last Ultomiris treated follow-up date (as defined in Section 1.2.2 of the SAP [Appendix B]).

For further details, see Section 1.2.2 of the SAP (Appendix B).

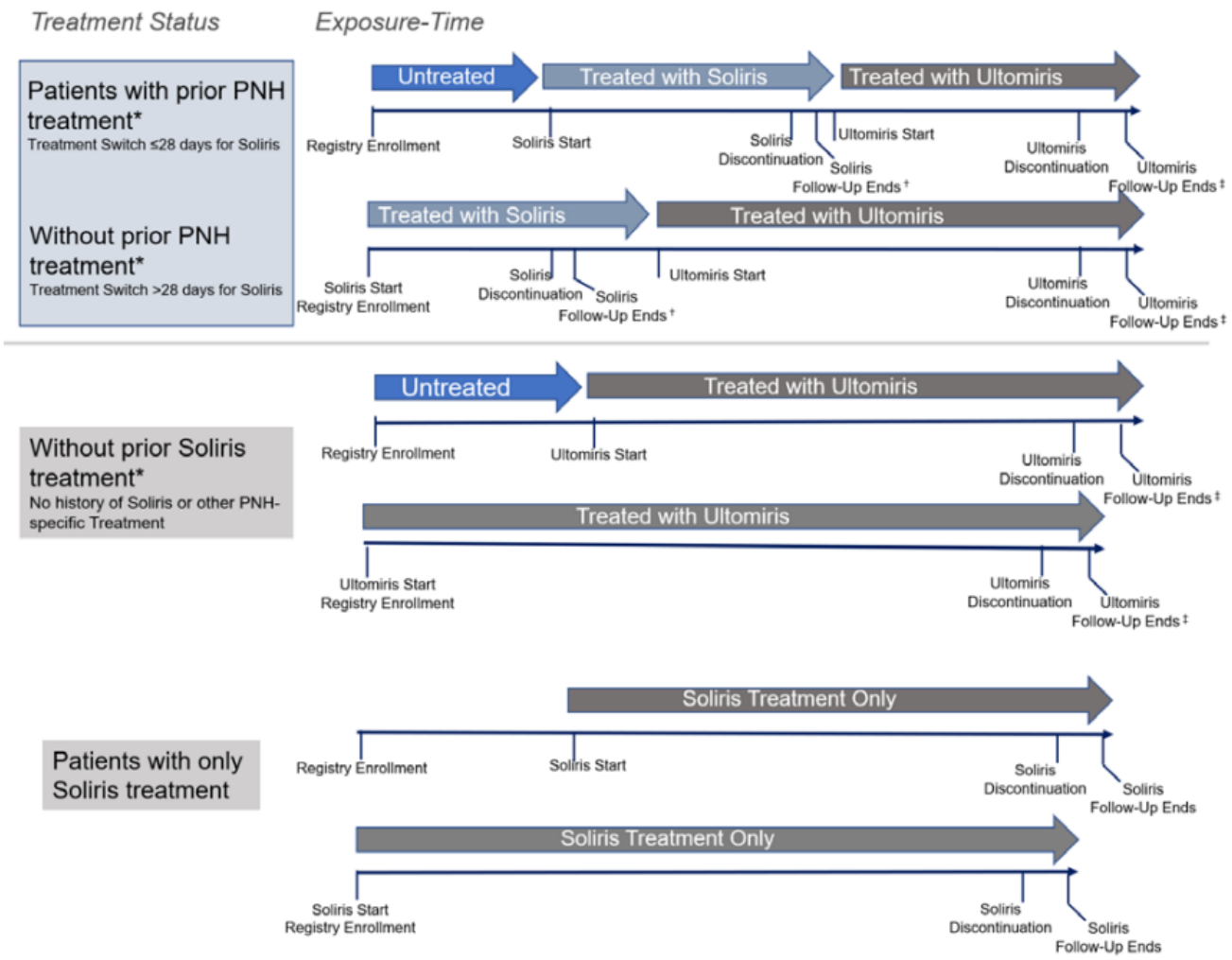
Definitions of exposure periods are illustrated in Figure 1.

3.2.3.2. Definitions of Exposure Periods in IPIG PNH Registry

- Untreated period: This period included the time from enrollment to last untreated follow-up date (as defined in Section 2.1.4 of Appendix 1 of the SAP [Appendix B]).
- Treated with Soliris (prior to Ultomiris switch) (Soliris exposure period): This period was from Soliris initiation date to last Soliris treated follow-up date (as defined in Section 2.1.4 of Appendix 1 of the SAP [Appendix B]).
- Treated with Ultomiris (Ultomiris exposure period): This period was from Ultomiris initiation date to last Ultomiris-treated follow-up date (as defined in Section 2.1.4 of Appendix 1 of the SAP [Appendix B]).

For further details, see Section 2.1.4 of Appendix 1 of the SAP (Appendix B).

Figure 1: Exposure Periods During Alexion PNH Registry Follow-up for Ultomiris-treated Participants



*Prior was defined as Soliris or other PNH-specific treatment within at least 28 days of Ultomiris initiation. Participants in Treatment Status 'Without Prior Soliris Treatment' still contributed to Soliris person time (eg, if treatment was > 4 weeks from Ultomiris initiation).
†Minimum of 4 weeks following Soliris discontinuation and the date prior to Ultomiris start.
‡Last Ultomiris follow-up date was minimum of 16 weeks after Ultomiris discontinuation, date of new non-Ultomiris treatment, or date of data cutoff.
Abbreviation: PNH = paroxysmal nocturnal hemoglobinuria; SAP = Statistical Analysis Plan.
Source: SAP version 1.0 dated 15 Apr 2025 (Appendix B)

3.2.4. Time Points of Interest

- Initiation of Ultomiris
- Initiation of Soliris
- Date of enrollment in the Alexion PNH Registry or the IPIG PNH Registry where applicable

- Last Registry follow-up date
- Last Ultomiris treated follow-up date
- Last Soliris treated follow-up date
- Last untreated follow-up date.

Definitions of timepoints of interest are described in Section 1.2.3 of the SAP (Appendix B) and Section 2.1.5 of Appendix 1 of the SAP (Appendix B).

3.2.5. Analysis Periods

Two different periods were considered when reporting the outcomes and variables summary for the Alexion PNH Registry dataset, as follows:

- The cumulative analysis included all events and person-time accrued from Registry enrollment until last Registry follow-up date or date of death.
- The analysis period included only events and person-time accrued during the current analysis period from 06 Jan 2023 until the analysis period end (cutoff) date of 06 Jan 2025.

For the IPIG PNH Registry dataset, outcomes and variables summary were reported only for the cumulative period from first participant-in in the Alexion Silo of the IPIG PNH Registry (21 May 2024) until the time of data extraction ie, data cutoff date of 13 Jan 2025.

More details are presented in Section 1.2.4 of the SAP (Appendix B) and Section 2.1.6 of Appendix 1 of the SAP (Appendix B).

3.2.6. Outcomes of Interest

3.2.6.1. Targeted Clinical and Safety Events

3.2.6.1.1. Reportable Adverse Events (SAEs and Special Events)

Alexion PNH Registry

The AEs were collected for participants who were treated with Ultomiris including the following:

- Special events regarding the medicinal product (overdose, misuse, medication error, occupational exposure of falsified products, and/or lack of therapeutic efficacy).
- SAEs (congenital anomaly or birth defect, persistent or significant disability/incapacity, resulting in death, requiring or prolonging hospitalization, life-threatening, and/or other medically important serious event).

For further details, see Section 1.3.1.1 of the SAP (Appendix B).

IPIG PNH Registry

All AEs including the targeted clinical events included participants from the full Ultomiris study population (Section 3.2.1). For those previously enrolled in the Alexion PNH Registry and who initiated Ultomiris prior to IPIG PNH Registry enrollment, any clinical or AE report from IPIG

PNH Registry enrollment through data cutoff date (13 Jan 2025) were summarized in the tables. For participants included in the IPIG PNH Registry Study Population (who initiated Ultomiris on or after IPIG PNH Registry enrollment), clinical or AEs that occurred on or after Ultomiris initiation were summarized in the tables. Clinical and AEs planned to be collected in the IPIG PNH Registry are listed in Section 3.2.6.1.2.

The clinical and AEs that were planned to be collected in the IPIG PNH Registry are detailed in Section 3.2.6.1.2 under subsection IPIG PNH Registry.

For further details, see Section 2.1.7.1 of Appendix 1 the SAP (Appendix B).

3.2.6.1.2. Targeted Clinical Events

Alexion PNH Registry

The incidence and outcomes of the following targeted clinical events were collected:

- thrombotic event (TE)
- non-thrombotic major adverse vascular event (non-TE MAVE)
- major adverse vascular event (MAVE)
- Malignancy
- Infection
- Death
- bone marrow transplant (BMT)
- Pregnancy outcomes
- Other targeted clinical events of interest:
  - Impaired renal function (IRF)
  - Impaired hepatic function (IHF)
  - Pulmonary hypertension
- Ultomiris infusion reaction

For further details, see Section 1.3.1.2 of the SAP (Appendix B).

IPIG PNH Registry

All AEs including the targeted clinical events planned to be collected were the same as those listed above in this section for the Alexion PNH Registry. Those not listed above/with slight differences were as follows:

- Pregnancy: pregnancy, exposure during lactation, and neonatal follow-up.
- Severe hepatic impairment
- Potential breakthrough hemolysis
- MAVE, infections, malignancies, and Ultomiris infusion reactions: please note that a list of types of MAVE, infections, malignancies, and Ultomiris infusion reactions was

included in Section 2.1.7.1 of Appendix 1 of the SAP (Appendix B). These were not mentioned specifically for MAVE, infections, malignancies, and Ultomiris infusion reactions in the Alexion PNH Registry.

- Bone marrow disorder (BMD): Acute myelogenous leukemia, aplastic or hypoplastic anemia, myelodysplastic syndrome, myeloproliferative neoplasm, autoimmune hemolytic anemia (AIHA), idiopathic thrombocytopenic purpura (ITP), thrombotic thrombocytopenic purpura (TTP), antiphospholipid syndrome (APS), and other.

For further details, see Section 2.1.7.1 of Appendix 1 of the SAP (Appendix B).

3.2.6.2. Medical History

Alexion PNH Registry

Medical history included history of targeted clinical events: BMD, MAVE, TE, non-TE MAVE, IRF, IHF, pulmonary hypertension, malignancy, infection, infusion reactions, pregnancy (female only), and participants' partner pregnancy.

Medical history also included concomitant medications and treatments at Ultomiris initiation.

For further details, see details in Section 1.3.2.1 of the SAP (Appendix B).

IPIG PNH Registry

As participants' medical history prior to Ultomiris initiation was already reported for the Alexion PNH Registry study population; the medical history table included participants from the IPIG PNH Registry study population.

Medical history also included concomitant medications and treatments within 6 months prior to IPIG PNH Registry enrollment or Ultomiris initiation, whichever was later.

For further details, see Sections 2.1.7.2, 2.1.7.3, 2.1.7.4 of Appendix 1 of the SAP (Appendix B).

3.2.6.3. Laboratory Measures

Alexion PNH Registry

Laboratory values included glycophosphatidylinositol (GPI)-deficient granulocytes, GPI-deficient erythrocytes (%), lactate dehydrogenase (LDH; U/L), LDH ratio, hemoglobin (g/L), haptoglobin (g/L), platelets ($\times 10^9$/L), serum creatinine (µmol/L), estimated glomerular filtration rate (eGFR; mL/min/1.73 m^2), absolute reticulocytes ($\times 10^9$/L), total red blood cell (RBC) ($\times 10^{12}$/L), and total white blood cell (WBC, $\times 10^9$/L).

For further details, see Section 1.3.2.2 of the SAP (Appendix B).

IPIG PNH Registry

The following laboratory values were presented, with the units indicated: Percent GPI-deficient granulocytes, LDH (U/L), LDH ratio (× upper limit of normal [ULN]), hemoglobin (g/dL), haptoglobin (µmol/L), platelets ($\times 10^9$/L), serum creatinine (µmol/L), eGFR (mL/min/1.73 m^2), absolute neutrophils ($\times 10^9$/µL), absolute reticulocytes ($\times 10^9$/L), and total WBC count ($\times 10^9$/L).

For further details, see Section 2.1.7.5 of Appendix 1 of the SAP (Appendix B).

3.2.7. Covariates

Alexion PNH Registry

The following covariates were used in the multivariable regression models described in Section 3.3.4:

- History of BMD at Baseline.
- History of aplastic anemia at Baseline.
- Use of Immunosuppressive concomitant medication at Baseline.
- History of TE at Baseline.
- History of MAVE at Baseline.
- History of LDH at Baseline.

These variables were added to the regression model alongside gender, age at Baseline (as defined in Section 3.2.8).

For further details on the covariates, see Section 1.3.3 of the SAP (Appendix B).

IPIG PNH Registry

Covariates were not applicable (see Section 3.3.2 for details).

3.2.8. Additional Variables of Interest

Alexion PNH Registry

- PNH disease start: Earliest of: date of first reported PNH symptom, date of first detected GPI-deficient granulocytes, or PNH diagnosis date.
- Age group at enrollment, PNH disease start, and Ultomiris initiation.
- Gender.
- Race.
- Ethnicity.
- Discontinuation from the Alexion PNH Registry.
- Discontinuation from Ultomiris treatment.
- Weight at Initiation of Ultomiris, if available; if not available, first reported weight after initiation of Ultomiris.

For further details, see Section 1.3.4 of the SAP (Appendix B).

IPIG PNH Registry

Additional variables of interest were the same as those listed above for Alexion PNH Registry. Those not listed above/with slight differences were as follows:

- PNH Disease start: Earliest of: Date from either the Alexion or IPIG PNH Registry of first reported PNH symptom, first detected GPI-deficient granulocytes, or enrollment date, as well as the PNH diagnosis date from the Alexion PNH Registry.

- Discontinuation from the Registry.

For further details, see Section 2.1.7.6 of Appendix 1 of the SAP (Appendix B).

3.3. Statistical Methods

This was a descriptive analysis with no prespecified hypotheses. If there was more than one assessment with multiple dates within the window of interest, the value closest to the date of interest was used. If there were pre- and post-equally close values, the pre- value was used for analysis. For continuous variables, if there were multiple values on the same date, the mean of the values was taken. For categorical variables, if there were multiple conflicting values on the same date, the value on that date was set to missing.

Descriptive analyses (means [standard deviation] or medians [minimum, maximum] or first quartile [Q1], third quartile [Q3]) for continuous variables; frequencies and percentages for categorical variables were planned.

Participant demographics, medical history, targeted clinical events, laboratory values, concomitant medication, prior treatment with Soliris, and Ultomiris dose were summarized at initiation of Ultomiris using descriptive analyses.

Treatment and registry discontinuation along with associated reasons, pregnancy and fetal outcomes, and SAEs collected during Registry follow-up were also summarized.

Please find further details in the SAP (Appendix B).

3.3.1. Conventions

Please find the details in Section 5.3.4 of the SAP (Appendix B) and Section 4.2.2 of Appendix 1 of the SAP (Appendix B).

3.3.2. Event Rates

Targeted clinical events, including death, MAVE, TE, non-TE MAVE, infection, malignancy, IRF, IHF, Ultomiris infusion reactions, pulmonary hypertension, and BMT were summarized by event rates based on the exposure period (detailed in Section 3.2.3). Pregnancy outcomes were also summarized by the defined exposure period.

The event rates were calculated by the total number of events divided by the person-years. Person-years were calculated per the definition of exposure period as defined in Section 1.2.2 of the SAP (Appendix B) for all participants included in the study population, regardless of whether they had an event. The event rate was calculated using Poisson regression with over-dispersion or generalized estimating equations with a log link, as was appropriate.

Please find further details on event rates in Section 5.3.1 of the SAP (Appendix B).

Considering that minimal follow-up time was available for participants in the IPIG PNH registry, targeted clinical events of interest were described in frequencies based on the exposure period defined in Section 3.2.3 and Figure 1, where feasible. Otherwise, event details were described through listings.

3.3.3. Subgroup Analyses:

Participants ever treated with Ultomiris in the study population were stratified by the following subgroups:

- Participants with untreated person-time.
- Treated with Ultomiris.
- Treated with Soliris (Prior to Ultomiris Switch).

In addition to the above groups, incidence rate analyses were also performed on participants treated with Soliris only:

- Soliris only treated participants (only for the Alexion PNH Registry analysis set).

Please find further details in Section 5.3.1.1 of the SAP (Appendix B).

3.3.4. Covariates for Multivariable Regression Models Specific to Alexion PNH Registry:

The following analysis employed the indicated covariates to control for potential confounding in the rate models:

- Analysis of infections used age, gender, history of aplastic anemia at Baseline, and use of immunosuppressive concomitant medication at Baseline as covariates.
- Analysis of MAVE/TEs/non-TE MAVE used age at Baseline, gender, LDH at Baseline, and history of MAVEs at Baseline as covariates.
- Analysis of malignancies used age, gender, and history of BMD at Baseline as covariates.

3.3.5. Sensitivity Analysis Specific to Alexion PNH Registry

A sensitivity analysis was conducted, which excluded participants missing clone size at enrollment, and participants with clone size < 1% at enrollment. The analysis repeated the rate analyses for the cumulative period for the following events: MAVE, TEs, malignancies, infections, IRF, IHF, PH, pregnancy, BMT, and deaths. Restricting these analyses to participants with a known clone size ≥ 1% at enrollment was to be applied to all Ultomiris-treated participants, as well as Soliris-treated participants, and participants with untreated person time.

Please find further details in Section 5.4 of the SAP (Appendix B).

4. RESULTS

Note: The tables (in- and post-text) utilize the generic names ravulizumab and eculizumab while the brand names Ultomiris and Soliris, respectively, are used in the text. Further, the tables used the terms “patient” and “subject” while the text mentions the term “participant”.

4.1. Disposition

4.1.1. Alexion PNH Registry Dataset

Description of the analysis set is provided in Section 3.2.1.1. The study population included participants enrolled in this registry as of 06 Jan 2025.

Cumulative

A total of 5976 participants were enrolled in the Alexion PNH Registry as of 06 Jan 2025 including 1245 participants in the study population. Of these, 532 participants were treated with Ultomiris. Thirty participants were considered as frequent treatment switchers, which refers to participants who switched between Soliris and Ultomiris treatment more than once during their participation in the Alexion PNH Registry. These participants were not included in the analysis set but are further described (Table 2; Listing 15 and Listing 16 Analysis: Ravuema202501). The study population included in this analysis set is summarized in Table 2.

Sensitivity analysis was performed in the cumulative study population and described in Post-text Table 1.3 Analysis: Ravuema202501. A total of 916 of 5976 participants were included in the study population with clone size ≥ 1%. Of these, 392 participants were treated with Ultomiris. Thirty participants from the sensitivity analysis were considered as frequent treatment switchers.

Analysis Period (06 Jan 2023 to 06 Jan 2025)

A total of 1765 participants were enrolled in the Alexion PNH Registry during the analysis period including 597 participants in the study population. Of these, 493 participants were treated with Ultomiris.

Twenty-five participants were considered as frequent treatment switchers. These participants were not included in the analysis set but are further described (Table 3; Listing 15 and Listing 16 Analysis: Ravuema202501). The study population included in this analysis set is summarized in Table 3.

Table 2: Study Population, Cumulative (Alexion PNH Registry)

	N
Patients ever enrolled in registry as of 06 Jan 2025	5976
Patients in study population[a]	1245
All ravulizumab patients	532
Prior eculizumab treatment[b]	301
Without prior eculizumab treatment[c]	161

Table 2: Study Population, Cumulative (Alexion PNH Registry)

	N
Patients never treated with eculizumab before ravulizumab initiation	59
Eculizumab was discontinued at least 28 days prior to ravulizumab initiation	102
Prior eculizumab treatment unknown[d]	70
Treated with eculizumab only	713
Patients with untreated person time[e]	252
Frequent treatment switchers[f]	30

[a] Study population includes patients ever enrolled in the registry as of 06 Jan 2025. who had non-missing and valid enrollment date, date of birth, sex. In addition, the study population only includes subjects treated with ravulizumab or treated with eculizumab only.
[b] Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. There were 27 patients who discontinued eculizumab between 17 and 28 days of ravulizumab initiation.
[c] Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.
[d] Patients were classified into the Prior Eculizumab Treatment Unknown group due to unknown prior eculizumab treatment history or because of a missing eculizumab discontinuation date.
[e] Patients with untreated person time were never treated with any anticomplement therapies on and prior to enrollment and could receive eculizumab, ravulizumab, or other anticomplement therapies after enrollment. They contributed information between registry enrollment and last untreated follow-up date.
[f] Frequent treatment switchers refer to patients who switched between eculizumab and ravulizumab treatment more than once in the registry. These patients were not to be included in the analysis.
Abbreviations: N = number of patients; PNH = paroxysmal nocturnal hemoglobinuria
Source: Post-text Table 1.1 Analysis: Ravuema202501

Table 3: Study Population, During the Analysis Period[a] (Alexion PNH Registry)

	N
Patients actively enrolled in registry between 06 Jan 2023 and 06 Jan 2025	1765
Patients in study population[b]	597
All ravulizumab patients	493
Prior eculizumab treatment[c]	278
Without prior eculizumab treatment[d]	152
Patients never treated with eculizumab before ravulizumab initiation	58
Eculizumab was discontinued at least 28 days prior to ravulizumab initiation	94
Prior eculizumab treatment unknown[e]	63
Treated with eculizumab only	104

Table 3: Study Population, During the Analysis Period[a] (Alexion PNH Registry)

	N
Patients with untreated person time[f]	239
Frequent treatment switchers[g]	25

[a] The analysis period is from 06 Jan 2023 to 06 Jan 2025.
[b] Study population includes patients actively enrolled in the registry between 06 Jan 2023 and 06 Jan 2025. who had non-missing and valid enrollment date, date of birth, sex. In addition, the study population only includes subjects treated with ravulizumab or treated with eculizumab only.
[c] Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. There were 24 patients who discontinued eculizumab between 17 and 28 days of ravulizumab initiation.
[d] Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.
[e] Patients were classified into the Prior Eculizumab Treatment Unknown group due to unknown prior eculizumab treatment history or because of a missing eculizumab discontinuation date.
[f] Patients with untreated person time were never treated with any anticomplement therapies on and prior to enrollment and could receive eculizumab, ravulizumab, or other anticomplement therapies after enrollment. They contributed information between registry enrollment and last untreated follow-up date.
[g] Frequent treatment switchers refer to patients switched between eculizumab and ravulizumab treatment more than once in the registry. These patients were not to be included in the analysis.
Abbreviations: N = number of patients; PNH = paroxysmal nocturnal hemoglobinuria
Source: Post-text Table 1.2 Analysis: Ravuema202501

4.1.2. IPIG PNH Registry Dataset

Description of the analysis set is provided in Section 3.2.1.2. The study population included participants enrolled in this registry as of 13 Jan 2025.

A total of 123 participants were enrolled in the IPIG PNH Registry including 81 participants who were also present in the Alexion PNH Registry. A total of 62 participants were treated with Ultomiris (ie, Ultomiris study population) including 56 participants who were also present in the Alexion PNH Registry (ie, Alexion PNH Registry study population) and 6 participants without prior participation in the Alexion PNH Registry (ie, IPIG PNH Registry study population).

There were no frequent treatment switchers in the IPIG PNH Registry. The study population included in the IPIG PNH Registry is summarized in Table 4.

Table 4: Study Population (IPIG PNH Registry)

	N
Patients ever enrolled in IPIG PNH Registry as of 13 Jan 2025	123
IPIG PNH Registry patients also present in Alexion PNH Registry[a]	81
Ravulizumab Study Population[b]	62
Alexion PNH Registry Study Population[d]	56
Prior eculizumab treatment[c]	46
Without prior eculizumab treatment	9
Prior eculizumab treatment unknown	1

Table 4: Study Population (IPIG PNH Registry)

	N
IPIG PNH Registry Study Population[e]	6
Prior eculizumab treatment[c]	1
Without prior eculizumab treatment	5
Prior eculizumab treatment unknown	0
Frequent treatment switchers[f]	0

[a] Based on matching participant IDs provided in both Registries.
[b] If the participant was enrolled in the Alexion PNH Registry and initiated ravulizumab in the Alexion PNH Registry, then the information regarding enrollment date and ravulizumab initiation date is based on the Alexion PNH Registry data. Otherwise, if ravulizumab is initiated in the IPIG PNH Registry, then information is based on the IPIG PNH Registry data.
[c] Prior eculizumab treatment indicates that eculizumab was discontinued within 28 days of ravulizumab initiation. Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation. Participants were classified into the Prior Eculizumab Treatment Unknown group due to unknown prior eculizumab treatment history or because of a missing eculizumab discontinuation date.
[d] Participants enrolled in the Alexion PNH Registry and initiated ravulizumab in the Alexion PNH Registry on or after enrollment.
[e] Participants who initiated ravulizumab on or after enrollment in the IPIG PNH irrespective of their participation in the Alexion PNH Registry.
[f] Frequent treatment switchers refer to patients who switched between eculizumab and ravulizumab treatment more than once in either of the registries. These patients were not to be included in the analysis.
Abbreviations: ID = identification number; IPIG = International PNH Interest Group; N = number of patients; PNH = paroxysmal nocturnal hemoglobinuria
Source: Post-text Table 1 Analysis: IPIG

4.2. Demographics

4.2.1. Alexion PNH Registry Dataset

Cumulative

The mean (SD) age at enrollment was 45.2 (16.98) years for all 532 Ultomiris-treated participants. The mean (SD) age at enrollment was 44.0 (16.78) years for participants with prior Soliris treatment, 47.7 (17.03) years for participants without prior Soliris treatment, and 44.3 (17.33) years for participants with unknown prior Soliris treatment.

The mean (SD) age at PNH disease start was 39.2 (17.53) years for all 532 Ultomiris-treated participants. The mean (SD) age at PNH disease start was 37.6 (17.07) years for participants with prior Soliris treatment, 42.0 (18.03) years for participants without prior Soliris treatment, and 39.5 (17.74) years for participants with unknown prior Soliris treatment.

The mean (SD) age at Ultomiris initiation was 52.1 (16.64) years for all 532 Ultomiris-treated participants. The mean (SD) age at Ultomiris initiation was 51.3 (16.69) years for participants with prior Soliris treatment, 53.9 (16.29) years for participants without prior Soliris treatment, and 51.1 (17.10) years for participants with unknown prior Soliris treatment.

Participant demographics are summarized in Table 5.

Analysis Period (06 Jan 2023 to 06 Jan 2025)

The mean (SD) age at enrollment was 45.2 (16.92) years for all 493 Ultomiris-treated participants. The mean (SD) age at enrollment was 44.0 (16.76) years for participants with prior Soliris treatment, 47.9 (16.94) years for participants without prior Soliris treatment, and 43.8 (17.08) years for participants with unknown prior Soliris treatment.

The mean (SD) age at PNH disease start was 39.1 (17.45) years for all 493 Ultomiris-treated participants. The mean (SD) age at PNH disease start was 37.6 (17.06) years for participants with prior Soliris treatment, 42.1 (17.90) years for participants without prior Soliris treatment, and 39.1 (17.38) years for participants with unknown prior Soliris treatment.

The mean (SD) age at Ultomiris initiation was 52.2 (16.55) years for all 493 Ultomiris-treated participants. The mean (SD) age at Ultomiris initiation was 51.3 (16.66) years for participants with prior Soliris treatment, 54.2 (16.15) years for participants without prior Soliris treatment, and 51.0 (16.86) years for participants with unknown prior Soliris treatment.

Participant demographics are summarized in Table 6.

Table 5: Patient Demographics, Cumulative and by Treatment Status (Ravulizumab Study Population)

	All Ravulizumab Patients[b] (N=532)	Prior Eculizumab Treatment[c] (N=301)	Without Prior Eculizumab Treatment[d] (N=161)	Prior Eculizumab Treatment Unknown (N=70)
Gender, n (%)				
n	532	301	161	70
Female	257 (48.3)	147 (48.8)	77 (47.8)	33 (47.1)
Male	275 (51.7)	154 (51.2)	84 (52.2)	37 (52.9)
Ethnicity, n (%)				
n	531	300	161	70
Not Hispanic/Latino	518 (97.6)	295 (98.3)	154 (95.7)	69 (98.6)
Hispanic/Latino	13 (2.4)	5 (1.7)	7 (4.3)	1 (1.4)
Race, n (%)				
n	530	299	161	70
Black or African descent	22 (4.2)	12 (4.0)	5 (3.1)	5 (7.1)
Asian	109 (20.6)	71 (23.7)	33 (20.5)	5 (7.1)
Native/Aboriginal	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Pacific Islander	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
White or Caucasian	387 (73.0)	212 (70.9)	118 (73.3)	57 (81.4)
Other (unlisted or multiple races)	12 (2.3)	4 (1.3)	5 (3.1)	3 (4.3)
Age at enrollment (years)				
n	532	301	161	70
Mean (SD)	45.2 (16.98)	44.0 (16.78)	47.7 (17.03)	44.3 (17.33)
Median (Q1, Q3)	43.6 (31.8, 59.7)	43.0 (30.7, 56.4)	47.8 (33.7, 62.7)	42.3 (30.9, 60.2)
Age group at enrollment, n (%)				
n	532	301	161	70

Table 5: Patient Demographics, Cumulative and by Treatment Status (Ravulizumab Study Population)

	All Ravulizumab Patients[b] (N=532)	Prior Eculizumab Treatment[c] (N=301)	Without Prior Eculizumab Treatment[d] (N=161)	Prior Eculizumab Treatment Unknown (N=70)
<2 years	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
2 to <12 years	1 (0.2)	1 (0.3)	0 (0.0)	0 (0.0)
12 to <18 years	10 (1.9)	7 (2.3)	2 (1.2)	1 (1.4)
18 to <30 years	101 (19.0)	63 (20.9)	23 (14.3)	15 (21.4)
30 to <50 years	220 (41.4)	126 (41.9)	68 (42.2)	26 (37.1)
50 to <65 years	112 (21.1)	59 (19.6)	37 (23.0)	16 (22.9)
65+ years	88 (16.5)	45 (15.0)	31 (19.3)	12 (17.1)
Age at PNH disease start (years)[a]				
n	532	301	161	70
Mean (SD)	39.2 (17.53)	37.6 (17.07)	42.0 (18.03)	39.5 (17.74)
Median (Q1, Q3)	35.3 (24.7, 52.0)	33.9 (24.1, 50.2)	37.1 (27.0, 58.9)	36.1 (23.7, 54.0)
Age group at PNH disease start, n (%)				
n	532	301	161	70
<2 years	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
2 to <12 years	9 (1.7)	6 (2.0)	1 (0.6)	2 (2.9)
12 to <18 years	28 (5.3)	23 (7.6)	4 (2.5)	1 (1.4)
18 to <30 years	162 (30.5)	93 (30.9)	45 (28.0)	24 (34.3)
30 to <50 years	183 (34.4)	103 (34.2)	60 (37.3)	20 (28.6)
50 to <65 years	92 (17.3)	47 (15.6)	28 (17.4)	17 (24.3)
65+ years	58 (10.9)	29 (9.6)	23 (14.3)	6 (8.6)
Years from PNH disease start to enrollment				
n	532	301	161	70

Table 5: Patient Demographics, Cumulative and by Treatment Status (Ravulizumab Study Population)

	All Ravulizumab Patients[b] (N=532)	Prior Eculizumab Treatment[c] (N=301)	Without Prior Eculizumab Treatment[d] (N=161)	Prior Eculizumab Treatment Unknown (N=70)
Mean (SD)	6.0 (8.02)	6.4 (8.09)	5.7 (8.54)	4.8 (6.29)
Median (Q1, Q3)	2.7 (0.6, 8.1)	3.1 (0.7, 9.4)	2.1 (0.4, 6.8)	2.4 (0.6, 6.7)
Years from PNH disease start to ravulizumab initiation				
n	532	301	161	70
Mean (SD)	12.9 (9.63)	13.7 (9.30)	11.9 (10.57)	11.6 (8.47)
Median (Q1, Q3)	10.9 (6.1, 17.6)	11.7 (7.1, 18.6)	9.7 (4.5, 16.2)	10.8 (6.3, 15.5)
Age at ravulizumab initiation (years)				
n	532	301	161	70
Mean (SD)	52.1 (16.64)	51.3 (16.69)	53.9 (16.29)	51.1 (17.10)
Median (Q1, Q3)	50.4 (39.3, 65.7)	50.1 (39.3, 64.6)	53.9 (40.5, 67.3)	48.4 (36.1, 64.7)
Age group at ravulizumab initiation, n (%)				
n	532	301	161	70
<2 years	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
2 to <12 years	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
12 to <18 years	1 (0.2)	0 (0.0)	1 (0.6)	0 (0.0)
18 to <30 years	43 (8.1)	27 (9.0)	10 (6.2)	6 (8.6)
30 to <50 years	214 (40.2)	123 (40.9)	60 (37.3)	31 (44.3)
50 to <65 years	133 (25.0)	76 (25.2)	41 (25.5)	16 (22.9)
65+ years	141 (26.5)	75 (24.9)	49 (30.4)	17 (24.3)

[a] PNH disease start is defined as the earliest date among date of PNH diagnosis, date of first PNH symptom, and date of laboratory test with reported granulocyte clone > 0.01%.
[b] Patients were classified into the Prior Eculizumab Treatment Unknown group due to unknown prior eculizumab treatment history or because of a missing eculizumab discontinuation date.

Table 5: Patient Demographics, Cumulative and by Treatment Status (Ravulizumab Study Population)

[c] Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. There were 27 patients who discontinued eculizumab between 17 and 28 days of ravulizumab initiation.
[d] Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.
Abbreviations: N/n = number of patients; PNH = paroxysmal nocturnal hemoglobinuria; Q1 = first quartile; Q3 = third quartile; SD: standard deviation
Source: Post-text Table 2.1 Analysis: Ravuema202501

Table 6: Patient Demographics, During the Analysis Period and by Treatment Status[a] (Ravulizumab Study Population)

	All Ravulizumab Patients[c] (N=493)	Prior Eculizumab Treatment[d] (N=278)	Without Prior Eculizumab Treatment[e] (N=152)	Prior Eculizumab Treatment Unknown (N=63)
Gender, n (%)				
n	493	278	152	63
Female	239 (48.5)	133 (47.8)	76 (50.0)	30 (47.6)
Male	254 (51.5)	145 (52.2)	76 (50.0)	33 (52.4)
Ethnicity, n (%)				
n	492	277	152	63
Not Hispanic/Latino	480 (97.6)	273 (98.6)	145 (95.4)	62 (98.4)
Hispanic/Latino	12 (2.4)	4 (1.4)	7 (4.6)	1 (1.6)
Race, n (%)				
n	491	276	152	63
Black or African descent	19 (3.9)	10 (3.6)	4 (2.6)	5 (7.9)
Asian	103 (21.0)	69 (25.0)	30 (19.7)	4 (6.3)
Native/Aboriginal	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Pacific Islander	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
White or Caucasian	358 (72.9)	193 (69.9)	114 (75.0)	51 (81.0)
Other (unlisted or multiple races)	11 (2.2)	4 (1.4)	4 (2.6)	3 (4.8)
Age at enrollment (years)				
n	493	278	152	63
Mean (SD)	45.2 (16.92)	44.0 (16.76)	47.9 (16.94)	43.8 (17.08)
Median (Q1, Q3)	43.5 (31.9, 59.7)	43.0 (30.7, 56.5)	47.9 (33.8, 62.8)	41.7 (30.3, 59.3)
Age group at enrollment, n (%)				
n	493	278	152	63

Table 6: Patient Demographics, During the Analysis Period and by Treatment Status[a] (Ravulizumab Study Population)

	All Ravulizumab Patients[c] (N=493)	Prior Eculizumab Treatment[d] (N=278)	Without Prior Eculizumab Treatment[e] (N=152)	Prior Eculizumab Treatment Unknown (N=63)
<2 years	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
2 to <12 years	1 (0.2)	1 (0.4)	0 (0.0)	0 (0.0)
12 to <18 years	9 (1.8)	6 (2.2)	2 (1.3)	1 (1.6)
18 to <30 years	93 (18.9)	58 (20.9)	21 (13.8)	14 (22.2)
30 to <50 years	205 (41.6)	117 (42.1)	64 (42.1)	24 (38.1)
50 to <65 years	103 (20.9)	55 (19.8)	35 (23.0)	13 (20.6)
65+ years	82 (16.6)	41 (14.7)	30 (19.7)	11 (17.5)
Age at PNH disease start (years)[b]				
n	493	278	152	63
Mean (SD)	39.1 (17.45)	37.6 (17.06)	42.1 (17.90)	39.1 (17.38)
Median (Q1, Q3)	35.0 (24.9, 51.6)	33.9 (24.0, 49.6)	37.8 (27.0, 59.3)	36.0 (24.9, 54.0)
Age group at PNH disease start, n (%)				
n	493	278	152	63
<2 years	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
2 to <12 years	8 (1.6)	5 (1.8)	1 (0.7)	2 (3.2)
12 to <18 years	27 (5.5)	22 (7.9)	4 (2.6)	1 (1.6)
18 to <30 years	149 (30.2)	86 (30.9)	42 (27.6)	21 (33.3)
30 to <50 years	173 (35.1)	96 (34.5)	57 (37.5)	20 (31.7)
50 to <65 years	83 (16.8)	43 (15.5)	26 (17.1)	14 (22.2)
65+ years	53 (10.8)	26 (9.4)	22 (14.5)	5 (7.9)
Years from PNH disease start to enrollment				
n	493	278	152	63

Table 6: Patient Demographics, During the Analysis Period and by Treatment Status[a] (Ravulizumab Study Population)

	All Ravulizumab Patients[c] (N=493)	Prior Eculizumab Treatment[d] (N=278)	Without Prior Eculizumab Treatment[e] (N=152)	Prior Eculizumab Treatment Unknown (N=63)
Mean (SD)	6.0 (8.12)	6.4 (8.14)	5.8 (8.71)	4.7 (6.37)
Median (Q1, Q3)	2.7 (0.6, 8.1)	3.1 (0.7, 9.5)	2.2 (0.4, 6.6)	2.3 (0.6, 6.7)
Years from PNH disease start to ravulizumab initiation				
n	493	278	152	63
Mean (SD)	13.0 (9.74)	13.8 (9.35)	12.2 (10.72)	11.9 (8.71)
Median (Q1, Q3)	11.2 (6.1, 17.7)	11.8 (7.1, 18.7)	9.9 (4.5, 16.2)	11.1 (6.3, 15.7)
Age at ravulizumab initiation (years)				
n	493	278	152	63
Mean (SD)	52.2 (16.55)	51.3 (16.66)	54.2 (16.15)	51.0 (16.86)
Median (Q1, Q3)	50.4 (39.5, 66.2)	49.6 (39.3, 64.6)	54.7 (40.6, 68.2)	48.1 (36.1, 64.7)
Age group at ravulizumab initiation, n (%)				
n	493	278	152	63
<2 years	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
2 to <12 years	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
12 to <18 years	1 (0.2)	0 (0.0)	1 (0.7)	0 (0.0)
18 to <30 years	37 (7.5)	23 (8.3)	9 (5.9)	5 (7.9)
30 to <50 years	202 (41.0)	117 (42.1)	56 (36.8)	29 (46.0)
50 to <65 years	121 (24.5)	69 (24.8)	38 (25.0)	14 (22.2)
65+ years	132 (26.8)	69 (24.8)	48 (31.6)	15 (23.8)

[a] Includes patients actively enrolled in the registry during the analysis period, which covers the time period from 06 Jan 2023 to 06 Jan 2025.
[b] PNH disease start is defined as the earliest date among date of PNH diagnosis, date of first PNH symptom, and date of laboratory test with reported granulocyte clone > 0.01%.

Table 6: Patient Demographics, During the Analysis Period and by Treatment Status[a] (Ravulizumab Study Population)

[c] Patients were classified into the Prior Eculizumab Treatment Unknown group due to unknown prior eculizumab treatment history or because of a missing eculizumab discontinuation date.
[d] Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. There were 24 patients who discontinued eculizumab between 17 and 28 days of ravulizumab initiation.
[e] Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.
Abbreviations: N/n = number of patients; PNH = paroxysmal nocturnal hemoglobinuria; Q1 = first quartile; Q3 = third quartile; SD: standard deviation
Source: Post-text Table 2.2 Analysis: Ravuema202501

4.2.2. IPIG PNH Registry Dataset

The demographic characteristics of the 56 participants who transitioned from the Alexion PNH Registry to the IPIG PNH Registry (ie, Alexion PNH Registry study population as described in Section 3.2.1.1) have been previously documented (Section 4.2.1; Table 5; Table 6). In contrast, Table 7 exclusively presents the demographic characteristics of the 6 participants who initiated Ultomiris on or after enrollment in the IPIG PNH Registry (ie, IPIG PNH Registry study population as described in Section 3.2.1.2) as of the data cutoff date (13 Jan 2025).

The mean (SD) age at enrollment was 48.3 (19.93) years for all 6 Ultomiris-treated participants. The mean (SD) age at enrollment was 32.0 (not applicable) years for the participant with prior Soliris treatment, 51.6 (20.40) years for participants without prior Soliris treatment, and there were no participants with unknown prior Soliris treatment.

The mean (SD) age at PNH disease start was 44.7 (23.42) years for all 6 Ultomiris-treated participants. The mean (SD) age at PNH disease start was 14.0 (not applicable) years for the participant with prior Soliris treatment, and 50.8 (20.09) years for participants without prior Soliris treatment.

The mean (SD) age at Ultomiris initiation was 48.5 (19.77) years for all 6 Ultomiris-treated participants. The mean (SD) age at Ultomiris initiation was 33.0 (not applicable) years for the participant with prior Soliris treatment, and 51.6 (20.40) years for participants without prior Soliris treatment.

Participant demographics are summarized in Table 7.

Table 7: Patient Demographics, by Treatment Status (IPIG PNH Registry Study Population)

	All Ravulizumab Patients[b] (N=6)	Prior Eculizumab Treatment[c] (N=1)	Without Prior Eculizumab Treatment[d] (N=5)	Prior Eculizumab Treatment Unknown (N=0)
Gender, n (%)				
n	6	1	5	0
Male	3 (50.0)	0 (0.0)	3 (60.0)	0 (0.0)
Female	3 (50.0)	1 (100.0)	2 (40.0)	0 (0.0)
Ethnicity, n (%)				
n	6	1	5	0
Not Hispanic or Latino	5 (83.3)	0 (0.0)	5 (100.0)	0 (0.0)
Unknown	1 (16.7)	1 (100.0)	0 (0.0)	0 (0.0)
Race, n (%)				
n	6	1	5	0
White	4 (66.7)	0 (0.0)	4 (80.0)	0 (0.0)

Table 7: Patient Demographics, by Treatment Status (IPIG PNH Registry Study Population)

	All Ravulizumab Patients[b] (N=6)	Prior Eculizumab Treatment[c] (N=1)	Without Prior Eculizumab Treatment[d] (N=5)	Prior Eculizumab Treatment Unknown (N=0)
Asian	1 (16.7)	0 (0.0)	1 (20.0)	0 (0.0)
Not known	1 (16.7)	1 (100.0)	0 (0.0)	0 (0.0)
Age at enrollment (years)				
n	6	1	5	0
Mean (SD)	48.3 (19.93)	32.0 (---)	51.6 (20.40)	-- (---)
Median (Q1, Q3)	39.5 (32.0, 70.0)	32.0 (32.0, 32.0)	41.0 (38.0, 70.0)	-- (--, --)
Age group at enrollment, n (%)				
n	6	1	5	0
<2 years	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
2 to <12 years	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
12 to <18 years	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
18 to <30 years	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
30 to <50 years	4 (66.7)	1 (100.0)	3 (60.0)	0 (0.0)
50 to <65 years	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
65+ years	2 (33.3)	0 (0.0)	2 (40.0)	0 (0.0)
Age at PNH disease start (years)[a]				
n	6	1	5	0
Mean (SD)	44.7 (23.42)	14.0 (---)	50.8 (20.09)	-- (---)
Median (Q1, Q3)	38.5 (32.0, 70.0)	14.0 (14.0, 14.0)	40.0 (37.0, 70.0)	-- (--, --)
Age group at PNH disease start, n (%)				
n	6	1	5	0
<2 years	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
2 to <12 years	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
12 to <18 years	1 (16.7)	1 (100.0)	0 (0.0)	0 (0.0)
18 to <30 years	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
30 to <50 years	3 (50.0)	0 (0.0)	3 (60.0)	0 (0.0)
50 to <65 years	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

Table 7: Patient Demographics, by Treatment Status (IPIG PNH Registry Study Population)

	All Ravulizumab Patients[b] (N=6)	Prior Eculizumab Treatment[c] (N=1)	Without Prior Eculizumab Treatment[d] (N=5)	Prior Eculizumab Treatment Unknown (N=0)
65+ years	2 (33.3)	0 (0.0)	2 (40.0)	0 (0.0)
Years from PNH disease start to enrollment				
n	6	1	5	0
Mean (SD)	3.9 (7.42)	19.0 (---)	0.9 (0.65)	-- (---)
Median (Q1, Q3)	1.1 (0.3, 1.8)	19.0 (19.0, 19.0)	1.1 (0.3, 1.1)	-- (--, --)
Years from PNH disease start to ravulizumab initiation				
n	6	1	5	0
Mean (SD)	4.0 (7.42)	19.1 (---)	1.0 (0.60)	-- (---)
Median (Q1, Q3)	1.1 (0.5, 1.8)	19.1 (19.1, 19.1)	1.1 (0.5, 1.1)	-- (--, --)
Age at ravulizumab initiation (years)				
n	6	1	5	0
Mean (SD)	48.5 (19.77)	33.0 (---)	51.6 (20.40)	-- (---)
Median (Q1, Q3)	39.5 (33.0, 70.0)	33.0 (33.0, 33.0)	41.0 (38.0, 70.0)	-- (--, --)
Age group at ravulizumab initiation, n (%)				
n	6	1	5	0
<2 years	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
2 to <12 years	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
12 to <18 years	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
18 to <30 years	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
30 to <50 years	4 (66.7)	1 (100.0)	3 (60.0)	0 (0.0)
50 to <65 years	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
65+ years	2 (33.3)	0 (0.0)	2 (40.0)	0 (0.0)

[a] PNH disease start is defined as the earliest date among date of PNH diagnosis, date of first PNH symptom, and date of first detected PNH clone.
[b] Patients were classified into the Prior Eculizumab Treatment Unknown group due to unknown prior eculizumab treatment history or because of a missing eculizumab discontinuation date.

Table7: Patient Demographics, by Treatment Status (IPIG PNH Registry Study Population)

[c] Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation.
[d] Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.
Abbreviations: N/n = number of patients; IPIG = International PNH Interest Group; PNH = paroxysmal nocturnal hemoglobinuria; Q1 = first quartile; Q3 = third quartile; SD = standard deviation
Source: Post-text Table 2 Analysis: IPIG

4.3. Disposition at Last Registry Follow-up Date

4.3.1. Alexion PNH Registry Dataset

Cumulative

As of the data cutoff date (06 Jan 2025), 466 (87.6%) out of 532 Ultomiris-treated participants discontinued from the Alexion PNH Registry. These included 244 (81.1%) participants with prior Soliris treatment, 153 (95.0%) participants without prior Soliris treatment, and 69 (98.6%) participants with unknown prior Soliris treatment status.

Reasons for discontinuation were: participant died (20 [4.3%] participants); participant enrolled in a clinical study of PNH treatment (19 [4.1%] participants), participant choice (4 [0.9%] participants), participant was treated by another physician (2 [0.4%] participants), participant received BMT (3 [0.6] participants), and other reasons (210 [45.1%] participants) (Table 8).

Other reasons for discontinuation included the following:

- site closure reported in 78 (43.33%) participants with prior Soliris treatment, 74 (41.11%) participants without prior Soliris treatment, and 28 (15.56%) participants with unknown prior Soliris treatment and
- participant enrolled in a clinical study for PNH therapy, treated by ASPAVELI®, and participant withdrew consent (1 participant, each, Listing 1 Analysis: Ravuema202501).

Analysis Period (06 Jan 2023 to 06 Jan 2025)

During the analysis period, 430 (87.2%) out of 493 Ultomiris-treated participants discontinued from the Alexion PNH Registry. These included 224 (80.6%) participants with prior Soliris treatment, 144 (94.7%) participants without prior Soliris treatment, and 62(98.4%) participants with unknown prior Soliris treatment.

Reasons for discontinuation were: participant died and participant enrolled in a clinical study of PNH treatment (12 [2.8%] participants, each), participant choice (1 [0.2%] participant), and other reasons (197 [45.8%] participants) (Table 9).

Other reasons for discontinuation included the following:

- site closure reported in 78 (43.82%) participants with prior Soliris treatment, 74 (41.57%) participants without prior Soliris treatment, and 26 (14.61%) participants with unknown prior Soliris treatment and

- participant enrolled in a study for PNH therapy, treated by Aspaveli (1 participant). (Listing 1.1 Analysis: Ravuema202501).

Table 8: Patient Disposition at Last Registry Follow-Up Date, Cumulative and by Treatment Status (Ravulizumab Study Population)

	All Ravulizumab Patients[a] (N=532)	Prior Eculizumab Treatment[b] (N=301)	Without Prior Eculizumab Treatment[c] (N=161)	Prior Eculizumab Treatment Unknown (N=70)
Registry discontinuation, n (%)				
n	532	301	161	70
No	66 (12.4)	57 (18.9)	8 (5.0)	1 (1.4)
Yes	466 (87.6)	244 (81.1)	153 (95.0)	69 (98.6)
Reported reason for registry discontinuation, n (%)				
n	466	244	153	69
Patient choice	4 (0.9)	1 (0.4)	3 (2.0)	0 (0.0)
Patient received a bone marrow transplant	3 (0.6)	1 (0.4)	1 (0.7)	1 (1.4)
Patient is being treated by another physician	2 (0.4)	1 (0.4)	1 (0.7)	0 (0.0)
Patient enrolled in a clinical trial of PNH treatment	19 (4.1)	15 (6.1)	3 (2.0)	1 (1.4)
Patient died	20 (4.3)	9 (3.7)	10 (6.5)	1 (1.4)
Enrollment in the IPIG PNH Registry	207 (44.4)	124 (50.8)	53 (34.6)	30 (43.5)
Other	210 (45.1)	93 (38.1)	81 (52.9)	36 (52.2)
Unknown	1 (0.2)	0 (0.0)	1 (0.7)	0 (0.0)

[a] Patients were classified into the Prior Eculizumab Treatment Unknown group due to unknown prior eculizumab treatment history or because of a missing eculizumab discontinuation date.
[b] Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. There were 27 patients who discontinued eculizumab between 17 and 28 days of ravulizumab initiation.
[c] Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.
Abbreviations: N/n = number of patients; IPIG = International PNH Interest Group; PNH = paroxysmal nocturnal hemoglobinuria
Source: Post-text Table 3.1 Analysis: Ravuema202501

Table 9: Patient Disposition at Last Registry Follow-Up Date, During the Analysis Period and by Treatment Status[a] (Ravulizumab Study Population)

	All Ravulizumab Patients[b] (N=493)	Prior Eculizumab Treatment[c] (N=278)	Without Prior Eculizumab Treatment[d] (N=152)	Prior Eculizumab Treatment Unknown (N=63)
Registry discontinuation, n (%)				
n	493	278	152	63
No	63 (12.8)	54 (19.4)	8 (5.3)	1 (1.6)
Yes	430 (87.2)	224 (80.6)	144 (94.7)	62 (98.4)
Reported reason for registry discontinuation, n (%)				
n	430	224	144	62
Patient choice	1 (0.2)	1 (0.4)	0 (0.0)	0 (0.0)
Patient received a bone marrow transplant	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Patient is being treated by another physician	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Patient enrolled in a clinical trial of PNH treatment	12 (2.8)	10 (4.5)	2 (1.4)	0 (0.0)
Patient died	12 (2.8)	4 (1.8)	8 (5.6)	0 (0.0)
Enrollment in the IPIG PNH Registry	207 (48.1)	124 (55.4)	53 (36.8)	30 (48.4)
Other	197 (45.8)	85 (37.9)	80 (55.6)	32 (51.6)
Unknown	1 (0.2)	0 (0.0)	1 (0.7)	0 (0.0)

[a] Includes patients actively enrolled in the registry during the analysis period, which covers the time period from 06 Jan 2023 to 06 Jan 2025.
[b] Patients were classified into the Prior Eculizumab Treatment Unknown group due to unknown prior eculizumab treatment history or because of a missing eculizumab discontinuation date.
[c] Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. There were 24 patients who discontinued eculizumab between 17 and 28 days of ravulizumab initiation.
[d] Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.
Abbreviations: N/n = number of patients; IPIG = International PNH Interest Group; PNH = paroxysmal nocturnal hemoglobinuria
Source: Post-text Table 3.2 Analysis: Ravuema202501

4.3.2. IPIG PNH Registry Dataset

As of the data cutoff date (13 Jan 2025), 1 (1.6%) out of 62 Ultomiris-treated participants discontinued from the IPIG PNH Registry. These included 1 (2.1%) participant with prior Soliris treatment. No participants without prior Soliris treatment or with unknown prior Soliris treatment discontinued from the IPIG PNH Registry.

Reason for discontinuation was participant died (1 [100%] participant) (Table 10, Listing 1 Analysis: IPIG).

Table 10: Patient Disposition at Last Registry Follow-Up Date, by Treatment Status (Ravulizumab Study Population)

	All Ravulizumab Patients[a] (N=62)	Prior Eculizumab Treatment[b] (N=47)	Without Prior Eculizumab Treatment[c] (N=14)	Prior Eculizumab Treatment Unknown (N=1)
Registry discontinuation, n (%)				
N	62	47	14	1
No	61 (98.4)	46 (97.9)	14 (100.0)	1 (100.0)
Yes	1 (1.6)	1 (2.1)	0 (0.0)	0 (0.0)
Reported reason for registry discontinuation, n (%)				
N	1	1	0	0
The patient (or legally authorized representative) requests discontinuation from the PNH registry for any reason	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Lost to follow-up	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Subject withdrawal of consent	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Death of patient	1 (100.0)	1 (100.0)	0 (0.0)	0 (0.0)
Bone marrow transplant	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Other reason	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

[a] Patients were classified into the Prior Eculizumab Treatment Unknown group due to unknown prior eculizumab treatment history or because of a missing eculizumab discontinuation date.
[b] Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation.
[c] Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.
Abbreviations: N/n = number of patients; PNH = paroxysmal nocturnal hemoglobinuria
Source: Post-text Table 3 Analysis: IPIG

4.4. Ultomiris Treatment Information

4.4.1. Alexion PNH Registry Dataset

Cumulative

Out of 532 participants treated with Ultomiris, 62 (11.7%) participants discontinued treatment with Ultomiris. The reasons for discontinuation included physician decision and death (10 [16.1%] participants each); cost or access consideration and AE (1 [1.6%] participant each); lack of efficacy (9 [14.5%] participants); switch to other anticomplement treatment (15 [24.2%] participants); due to participant choice (3 [4.8%] participants), switch to Soliris IV (5 [8.1%] participants) and unknown reason (8 [12.9%] participants) (Post-text Table 4.1 and Listing 2 Analysis: Ravuema202501).

A total of 481 out of 532 participants treated with Ultomiris reported receipt of meningococcal vaccine prior to the start of Ultomiris treatment (Post-text Table 5.1 Analysis: Ravuema202501).

The majority of Ultomiris-treated participants (337 [67.1%]) out of 502 participants with analyzable data) received the first dose of Ultomiris 2700 mg. Out of 505 participants who received subsequent doses of Ultomiris as of the data cutoff date, 294 (58.2%) participants received all subsequent doses that were ≥ 3300 to < 3600 mg every 8 weeks. There were 74 (14.7%) participants who had subsequent doses categorized as “other” or “unknown”. A total of 337 (66.7%) participants out of 505 participants with analyzable data received a last dose of 3300 mg Ultomiris. There were 12 (2.4%) participants who received a last dose of Ultomiris categorized as “other” (Post-text Table 5.1 Analysis: Ravuema202501).

Analysis Period (06 Jan 2023 to 06 Jan 2025)

Out of 493 participants treated with Ultomiris, 46 (9.3%) participants discontinued treatment with Ultomiris. The reasons for discontinuation included physician decision and lack of efficacy (7 [15.2%]) participants each); death (6 [13.0%]); AE (1 [2.2%]); switch to other anticomplement treatment (14 [30.4%]) participants; due to participant choice and switch to Soliris IV (2 [4.3%] participants each); and unknown reason (7 [15.2%] participants) (Post-text Table 4.2 and Listing 2.1 Analysis: Ravuema202501).

A total of 442 out of 493 participants treated with Ultomiris reported receipt of meningococcal vaccines prior to the start of Ultomiris treatment (Post-text Table 5.2 Analysis: Ravuema202501).

The majority of Ultomiris-treated participants (316 [67.5%]) out of 468 participants with analyzable data) received the first dose of Ultomiris 2700 mg. Out of 470 participants who received subsequent doses of Ultomiris, 279 (59.4%) received doses that were ≥ 3300 to < 3600 mg every 8 weeks. There were 65 (13.8%) participants who had subsequent doses categorized as “other” or “unknown”. Among the 473 participants with analyzable data, 318 (67.2%) participants received a last dose of 3300 mg Ultomiris. There were 11 (2.3%) participants who received a last dose of Ultomiris categorized as “other” (Post-text Table 5.2 Analysis: Ravuema202501).

4.4.2. IPIG PNH Registry Dataset

Out of 62 participants treated with Ultomiris, 1 (1.6%) participant discontinued treatment with Ultomiris. The reason for discontinuation was physician decision. No record of discontinuation was reported for 61 (98.4%) participants (Post-text Table 4 and Listing 2 Analysis: IPIG).

Ultomiris treatment information for the 56 participants who transitioned from the Alexion PNH registry to the IPIG PNH Registry (ie, Alexion PNH Registry study population as described in Section 3.2.1.1) have been previously documented (Section 4.4.1, Post-text Table 5.1 and Post-text Table 5.2 Analysis: Ravuema202501). In contrast, Post-text Table 5 Analysis: IPIG exclusively presents Ultomiris treatment information for the 6 participants who initiated Ultomiris on or after enrollment in the IPIG PNH Registry (ie, IPIG PNH Registry study population as described in Section 3.2.1.2) as of the data cutoff date (13 Jan 2025).

All 6 participants treated with Ultomiris reported receipt of meningococcal vaccines prior to the start of Ultomiris treatment (Post-text Table 5 Analysis: IPIG).

The majority of Ultomiris-treated participants (4 [66.7%]) out of 6 participants with analyzable data) received the first dose of Ultomiris 3300 mg. No participants received any subsequent doses of Ultomiris (< 3000 mg to ≥ 3600 mg every 8 weeks) (Post-text Table 5 Analysis: IPIG).

4.5. Durations of Follow-up

4.5.1. Alexion PNH Registry Dataset

Cumulative

The mean (SD) duration from enrollment to last Registry follow-up was 9.4 (4.19) years for all Ultomiris-treated participants. The mean (SD) duration from enrollment to last Registry follow-up was 10.1 (3.70) years for participants with prior Soliris treatment, 8.0 (4.67) years for participants without prior Soliris treatment, and 9.2 (4.31) years for participants with unknown prior Soliris treatment. The mean (SD) duration of Ultomiris treatment follow-up was 2.2 (1.37) years for all Ultomiris-treated participants. The mean (SD) duration of Ultomiris treatment follow-up was 2.6 (1.27) years for participants with prior Soliris treatment, 1.6 (1.2) years for participants without prior Soliris treatment, and 1.9 (1.55) years for participants with unknown prior Soliris treatment (Post-text Table 6.1 Analysis: Ravuema202501).

Analysis Period (06 Jan 2023 to 06 Jan 2025)

The mean (SD) duration of follow-up during the analysis period was 1.2 (0.35) years for all Ultomiris-treated participants. The mean (SD) duration of follow-up during the analysis period was 1.2 (0.35) years for participants with prior Soliris treatment, 1.2 (0.31) years for participants without prior Soliris treatment, and 1.2 (0.39) years for participants with unknown prior Soliris treatment. The mean (SD) duration of Ultomiris treatment during the analysis period was 1.1 (0.42) years for all Ultomiris-treated participants. The mean (SD) duration of Ultomiris treatment during the analysis period was 1.2 (0.40) years for participants with prior Soliris treatment, 1.0 (0.40) year for participants without prior Soliris treatment, and 1.1 (0.51) years for participants with unknown prior Soliris treatment (Post-text Table 6.2 Analysis: Ravuema202501).

4.5.2. IPIG PNH Registry Dataset

As of the data cutoff date (13 Jan 2025), the mean (SD) duration from enrollment to last Registry follow-up was 0.4 (0.14) years for all Ultomiris-treated participants. The mean (SD) duration from enrollment to last Registry follow-up was 0.4 (0.14) years for participants with prior Soliris treatment, 0.5 (0.12) years for participants without prior Soliris treatment, and 0.3 (not applicable) years for the participant with unknown prior Soliris treatment. The mean (SD) duration of Ultomiris treatment follow-up was 2.8 (0.98) years for all Ultomiris-treated participants inclusive of treatment data from the Alexion PNH Registry. The mean (SD) duration of Ultomiris treatment follow-up was 3.1 (0.61) years for participants with prior Soliris treatment, 1.9 (1.43) years for participants without prior Soliris treatment, and 2.7 (not applicable) years for the participant with unknown prior Soliris treatment (Post-text Table 6 Analysis: IPIG).

4.6. Vital Status at Last Registry Follow-up

4.6.1. Alexion PNH Registry Dataset

Cumulative

At the last Registry follow-up date, there were 20 (3.8%) deaths reported in 532 Ultomiris-treated participants (Post-text Table 7.1 Analysis: Ravuema202501). This result encompasses deaths that occurred during both treated and untreated time periods. These included 9 (3.0%) out of 301 participants with prior Soliris treatment, 10 (6.2%) out of 161 participants without prior Soliris treatment, and 1 (1.4%) out of 70 participants with unknown prior Soliris treatment.

Analysis Period (06 Jan 2023 to 06 Jan 2025)

At the last Registry follow-up date, there were 12 (2.4%) deaths reported in 493 Ultomiris-treated participants (Post-text Table 7.2 Analysis: Ravuema202501). These included 4 (1.4%) out of 278 participants with prior Soliris treatment and 8 (5.3%) out of 152 participants without prior Soliris treatment. No deaths were reported in participants with unknown prior Soliris treatment.

4.6.2. IPIG PNH Registry Dataset

At the last Registry follow-up date, there was 1 (1.6%) death reported in 6 Ultomiris-treated participants (Post-text Table 7 Analysis: IPIG), including 1 (2.1%) out of 47 participants with prior Soliris treatment. No death was reported in 14 participants without prior Soliris treatment and no death were reported in the participant with unknown prior Soliris treatment as of the data cutoff date (13 Jan 2025).

4.7. Targeted Clinical and Safety Events

4.7.1. Reportable Adverse Events (SAEs and Special Events)

4.7.1.1. Death

4.7.1.1.1. Alexion PNH Registry Dataset

Cumulative

A total of 17 deaths were reported during Ultomiris treatment and 78 deaths were reported in those treated only with Soliris. No deaths were reported in 252 participants with untreated person-time while untreated and in 299 participants treated with Soliris prior to Ultomiris. These results only include deaths that occurred during Ultomiris-treated time.

The estimated death rate was 1.5 per 100 person-years (95% CI: 0.9, 2.4) in participants while treated with Ultomiris and 2.4 per 100 person-years (95% CI: 1.9, 3.0) in participants treated only with Soliris (Table 11). For further details, see Listing 3 Analysis: Ravuema202501.

Analysis Period (06 Jan 2023 to 06 Jan 2025)

A total of 10 deaths were reported during Ultomiris treatment and 3 deaths were reported in those treated with Soliris only. No deaths were reported in 23 participants with untreated person-time while untreated and in 14 participants treated with Soliris prior to Ultomiris.

The estimated death rate was 2.0 per 100 person-years (95% CI: 1.1, 3.7) in participants while treated with Ultomiris and 3.5 per 100 person-years (95% CI: 1.1, 10.8) in participants treated only with Soliris (Table 12). For further details, see Listing 3.1 Analysis: Ravuema202501.

Table 11: Rates of Death, Cumulative and by Exposure Period (Study Population)

	Patients with Untreated Person Time (N=252)	Treated with Eculizumab (Prior to Ravulizumab Switch) (N=301)	Treated with Ravulizumab (N=532)	Treated with Eculizumab Only (N=713)
All patients				
Total patients at risk	252	299	525	709
Number of patients with events	0	0	17	78
Incidence (percent of population at risk, %)	0.0	0.0	3.2	11.0
Number of events	0	0	17	78
Person-years	609.7	2181.6	1155.4	3256.6
Rate per 100 person-years	0.0	0.0	1.5	2.4
Estimated rate per 100 person-years[a]	n/a	n/a	1.5	2.4

Table 11: Rates of Death, Cumulative and by Exposure Period (Study Population)

	Patients with Untreated Person Time (N=252)	Treated with Eculizumab (Prior to Ravulizumab Switch) (N=301)	Treated with Ravulizumab (N=532)	Treated with Eculizumab Only (N=713)
95% CI	(n/a)	(n/a)	(0.9, 2.4)	(1.9, 3.0)

[a] Poisson regression estimate of incidence density.
Abbreviations: CI = confidence interval; n/a = not available; N/n = number of patients
Source: Post-text Table 21.1 Analysis: Ravuema202501

Table 12: Rates of Death, During the Analysis Period and by Exposure Period[a] (Study Population)

	Patients with Untreated Person Time (N=239)	Treated with Eculizumab (Prior to Ravulizumab Switch) (N=278)	Treated with Ravulizumab (N=493)	Treated with Eculizumab Only (N=104)
All patients				
Total patients at risk	23	14	452	77
Number of patients with events	0	0	10	3
Incidence (percent of population at risk, %)	0.0	0.0	2.2	3.9
Number of events	0	0	10	3
Person-years	9.7	5.6	500.0	86.0
Rate per 100 person-years	0.0	0.0	2.0	3.5
Estimated rate per 100 person-years[b]	n/a	n/a	2.0	3.5
95% CI	(n/a)	(n/a)	(1.1, 3.7)	(1.1, 10.8)

[a] The analysis period was from 06 Jan 2023 to 06 Jan 2025.
[b] Poisson regression estimate of incidence density.
Abbreviations: CI = confidence interval; n/a = not available; N/n = number of patients
Source: Post-text Table 21.2 Analysis: Ravuema202501

4.7.1.1.2. IPIG PNH Registry Dataset

As of the data cutoff date (13 Jan 2025), 1 participant died while treated with Ultomiris (Listing 3 Analysis: IPIG). Details are provided in Section 4.7.2.3.2.

4.7.1.2. Serious Adverse Events and Special Events

4.7.1.2.1. Alexion PNH Registry Dataset

Of the 532 participants treated with Ultomiris in this Registry as of 06 Jan 2025, a total of 257 SAEs were reported in 119 participants (211 SAEs in 90 participants with prior Soliris treatment, 31 SAEs in 22 participants without prior Soliris treatment, and 15 SAEs in 7 participants with unknown treatment status). Of these, 236 SAEs in 112 participants required hospitalization (196 SAEs in 85 participants with prior Soliris treatment, 26 SAEs in 20 participants without prior Soliris treatment, and 14 SAEs in 7 participants with unknown treatment status). A total of 13 SAEs in 10 participants were categorized as fatal. Details of these SAEs that occurred in Ultomiris-treated participants enrolled in the Alexion PNH Registry as of 06 Jan 2025 are presented in Listing 14 Analysis: Ravuema202501. These reported SAEs did not reveal any new safety concerns.

One SAE of hemolytic crisis reported in 1 participant was considered as a special event due to lack of therapeutic efficacy. The outcome of this event was reported as resolved.

4.7.1.2.2. IPIG PNH Registry Dataset

As of the data cutoff date (13 Jan 2025), out of the 62 participants treated with Ultomiris, a total of 4 SAEs were reported in 4 participants (3 SAEs [acute cardiac failure, pyrexia, and worsening of gallstone disease] in 3 participants with prior Soliris treatment and 1 SAE [prostate cancer] in 1 participant without prior Soliris treatment). The SAEs, acute cardiac failure (1 participant; Section 4.7.2.3.2) had fatal outcome; prostate cancer (1 participant, Section 4.7.2.4.2) had the outcome reported as not resolved; and pyrexia and worsening of gallstone disease (1 participant, each) which had the outcomes reported as resolved (Post-text Table 8.2 and Listing 14 Analysis: IPIG).

4.7.2. Targeted Clinical Events

Safety events in this analysis were stratified by exposure period during Registry follow-up- as described in Section 3.3.1.

4.7.2.1. Thrombotic Events

4.7.2.1.1. Alexion PNH Registry Dataset

Cumulative

Out of 252 participants with untreated person-time at risk, 18 TEs were reported in 16 participants while untreated. Out of 299 participants treated with Soliris prior to Ultomiris at risk, 15 TEs were reported in 15 participants while treated with Soliris. Out of 525 participants at risk, 4 TEs were reported in 3 participants while treated with Ultomiris. Out of 711 participants treated only with Soliris at risk, 21 TEs were reported in 19 participants (Table 13).

The adjusted TE rate was 4.2 per 100 person-years (95% CI: 2.4, 7.1) in participants with untreated person-time while untreated, 0.7 per 100 person-years (95% CI: 0.3, 1.3) in participants treated with Soliris prior to Ultomiris, 0.5 per 100 person-years (95% CI: 0.2, 1.4) in participants while treated with Ultomiris, and 0.7 per 100 person-years (95% CI: 0.4, 1.2) in participants treated only with Soliris (Table 13).

Table 13: Adjusted Rates of Thrombotic Events, Cumulative and by Exposure Period (Study Population)

	Patients with Untreated Person-Time (N=252)	Treated with Eculizumab (Prior to Ravulizumab Switch) (N=301)	Treated with Ravulizumab (N=532)	Treated with Eculizumab Only (N=713)
All patients				
Total patients at risk	252	299	525	711
Number of patients with events	16	15	3	19
Incidence (percent of population at risk, %)	6.3	5.0	0.6	2.7
Number of events	18	15	4	21
Person-years	609.7	2181.6	1155.4	3258.0
Rate per 100 person-years	3.0	0.7	0.3	0.6
Adjusted rate per 100 person-years[a]	4.2	0.7	0.5	0.7
95% CI	(2.4, 7.1)	(0.3, 1.3)	(0.2, 1.4)	(0.4, 1.2)

[a] Poisson regression estimate of incidence density. The adjusted multivariable regression model includes the following covariates: age at Baseline, gender, LDH at Baseline, and history of MAVEs at Baseline.
[b] Baseline is defined as the enrollment date for 'patients with untreated person-time' and the ravulizumab treatment initiation date for patients in 'treated with ravulizumab' group. For patients included in the group of 'treated with eculizumab (prior to ravulizumab switch)' and 'treated with eculizumab only', Baseline is the eculizumab treatment initiation date.
Abbreviations: CI = confidence interval; LDH = lactate dehydrogenase; MAVE = major adverse vascular event; N = number of patients
Source: Post-text Table 11.1.2 Analysis: Ravuema202501

Analysis Period (06 Jan 2023 to 06 Jan 2025)

Out of 23 participants with untreated person-time at risk, 1 TE was reported in 1 participant while untreated. Out of 14 participants treated with Soliris prior to Ultomiris at risk, no TEs were reported in any participant while treated with Soliris. Out of 452 participants at risk, 2 TEs were reported in 1 participant while treated with Ultomiris. Out of 78 participants treated only with Soliris at risk, no TEs were reported in any participant while treated only with Soliris.

The estimated TE rate was 10.3 per 100 person-years (95% CI: 1.5, 73.4) in participants while untreated, 0.4 per 100 person-years (95% CI: 0.1, 1.6) in participants while treated with Ultomiris (Table 14).

Table 14: Rates of Thrombotic Events, During the Analysis Period and by Exposure Period[a] (Study Population)

	Patients with Untreated Person-Time (N=239)	Treated with Eculizumab (Prior to Ravulizumab Switch) (N=278)	Treated with Ravulizumab (N=493)	Treated with Eculizumab Only (N=104)
All patients				
Total patients at risk	23	14	452	78
Number of patients with events	1	0	1	0
Incidence (percent of population at risk, %)	4.3	0.0	0.2	0.0
Number of events	1	0	2	0
Person-years	9.7	5.6	500.0	86.2
Rate per 100 person-years	10.3	0.0	0.4	0.0
Estimated rate per 100 person-years[b]	10.3	n/a	0.4	n/a
95% CI	(1.5, 73.4)	(n/a)	(0.1, 1.6)	(n/a)

[a] The analysis period is from 06 Jan 2023 to cutoff date 06 Jan 2025.
[b] Poisson regression estimate of incidence density.
Abbreviations: CI = confidence interval; N = number of patients
Source: Post-text Table 11.1.3 Analysis: Ravuema202501

4.7.2.1.2. IPIG PNH Registry Dataset

As of the data cutoff date (13 Jan 2025), no TEs were reported (Post-text Table 8.2 Analysis: IPIG).

4.7.2.2. Non-thrombotic Major Adverse Vascular Events

4.7.2.2.1. Alexion PNH Registry Dataset

Cumulative

Out of 252 participants with untreated person-time at risk, 8 non-TE MAVEs were reported in 7 participants while untreated. Out of 299 participants treated with Soliris prior to Ultomiris at risk, 4 non-TE MAVEs were reported in 4 participants while treated with Soliris. Out of 525 participants at risk, 2 non-TE MAVEs were reported in 2 participants while treated with Ultomiris. Out of 711 participants treated only with Soliris at risk, 15 non-TE MAVEs were reported in 13 participants while treated only with Soliris.

The adjusted non-TE MAVE rate was 1.7 per 100 person-years (95% CI: 0.7, 3.9) in participants with untreated person-time while untreated, 0.1 per 100 person-years (95% CI: 0.0, 0.5) in participants treated with Soliris prior to Ultomiris, 0.3 per 100 person-years (95% CI: 0.1, 1.3) in participants while treated with Ultomiris, and 0.4 per 1 00 person-years (95% CI: 0.2, 0.7) in participants treated only with Soliris (Table 15).

Table 15: Adjusted Rates of Non-Thrombotic Major Adverse Vascular Events, Cumulative and by Exposure Period (Study Population)

	Patients with Untreated Person-Time (N=252)	Treated with Eculizumab (Prior to Ravulizumab Switch) (N=301)	Treated with Ravulizumab (N=532)	Treated with Eculizumab Only (N=713)
All patients				
Total patients at risk	252	299	525	711
Number of patients with events	7	4	2	13
Incidence (percent of population at risk, %)	2.8	1.3	0.4	1.8
Number of events	8	4	2	15
Person-years	609.7	2181.6	1155.4	3258.0
Rate per 100 person-years	1.3	0.2	0.2	0.5
Adjusted rate per 100 person-years[a]	1.7	0.1	0.3	0.4
95% CI	(0.7, 3.9)	(0.0, 0.5)	(0.1, 1.3)	(0.2, 0.7)

[a] Poisson regression estimate of incidence density. The adjusted multivariable regression model includes the following covariates: age at Baseline, gender, LDH at Baseline, and history of MAVEs at Baseline.
[b] Baseline is defined as the enrollment date for 'patients with untreated person-time' and the ravulizumab treatment initiation date for patients in 'treated with ravulizumab' group. For patients included in the group of 'treated with eculizumab (prior to ravulizumab switch)' and 'treated with eculizumab only', Baseline is the eculizumab treatment initiation date.
Abbreviations: CI = confidence interval; LDH = lactate dehydrogenase; MAVE = major adverse vascular event; N = number of patients
Source: Post-text Table 11.2.2 Analysis: Ravuema202501

Analysis Period (06 Jan 2023 to 06 Jan 2025)

Out of 452 participants treated with Ultomiris at risk, 1 non-TE MAVE was reported in 1 participant while treated with Ultomiris and out of the 78 participants treated only with Soliris at risk, 1 non-TE MAVE was reported in 1 participant while treated only with Soliris. No non-TE MAVEs were reported in 23 participants with untreated person-time at risk and 14 participants treated with Soliris prior to Ultomiris at risk.

The estimated non-TE MAVE rate was 0.2 per 100 person-years (95% CI: 0.0, 1.4) in participants while treated with Ultomiris and 1.2 per 100 person-years (95% CI: 0.2, 8.2) in participants treated only with Soliris (Table 16).

Table 16: Rates of Non-Thrombotic Major Adverse Vascular Events, During the Analysis Period and by Exposure Period[a] (Study Population)

	Patients with Untreated Person-Time (N=239)	Treated with Eculizumab (Prior to Ravulizumab Switch) (N=278)	Treated with Ravulizumab (N=493)	Treated with Eculizumab Only (N=104)
All patients				
Total patients at risk	23	14	452	78
Number of patients with events	0	0	1	1
Incidence (percent of population at risk, %)	0.0	0.0	0.2	1.3
Number of events	0	0	1	1
Person-years	9.7	5.6	500.0	86.2
Rate per 100 person-years	0.0	0.0	0.2	1.2
Estimated rate per 100 person-years[b]	n/a	n/a	0.2	1.2
95% CI	(n/a)	(n/a)	(0.0, 1.4)	(0.2, 8.2)

[a] The analysis period is from 06 Jan 2023 to cutoff date 06 Jan 2025.
[b] Poisson regression estimate of incidence density.
Abbreviations: CI = confidence interval; n/a = not available; N = number of patients
Source: Post-text Table 11.2.3 Analysis: Ravuema202501

4.7.2.2.2. IPIG PNH Registry Dataset

As of the data cutoff date (13 Jan 2025), no non-TE MAVEs were reported (Post-text Table 8.2 Analysis: IPIG).

4.7.2.3. Major Adverse Vascular Events

4.7.2.3.1. Alexion PNH Registry Dataset

Cumulative

Out of 252 participants with untreated person-time at risk, 26 MAVEs were reported in 22 participants while untreated. Out of 299 participants treated with Soliris prior to Ultomiris at risk, 19 MAVEs were reported in 19 participants while treated with Soliris prior to Ultomiris. Out of 525 participants treated with Ultomiris at risk, 6 MAVEs were reported in 5 participants while treated with Ultomiris. Out of 711 participants treated only with Soliris at risk, 36 MAVEs were reported in 31 participants while treated only with Soliris (Table 17).

The adjusted MAVE rates were 5.9 per 100 person-years (95% CI: 3.7, 9.2) in participants with untreated person-time while untreated, 0.8 per 100 person-years (95% CI: 0.4, 1.5) in participants treated with Soliris prior to Ultomiris, 0.8 per 100 person-years (95% CI: 0.4, 1.9) in participants while treated with Ultomiris, and 1.1 per 100 person-years (95% CI: 0.7, 1.6) in participants treated only with Soliris (Table 17; Listing 4 Analysis: Ravuema202501).

Analysis Period (06 Jan 2023 to 06 Jan 2025)

Out of 23 participants with untreated person-time at risk, 1 MAVE was reported in 1 participant while untreated. Out of 14 participants treated with Soliris prior to Ultomiris at risk, no MAVE were reported while treated with Soliris prior to Ultomiris. Out of 452 participants treated with Ultomiris at risk, 3 MAVEs were reported in 2 participants while treated with Ultomiris. Out of 78 participants treated only with Soliris at risk, 1 MAVE was reported in 1 participant while treated only with Soliris.

The estimated MAVE rates were 10.3 per 100 person-years (95% CI: 1.5, 73.4) in participants with untreated person-time while untreated, 0.6 per 100 person-years (95% CI: 0.2 1.9) in participants while treated with Ultomiris, and 1.2 per 100 person-years (95% CI: 0.2, 8.2) in participants treated only with Soliris (Table 18 and Listing 4 Analysis: Ravuema202501).

4.7.2.3.2. IPIG PNH Registry Dataset

As of the data cutoff date (13 Jan 2025), 1 MAVE (acute cardiac failure) was reported in 1 participant while treated with Ultomiris. The outcome was reported as fatal (Listing 4 Analysis: IPIG).

Table 17: Adjusted Rates of Major Adverse Vascular Events, Cumulative and by Exposure Period[a] (Study Population)

	Patients with Untreated Person-Time (N=252)	Treated with Eculizumab (Prior to Ravulizumab Switch) (N=301)	Treated with Ravulizumab (N=532)	Treated with Eculizumab Only (N=713)
All patients				
Total patients at risk	252	299	525	711
Number of patients with events	22	19	5	31
Incidence (percent of population at risk, %)	8.7	6.4	1.0	4.4
Number of events	26	19	6	36
Person-years	609.7	2181.6	1155.4	3258.0
Rate per 100 person-years	4.3	0.9	0.5	1.1
Adjusted rate per 100 person-years[a]	5.9	0.8	0.8	1.1
95% CI	(3.7, 9.2)	(0.4, 1.5)	(0.4, 1.9)	(0.7, 1.6)

[a] Poisson regression estimate of incidence density. The adjusted multivariable regression model includes the following covariates: age at Baseline, gender, LDH at Baseline, and history of MAVEs at Baseline.
[b] Baseline is defined as the enrollment date for 'patients with untreated person-time' and the ravulizumab treatment initiation date for patients in 'treated with ravulizumab' group. For patients included in the group of 'treated with eculizumab (prior to ravulizumab switch)' and 'treated with eculizumab only', Baseline is the eculizumab treatment initiation date.
Abbreviations: CI = confidence interval; LDH = lactate dehydrogenase; MAVE = major adverse vascular event; N = number of patients
TeSource: Post-text Table 11.2 Analysis: Ravuema202501

Table 18: Rates of Major Adverse Vascular Events, During the Analysis Period and by Exposure Period[a] (Study Population)

	Patients with Untreated Person-Time (N=239)	Treated with Eculizumab (Prior to Ravulizumab Switch) (N=278)	Treated with Ravulizumab (N=493)	Treated with Eculizumab Only (N=104)
All patients				
Total patients at risk	23	14	452	78
Number of patients with events	1	0	2	1
Incidence (percent of population at risk, %)	4.3	0.0	0.4	1.3
Number of events	1	0	3	1
Person-years	9.7	5.6	500.0	86.2
Rate per 100 person-years	10.3	0.0	0.6	1.2
Estimated rate per 100 person-years[b]	10.3	n/a	0.6	1.2
95% CI	(1.5, 73.4)	(n/a)	(0.2, 1.9)	(0.2, 8.2)

[a] The analysis period is from 06 Jan 2023 to 06 Jan 2025.
[b] Poisson regression estimate of incidence density.
Abbreviations: CI = confidence interval; n/a = not available; N = number of patients
Source: Post-text Table 11.3 Analysis: Ravuema202501

4.7.2.4. Malignancy

4.7.2.4.1. Alexion PNH Registry Dataset

Cumulative

Out of 252 participants with untreated person-time at risk, 4 malignancies were reported in 4 participants while untreated. Out of 299 participants treated with Soliris prior to Ultomiris at risk, 19 malignancies were reported in 17 participants while treated only with Soliris (Table 19). Out of 525 participants at risk, 21 malignancies were reported in 19 participants while treated with Ultomiris. These 21 malignancies included solid tumor reported in 14 (66.7%) participants (mostly colorectal, non-malignant skin cancer [NMSC], and other: 2 [9.5%] participants each) and hematologic malignancy reported in 7 (33.3%) participants (mostly myelodysplastic syndrome [MDS]: 5 [23.8%] participants) (Post-text Table 12.5 Analysis: Ravuema202501).

The adjusted reported malignancy rate was 0.5 per 100 person-years (95% CI: 0.2, 1.3) in participants with untreated person-time while untreated, 0.7 per 100 person-years

(95% CI: 0.4, 1.1) in participants treated with Soliris prior to Ultomiris, 0.9 per 100 person-years (95% CI: 0.6, 1.5) in participants while treated with Ultomiris, and 1.0 per 100 person-years (95% CI: 0.7, 1.4) in participants treated only with Soliris (Table 19).

The adjusted reported hematologic malignancy rate was 0.0 per 100 person-years (95% CI: 0.0, 0.0) in participants with untreated person-time while untreated, 0.1 per 100 person-years (95% CI: 0.0, 0.4) in participants treated with Soliris prior to Ultomiris, 0.4 per 100 person-years (95% CI: 0.2, 0.8) in participants while treated with Ultomiris, and 0.5 per 100 person-years (95% CI: 0.3, 0.8) in participants treated only with Soliris (Post-text Table 12.1.2 Analysis: Ravuema202501).

Out of 252 participants with untreated person-time at risk, 3 confirmed malignancies were reported in 3 participants while untreated. Out of 299 participants treated with Soliris prior to Ultomiris at risk, 18 confirmed malignancies were reported in 16 participants while treated with Soliris. Out of 525 participants at risk, 21 confirmed malignancies were reported in 19 participants while treated with Ultomiris and out of 711 participants treated only with Soliris at risk, 45 confirmed malignancies were reported in 40 participants (Table 19).

The adjusted confirmed malignancy rate was 0.3 per 100 person-years (95% CI: 0.1, 1.1) in participants with untreated person-time while untreated, 0.6 per 100 person-years (95% CI: 0.4, 1.0) in participants treated with Soliris prior to Ultomiris, 0.9 per 100 person-years (95% CI: 0.5, 1.5) in participants while treated with Ultomiris, and 0.9 per 100 person-years (95% CI: 0.7, 1.3) in participants treated only with Soliris (Table 19).

The adjusted confirmed hematologic malignancy rate was 0.0 per 100 person-years (95% CI: 0.0, 0.0) in participants with untreated person-time while untreated, 0.1 per 100 person-years (95% CI: 0.0, 0.4) in participants treated with Soliris prior to Ultomiris, 0.4 per 100 person-years (95% CI: 0.2, 0.8) in participants while treated with Ultomiris, and 0.5 per 100 person-years (95% CI: 0.3, 0.8) in participants treated only with Soliris (Post-text Table 12.1.2 Analysis: Ravuema202501).

Analysis Period (06 Jan 2023 to 06 Jan 2025)

Out of 23 participants with untreated person-time at risk, 1 malignancy was reported in 1 participant while untreated. Out of 14 participants treated with Soliris prior to Ultomiris at risk, malignancy was not reported while treated with Soliris (Table 20). Out of 452 participants at risk, 7 malignancies were reported in 6 participants while treated with Ultomiris. These 7 malignancies included solid tumor reported in 5 (71.4%) participants (mostly colorectal: 2 [28.6%] participants) and hematologic malignancy reported in 2 (28.6%) participants (only MDS) (Post-text Table 12.6 Analysis: Ravuema202501).

The estimated reported malignancy rate was 10.3 per 100 person-years (95% CI: 1.5, 73.4) in participants with untreated person-time while untreated, 1.4 per 100 person-years (95% CI: 0.7, 2.9) in participants while treated with Ultomiris, and 3.5 per 100 person-years (95% CI: 1.1, 10.8) in participants treated only with Soliris.

Out of 23 participants with untreated person-time at risk, 1 confirmed malignancy was reported in 1 participant while untreated. Out of 14 participants treated with Soliris prior to Ultomiris at risk, no confirmed malignancy was reported while treated with Soliris. Out of 452 participants at risk, 7 confirmed malignancies were reported in 6 participants while treated with Ultomiris. Out

of 78 participants treated only with Soliris at risk, 3 confirmed malignancies were reported in 3 participants.

The estimated confirmed malignancy rate was 10.3 per 100 person-years (95% CI: 1.5, 73.4) in participants with untreated person-time while untreated, 1.4 per 100 person-years (95% CI: 0.7, 2.9) in participants while treated with Ultomiris, and 3.5 per 100 person-years (95% CI: 1.1, 10.8) in participants treated only with Soliris (Table 20 and Listing 5 Analysis: Ravuema202501).

Table 19: Adjusted Rates of Malignancy, Cumulative and by Exposure Period (Study Population)

	Patients with Untreated Person-Time (N=252)	Treated with Eculizumab (Prior to Ravulizumab Switch) (N=301)	Treated with Ravulizumab (N=532)	Treated with Eculizumab Only (N=713)
All patients				
All reported malignancy				
Total patients at risk	252	299	525	711
Number of patients with events	4	17	19	40
Incidence (percent of population at risk, %)	1.6	5.7	3.6	5.6
Number of events	4	19	21	45
Person-years	609.7	2181.6	1155.4	3258.0
Rate per 100 person-years	0.7	0.9	1.8	1.4
Adjusted rate per 100 person-years[a]	0.5	0.7	0.9	1.0
95% CI	(0.2, 1.3)	(0.4, 1.1)	(0.6, 1.5)	(0.7, 1.4)
All confirmed malignancy				
Total patients at risk	252	299	525	711
Number of patients with events	3	16	19	40
Incidence (percent of population at risk, %)	1.2	5.4	3.6	5.6
Number of events	3	18	21	45
Person-years	609.7	2181.6	1155.4	3258.0
Rate per 100 person-years	0.5	0.8	1.8	1.4

Table 19: Adjusted Rates of Malignancy, Cumulative and by Exposure Period (Study Population)

	Patients with Untreated Person-Time (N=252)	Treated with Eculizumab (Prior to Ravulizumab Switch) (N=301)	Treated with Ravulizumab (N=532)	Treated with Eculizumab Only (N=713)
Adjusted rate per 100 person-years[a]	0.3	0.6	0.9	0.9
95% CI	(0.1, 1.1)	(0.4, 1.0)	(0.5, 1.5)	(0.7, 1.3)

[a] Poisson regression estimate of incidence density. The adjusted multivariable regression model includes the following covariates: age at Baseline, gender, and history of BMD at Baseline.
[b] Baseline is defined as the enrollment date for 'patients with untreated person-time' and the ravulizumab treatment initiation date for patients in 'treated with ravulizumab' group. For patients included in the group of 'treated with eculizumab (prior to ravulizumab switch)' and 'treated with eculizumab only', Baseline is the eculizumab treatment initiation date.
Abbreviations: BMD = bone marrow disorder; CI = confidence interval; N = number of patients
Source: Post-text Table 12.2 Analysis: Ravuema202501

Table 20: Rates of Malignancy, During the Analysis Period and by Exposure Period[a] (Study Population)

	Patients with Untreated Person-Time (N=239)	Treated with Eculizumab (Prior to Ravulizumab Switch) (N=278)	Treated with Ravulizumab (N=493)	Treated with Eculizumab Only (N=104)
All patients				
All reported malignancy				
Total patients at risk	23	14	452	78
Number of patients with events	1	0	6	3
Incidence (percent of population at risk, %)	4.3	0.0	1.3	3.8
Number of events	1	0	7	3
Person-years	9.7	5.6	500.0	86.2
Rate per 100 person-years	10.3	0.0	1.4	3.5
Estimated rate per 100 person-years[b]	10.3	n/a	1.4	3.5
95% CI	(1.5, 73.4)	(n/a)	(0.7, 2.9)	(1.1, 10.8)
All confirmed malignancy				
Total patients at risk	23	14	452	78
Number of patients with events	1	0	6	3

Table 20: Rates of Malignancy, During the Analysis Period and by Exposure Period[a] (Study Population)

	Patients with Untreated Person-Time (N=239)	Treated with Eculizumab (Prior to Ravulizumab Switch) (N=278)	Treated with Ravulizumab (N=493)	Treated with Eculizumab Only (N=104)
Incidence (percent of population at risk, %)	4.3	0.0	1.3	3.8
Number of events	1	0	7	3
Person-years	9.7	5.6	500.0	86.2
Rate per 100 person-years	10.3	0.0	1.4	3.5
Estimated rate per 100 person-years[b]	10.3	n/a	1.4	3.5
95% CI	(1.5, 73.4)	(n/a)	(0.7, 2.9)	(1.1, 10.8)

[a] The analysis period is from 06 Jan 2023 to 06 Jan 2025.
[b] Poisson regression estimate of incidence density.
Abbreviations: CI = confidence interval; n/a = not available; N = number of patients
Source: Post-text Table 12.3 Analysis: Ravuema202501

4.7.2.4.2. IPIG PNH Registry Dataset

Malignancy results for the 56 participants who transitioned from the Alexion PNH registry to the IPIG PNH Registry (ie, Alexion PNH Registry study population as described in Section 3.2.1.1) have been previously documented (Section 4.7.2.4.1, Table 19, Table 20, and Listing 5 Analysis: Ravuema202501). In contrast, Listing 5 Analysis: IPIG exclusively presents malignancy results for the 6 participants who initiated Ultomiris on or after enrollment in the IPIG PNH Registry (ie, IPIG PNH Registry study population as described in Section 3.2.1.2) as of the data cutoff date (13 Jan 2025).

Out of 6 participants treated with Ultomiris, malignancy (prostate cancer) was reported in 1 participant while treated with Ultomiris. The outcome was reported as not resolved (Listing 5 Analysis: IPIG).

4.7.2.5. Infection

4.7.2.5.1. Alexion PNH Registry Dataset

Cumulative

A total of 34 out of 252 participants with untreated person-time had infection, which were other infection due to other organism (19 participants) and unknown organism (14 participants). A total of 64 out of 301 participants treated with Soliris prior to Ultomiris had infection, which were *Neisseria* infections (4 participants: meningococcal infection [3 participants; these participants were all vaccinated; Table 21; Listing 6 and Listing 7 Analysis: Ravuema202501] and unknown *Neisseria spp* infection [1 participant]) and other infection (59 participants: other organism [28 participants] and unknown organism [31 participants]). A total of 58 out of 532

participants treated with Ultomiris had infection, which were *Neisseria spp* infection (1 participant: gonorrhea) and other infection (55 participants: other organism [38 participants] and unknown organism [17 participants]). A total of 195 out of 713 participants treated only with Soliris had infection, which were *Neisseria spp* infections (7 participants: meningococcal infection [6 participants], gonorrhea [1 participant]); encapsulated bacterial infection (5 participants: *Haemophilus influenzae* infection [4 participants] and streptococcus pneumonia [1 participant]); *Aspergillus spp* infection (2 participants); and other infection (179 participants: other organism [64 participants] and unknown organism [115 participants]; Table 21).

The adjusted reported infection rate was 5.4 per 100 person-years (95% CI: 3.8, 7.8) in participants with untreated person-time while untreated, 3.0 per 100 person-years (95% CI: 2.3, 3.9) in participants treated with Soliris prior to Ultomiris, 5.1 per 100 person-years (95% CI: 3.8, 6.8) in participants while treated with Ultomiris, and 5.7 per 100 person-years (95% CI: 4.8, 6.7) in participants treated only with Soliris (Table 22).

For further details, see Listing 6 and Listing 7 Analysis: Ravuema202501.

Analysis Period (06 Jan 2023 to 06 Jan 2025)

A total of 2 out of 239 participants with untreated person-time had infection, which were other infection due to other organism. None out of 278 participants treated with Soliris prior to Ultomiris had infection. A total of 29 out of 493 participants treated with Ultomiris had infection, which was other infection (other organism [19 participants] and unknown organism [10 participants]). A total of 6 out of 104 participants treated only with Soliris had other infection (4 participants: other organism [1 participant] and unknown organism [3 participants]; 1 participant had streptococcus pneumonia infection Table 23). No *Neisseria spp*, *Haemophilus influenza*e, or *Aspergillus spp* infections were reported during this period.

The estimated reported infection rate was 20.7 per 100 person-years (95% CI: 5.2, 82.7) in participants with untreated person-time while untreated, 5.8 per 100 person-years (95% CI: 4.0, 8.3) in participants while treated with Ultomiris, and 7.0 per 100 person-years (95% CI: 3.1, 5.5) in participants treated only with Soliris (Table 24).

Table 21: Infection, Cumulative and by Exposure Period (Study Population)

	Patients with Untreated Person-Time (N=252)	Treated with Eculizumab (Prior to Ravulizumab Switch) (N=301)	Treated with Ravulizumab (N=532)	Treated with Eculizumab Only (N=713)
Infections reported, n	34	64	58	195
Neisseria, n (%)	0 (0.0)	4 (6.3)	1 (1.7)	7 (3.6)
Meningococcal, n (%)	0 (0.0)	3 (4.7)	0 (0.0)	6 (3.1)
Suspected meningococcal, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Gonorrhea, n (%)	0 (0.0)	0 (0.0)	1 (1.7)	1 (0.5)
Other, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

Table 21: Infection, Cumulative and by Exposure Period (Study Population)

	Patients with Untreated Person-Time (N=252)	Treated with Eculizumab (Prior to Ravulizumab Switch) (N=301)	Treated with Ravulizumab (N=532)	Treated with Eculizumab Only (N=713)
Unknown, n (%)	0 (0.0)	1 (1.6)	0 (0.0)	0 (0.0)
Encapsulated bacteria[a], n (%)	1 (2.9)	0 (0.0)	0 (0.0)	5 (2.6)
Streptococcus Pneumonia, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)
Haemophilus influenza, n (%)	1 (2.9)	0 (0.0)	0 (0.0)	4 (2.1)
Aspergillus, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	2 (1.0)
Other infection, n (%)	33 (97.1)	59 (92.2)	55 (94.8)	179 (91.8)
Other organism, n (%)	19 (55.9)	28 (43.8)	38 (65.5)	64 (32.8)
Unknown organism, n (%)	14 (41.2)	31 (48.4)	17 (29.3)	115 (59.0)

Note: The percentage is the percent of total number of infections reported for each exposure group.
[a] *Streptococcus pneumoniae*, *Haemophilus influenzae* only.
Abbreviation: N/n = number of patients
Source: Post-text Table 13.1 Analysis: Ravuema202501

Table 22: Adjusted Rates of Infection, Cumulative and by Exposure (Study Population)

	Patients with Untreated Person-Time (N=252)	Treated with Eculizumab (Prior to Ravulizumab Switch) (N=301)	Treated with Ravulizumab (N=532)	Treated with Eculizumab Only (N=713)
All patients				
Total patients at risk	252	299	525	711
Number of patients with events	20	42	46	113
Incidence (percent of population at risk, %)	7.9	14.0	8.8	15.9
Number of events	34	64	58	195
Person-years	609.7	2181.6	1155.4	3258.0
Rate per 100 person-years	5.6	2.9	5.0	6.0
Adjusted rate per 100 person-years[a]	5.4	3.0	5.1	5.7

Table 22: Adjusted Rates of Infection, Cumulative and by Exposure (Study Population)

	Patients with Untreated Person-Time (N=252)	Treated with Eculizumab (Prior to Ravulizumab Switch) (N=301)	Treated with Ravulizumab (N=532)	Treated with Eculizumab Only (N=713)
95% CI	(3.8, 7.8)	(2.3, 3.9)	(3.8, 6.8)	(4.8, 6.7)

[a] Poisson regression estimate of incidence density. The adjusted multivariable regression model includes the following covariates: age at Baseline, gender, history of aplastic anemia at Baseline, and use of immunosuppressive concomitant mediation at Baseline.
[b] Baseline is defined as the enrollment date for 'patients with untreated person-time' and the ravulizumab treatment initiation date for patients in 'treated with ravulizumab' group. For patients included in the group of 'treated with eculizumab (prior to ravulizumab switch)' and 'treated with eculizumab only', Baseline is the eculizumab treatment initiation date.
Abbreviations: CI = confidence interval; N = number of patients
Source: Post-text Table 14.2 Analysis: Ravuema202501

Table 23: Infection, During the Analysis Period and by Exposure Period[a] (Study Population)

	Patients with Untreated Person-Time (N=239)	Treated with Eculizumab (Prior to Ravulizumab Switch) (N=278)	Treated with Ravulizumab (N=493)	Treated with Eculizumab Only (N=104)
Infections reported, n	2	0	29	6[b]
Neisseria, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Meningococcal, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Suspected meningococcal, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Gonorrhea, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Other, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Unknown, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Encapsulated bacteria[c], n (%)	0 (0.0)	0 (0.0)	0 (0.0)	1 (16.7)
Streptococcus Pneumonia, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	1 (16.7)
Haemophilus influenza, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Aspergillus, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Other infection, n (%)	2 (100.0)	0 (0.0)	29 (100.0)	4 (66.7)
Other organism, n (%)	2 (100.0)	0 (0.0)	19 (65.5)	1 (16.7)
Unknown organism, n (%)	0 (0.0)	0 (0.0)	10 (34.5)	3 (50.0)

Table 23: Infection, During the Analysis Period and by Exposure Period[a] (Study Population)

Note: The percentage is the percent of total number of infections reported for each exposure group.
[a] The analysis period is from 06 Jan 2023 to 06 Jan 2025.
[b] One out of 6 participants had infection that could not be categorized and listed in this table.
[c] *Streptococcus pneumoniae*, *Haemophilus influenzae* only.
Abbreviations: N/n = number of patients
Source: Post-text Table 13.2 Analysis: Ravuema202501

Table 24: Rates of Infection, During the Analysis Period and by Exposure Period[a] (Study Population)

	Patients with Untreated Person-Time (N=239)	Treated with Eculizumab (Prior to Ravulizumab Switch) (N=278)	Treated with Ravulizumab (N=493)	Treated with Eculizumab Only (N=104)
All patients				
Total patients at risk	23	14	452	78
Number of patients with events	2	0	25	6
Incidence (percent of population at risk, %)	8.7	0.0	5.5	7.7
Number of events	2	0	29	6
Person-years	9.7	5.6	500.0	86.2
Rate per 100 person-years	20.7	0.0	5.8	7.0
Estimated rate per 100 person-years[b]	20.7	n/a	5.8	7.0
95% CI	(5.2, 82.7)	(n/a)	(4.0, 8.3)	(3.1, 15.5)

[a] The analysis period is from 06 Jan 2023 to 06 Jan 2025.
[b] Poisson regression estimate of incidence density.
Abbreviations: CI = confidence interval; n/a = not available; N = number of patients
Source: Post-text Table 14.3 Analysis: Ravuema202501

4.7.2.5.2. IPIG PNH Registry Dataset

As of the data cutoff date (13 Jan 2025), no infections were reported (Listing 6 Analysis: IPIG).

4.7.2.6. Bone Marrow Transplant

4.7.2.6.1. Alexion PNH Registry Dataset

Cumulative

Out of 252 participants with untreated person-time at risk, 1 participant had 2 BMTs while untreated. Out of 529 participants treated with Ultomiris at risk, 3 participants had 3 BMTs while treated with Ultomiris. Out of 713 participants treated only with Soliris at risk, 33 participants

had 33 BMTs. No BMTs were reported in 301 participants treated with Soliris prior to Ultomiris at risk.

The estimated BMT rate was 0.3 per 100 person-years (95% CI: 0.1, 1.3) in participants with untreated person-time while untreated, 0.3 per 100 person-years (95% CI: 0.1, 0.8) in participants while treated with Ultomiris, and 1.0 per 100 person-years (95% CI: 0.7, 1.4) in participants treated only with Soliris (Post-text Table 20.1 Analysis: Ravuema202501).

For further details, see Listing 13 Analysis: Ravuema202501.

Analysis Period (06 Jan 2023 to 06 Jan 2025)

Out of 454 participants at risk, 1 participant had 1 BMT while treated with Ultomiris. No BMTs were reported in 23 untreated participants at risk, 14 participants treated with Soliris (prior to Ultomiris switch) at risk, and 78 participants treated only with Soliris at risk.

The estimated BMT rate was 0.2 per 100 person-years (95% CI: 0.0, 1.4) in participants while treated with Ultomiris (Post-text Table 20.2 Analysis: Ravuema202501).

4.7.2.6.2. IPIG PNH Registry Dataset

As of the data cutoff date (13 Jan 2025), no BMTs were reported (Listing 13 Analysis: IPIG).

4.7.2.7. Pregnancy Outcomes During Follow-up

4.7.2.7.1. Alexion PNH Registry Dataset

During data collection, there was no differentiation between stillbirth and miscarriage.

Data on fetal outcomes were not collected.

Cumulative

The follow-up period was from Registry enrollment date to last untreated follow-up date for participants with untreated person-time, from Soliris treatment start date to last Soliris-treated follow-up date for participants previously treated with Soliris and Soliris only participants, and from Ultomiris treatment start date to last Ultomiris-treated follow-up date for participants treated with Ultomiris.

Out of 121 female participants with untreated person-time and with available data, 3 participants reported 3 pregnancy outcomes of 1 miscarriage/stillbirth, 1 live birth, and 1 abortion while untreated. Out of 147 female participants treated with Soliris prior to Ultomiris with available data, 26 participants reported 45 pregnancy outcomes of which 34 (75.6%) were live births, 4 (8.9%) were reported as abortions, and 7 (15.6%) were reported as miscarriages/stillbirths while treated with Soliris and prior to Ultomiris initiation. Out of 257 female participants with available data, 2 participants reported 3 pregnancy outcomes of 2 live births and 1 miscarriage/stillbirth while treated with Ultomiris. Out of 391 female participants treated only with Soliris with available data, 55 participants reported 85 pregnancy outcomes of 58 (68.2%) live births, 9 (10.6%) abortions, 17 (20.0%) miscarriages/stillbirths, and 1 (1.2%) missing outcomes.

Outcomes of pregnancy were reported for Ultomiris-treated female participants with available data by exposure period (Post-text Table 19.1 and Listing 12 Analysis: Ravuema202501).

Analysis Period (06 Jan 2023 to 06 Jan 2025)

The follow-up period was from registry enrollment date to last untreated follow-up date for patients with untreated person-time, from Soliris treatment start date to last Soliris-treated follow-up date for patients previously treated with Soliris and Soliris only patients, and from Ultomiris treatment start date to last Ultomiris-treated follow-up date for patients treated with Ultomiris.

Out of 56 female participants treated only with Soliris with available data, 2 participants reported 3 pregnancy outcomes of 1 (33.3%) live births, and 2 (66.7%) miscarriage/stillbirth. No pregnancy outcome was reported for 116 participants with untreated person-time while untreated, 133 participants treated with Soliris and prior to Ultomiris initiation, and 239 participants treated with Ultomiris.

Outcomes of pregnancy were reported for Ultomiris-treated female participants with available data by exposure period (Post-text Table 19.2 and Listing 12 Analysis: Ravuema202501).

4.7.2.7.2. IPIG PNH Registry Dataset

As of the data cutoff date (13 Jan 2025), no pregnancy cases were reported (Listing 12 Analysis: IPIG).

4.7.2.8. Impaired Renal Function

4.7.2.8.1. Alexion PNH Registry Dataset

Cumulative

Out of 252 participants with untreated person-time at risk, 23 participants had 31 IRF events while untreated. Out of 299 participants treated with Soliris prior to Ultomiris at risk, 17 participants had 20 IRF events while treated with Soliris. Out of 525 participants at risk, 3 participants had 3 IRF events while treated with Ultomiris. Out of 712 participants treated only with Soliris at risk, 45 participants had 55 IRF events.

The estimated IRF event rate was 5.1 per 100 person-years (95% CI: 3.6, 7.2) in participants with untreated person-time while untreated, 0.9 per 100 person-years (95% CI: 0.6, 1.4) in participants treated with Soliris prior to Ultomiris, 0.3 per 100 person-years (95% CI: 0.1, 0.8) in participants while treated with Ultomiris, and 1.7 per 100 person-years (95% CI: 1.3, 2.2) in participants treated only with Soliris (Table 25).

For further details, see Listing 8 Analysis: Ravuema202501.

Analysis Period (06 Jan 2023 to 06 Jan 2025)

Out of 23 participants at risk, 2 participants had 2 events while untreated. Out of 452 participants at risk, 2 participants had 2 IRF events while treated with Ultomiris. No IRF events were reported in 14 participants treated with Soliris prior to Ultomiris at risk and in 78 participants treated only with Soliris.

The estimated IRF event rate was 20.7 per 100 person-years (95% CI: 5.2, 82.7) in participants with untreated person-time while untreated and 0.4 per 100 person-years (95% CI: 0.1, 1.6) in participants while treated with Ultomiris (Table 26).

Table 25: Rates of Impaired Renal Function, Cumulative and by Exposure Period (Study Population)

	Patients with Untreated Person-Time (N=252)	Treated with Eculizumab (Prior to Ravulizumab Switch) (N=301)	Treated with Ravulizumab (N=532)	Treated with Eculizumab Only (N=713)
All patients				
Total patients at risk	252	299	525	712
Number of patients with events	23	17	3	45
Incidence (percent of population at risk, %)	9.1	5.7	0.6	6.3
Number of events	31	20	3	55
Person-years	609.7	2181.6	1155.4	3259.3
Rate per 100 person-years	5.1	0.9	0.3	1.7
Estimated rate per 100 person-years[a]	5.1	0.9	0.3	1.7
95% CI	(3.6, 7.2)	(0.6, 1.4)	(0.1, 0.8)	(1.3, 2.2)

[a] Poisson regression estimate of incidence density.
Abbreviations: CI = confidence interval; N = number of patients
Source: Post-text Table 15.1 Analysis: Ravuema202501

Table 26: Rates of Impaired Renal Function, During the Analysis Period and by Exposure Period[a] (Study Population)

	Patients with Untreated Person-Time (N=239)	Treated with Eculizumab (Prior to Ravulizumab Switch) (N=278)	Treated with Ravulizumab (N=493)	Treated with Eculizumab Only (N=104)
All patients				
Total patients at risk	23	14	452	78
Number of patients with events	2	0	2	0
Incidence (percent of population at risk, %)	8.7	0.0	0.4	0.0
Number of events	2	0	2	0
Person-years	9.7	5.6	500.0	86.2
Rate per 100 person-years	20.7	0.0	0.4	0.0
Estimated rate per 100 person-years[b]	20.7	n/a	0.4	n/a

Table 26: Rates of Impaired Renal Function, During the Analysis Period and by Exposure Period[a] (Study Population)

	Patients with Untreated Person-Time (N=239)	Treated with Eculizumab (Prior to Ravulizumab Switch) (N=278)	Treated with Ravulizumab (N=493)	Treated with Eculizumab Only (N=104)
95% CI	(5.2, 82.7)	(n/a)	(0.1, 1.6)	(n/a)

[a] The analysis period is from 06 Jan 2023 to 06 Jan 2025.
[b] Poisson regression estimate of incidence density.
Abbreviations: CI = confidence interval; n/a = not available; N = number of patients
Source: Post-text Table 15.2 Analysis: Ravuema202501

4.7.2.8.2. IPIG PNH Registry Dataset

As of the data cutoff date (13 Jan 2025), no IRF event was reported (Listing 8 Analysis: IPIG).

4.7.2.9. Impaired Hepatic Function

4.7.2.9.1. Alexion PNH Registry Dataset

Cumulative

Out of 252 participants with untreated person-time at risk, 1 participant had 2 IHF events while untreated. Out of 299 participants treated with Soliris prior to Ultomiris at risk, 11 participants had 11 IHF events while treated with Soliris prior to Ultomiris. Out of 525 participants treated with Ultomiris at risk, 6 participants had 8 events while treated with Ultomiris. Out of 711 participants treated only with Soliris at risk, 24 participants had 34 IHF events while treated with Soliris.

The estimated IHF event rate was 0.3 per 100 person-years (95% CI: 0.1, 1.3) in participants with untreated person-time while untreated, 0.5 per 100 person-years (95% CI: 0.3, 0.9) in participants treated with Soliris prior to Ultomiris, 0.7 per 100 person-years (95% CI: 0.3, 1.4) in participants while treated with Ultomiris, and 1.0 per 100 person-years (95% CI: 0.7, 1.5) in participants treated only with Soliris (Table 27).

For further details, see Listing 9 Analysis: Ravuema202501.

Analysis Period (06 Jan 2023 to 06 Jan 2025)

Out of 452 participants treated with Ultomiris at risk, 2 participants had 3 IHF events while treated with Ultomiris. No IHF events were reported in 23 participants with untreated person-time while untreated at risk, in 14 participants treated with Soliris prior to Ultomiris at risk, and in 78 participants at risk treated only with Soliris.

The estimated IHF event rate was 0.6 per 100 person-years (95% CI: 0.2, 1.9) in participants treated with Ultomiris (Table 28).

Table 27: Rates of Impaired Hepatic Function, Cumulative and by Exposure Period (Study Population)

	Patients with Untreated Person-Time (N=252)	Treated with Eculizumab (Prior to Ravulizumab Switch) (N=301)	Treated with Ravulizumab (N=532)	Treated with Eculizumab Only (N=713)
All patients				
Total patients at risk	252	299	525	711
Number of patients with events	1	11	6	24
Incidence (percent of population at risk, %)	0.4	3.7	1.1	3.4
Number of events	2	11	8	34
Person-years	609.7	2181.6	1155.4	3258.0
Rate per 100 person-years	0.3	0.5	0.7	1.0
Estimated rate per 100 person-years[a]	0.3	0.5	0.7	1.0
95% CI	(0.1, 1.3)	(0.3, 0.9)	(0.3, 1.4)	(0.7, 1.5)

[a] Poisson regression estimate of incidence density.
Abbreviations: CI = confidence interval; N = number of patients
Source: Post-text Table 16.1 Analysis: Ravuema202501

Table 28: Rates of Impaired Hepatic Function, During the Analysis Period and by Exposure Period[a] (Study Population)

	Patients with Untreated Person-Time (N=239)	Treated with Eculizumab (Prior to Ravulizumab Switch) (N=278)	Treated with Ravulizumab (N=493)	Treated with Eculizumab Only (N=104)
All patients				
Total patients at risk	23	14	452	78
Number of patients with events	0	0	2	0
Incidence (percent of population at risk, %)	0.0	0.0	0.4	0.0
Number of events	0	0	3	0
Person-years	9.7	5.6	500.0	86.2
Rate per 100 person-years	0.0	0.0	0.6	0.0
Estimated rate per 100 person- years[b]	n/a	n/a	0.6	n/a
95% CI	(n/a)	(n/a)	(0.2, 1.9)	(n/a)

Table 28: Rates of Impaired Hepatic Function, During the Analysis Period and by Exposure Period[a] (Study Population)

[a] The analysis period is from 06 Jan 2023 to 06 Jan 2025.
[b] Poisson regression estimate of incidence density.
Abbreviations: CI = confidence interval; n/a = not available; N = number of patients
Source: Post-text Table 16.2 Analysis: Ravuema202501

4.7.2.9.2. IPIG PNH Registry Dataset

As of the data cutoff date (13 Jan 2025), no IHF events were reported (Listing 9 Analysis: IPIG).

4.7.2.10. Pulmonary Hypertension

4.7.2.10.1. Alexion PNH Registry Dataset

Cumulative

Out of 252 participants at risk, 8 participants had 9 events of pulmonary hypertension while untreated. Out of 299 participants treated with Soliris prior to Ultomiris at risk, 5 participants had 6 events of pulmonary hypertension while treated with Soliris. Out of 525 participants at risk, 2 participants had 2 events of pulmonary hypertension while treated with Ultomiris. Out of 711 participants treated only with Soliris at risk, 17 participants had 20 events of pulmonary hypertension.

The estimated pulmonary hypertension event rate was 1.5 per 100 person-years (95% CI: 0.8, 2.8) in participants with untreated person-time while untreated, 0.3 per 100 person-years (95% CI: 0.1, 0.6) in participants treated with Soliris prior to Ultomiris, 0.2 per 100 person-years (95% CI: 0.0, 0.7) in participants while treated with Ultomiris, and 0.6 per 100 person-years (95% CI: 0.4, 1.0) in participants treated only with Soliris (Table 29).

For further details, see Listing 10 Analysis: Ravuema202501.

Analysis Period (06 Jan 2023 to 06 Jan 2025)

No events of pulmonary hypertension were reported in 23 participants with untreated person-time while untreated at risk, 14 participants treated with Soliris prior to Ultomiris at risk, 452 participants treated with Ultomiris at risk, and 78 participants treated only with Soliris at risk (Table 30).

Table 29: Rates of Pulmonary Hypertension, Cumulative and by Exposure Period (Study Population)

	Patients with Untreated Person-Time (N=252)	Treated with Eculizumab (Prior to Ravulizumab Switch) (N=301)	Treated with Ravulizumab (N=532)	Treated with Eculizumab Only (N=713)
All patients				
Total patients at risk	252	299	525	711

Table 29: Rates of Pulmonary Hypertension, Cumulative and by Exposure Period (Study Population)

	Patients with Untreated Person-Time (N=252)	Treated with Eculizumab (Prior to Ravulizumab Switch) (N=301)	Treated with Ravulizumab (N=532)	Treated with Eculizumab Only (N=713)
Number of patients with events	8	5	2	17
Incidence (percent of population at risk, %)	3.2	1.7	0.4	2.4
Number of events	9	6	2	20
Person-years	609.7	2181.6	1155.4	3258.0
Rate per 100 person-years	1.5	0.3	0.2	0.6
Estimated rate per 100 person-years[a]	1.5	0.3	0.2	0.6
95% CI	(0.8, 2.8)	(0.1, 0.6)	(0.0, 0.7)	(0.4, 1.0)

[a] Poisson regression estimate of incidence density.
Abbreviations: CI = confidence interval; N = number of patients
Source: Post-text Table 17.1 Analysis: Ravuema202501

Table 30: Rates of Pulmonary Hypertension, During the Analysis Period and by Exposure Period[a] (Study Population)

	Patients with Untreated Person-Time (N=239)	Treated with Eculizumab (Prior to Ravulizumab Switch) (N=278)	Treated with Ravulizumab (N=493)	Treated with Eculizumab Only (N=104)
All patients				
Total patients at risk	23	14	452	78
Number of patients with events	0	0	0	0
Incidence (percent of population at risk, %)	0.0	0.0	0.0	0.0
Number of events	0	0	0	0
Person-years	9.7	5.6	500.0	86.2
Rate per 100 person-years	0.0	0.0	0.0	0.0
Estimated rate per 100 person-years[b]	n/a	n/a	n/a	n/a
95% CI	(n/a)	(n/a)	(n/a)	(n/a)

[a] The analysis period is from 06 Jan 2023 to 06 Jan 2025.
[b] Poisson regression estimate of incidence density.
Abbreviations: CI = confidence interval; n/a = not available; N = number of patients
Source: Post-text Table 17.2 Analysis: Ravuema202501

4.7.2.10.2. IPIG PNH Registry Dataset

As of the data cutoff date (13 Jan 2025), no events of pulmonary hypertension (Listing 10 Analysis: IPIG) were reported.

4.7.2.11. Ultomiris Infusion Reactions

4.7.2.11.1. Alexion PNH Registry Dataset

Cumulative

Out of 523 participants at risk, 8 participants had 11 infusion reactions (all were nonserious) while treated with Ultomiris. Of these, infusion reactions resolved for 6 participants and were ongoing for 2 participants as of the data cutoff date (Listing 11 Analysis: Ravuema202501). The estimated rate of infusion reaction was 1.0 per 100 person-years (95% CI: 0.5, 1.7, Post-text Table 18.1 Analysis: Ravuema202501).

Analysis Period (06 Jan 2023 to 06 Jan 2025)

Out of 450 participants at risk, 2 participants had 5 infusion reactions while treated with Ultomiris. The estimated infusion reaction rate was 1.0 per 100 person-years (95% CI: 0.4, 2.4; Post-text Table 18.2 and Listing 11 Analysis: Ravuema202501).

4.7.2.11.2. IPIG PNH Registry Dataset

As of the data cutoff date (13 Jan 2025), no infusion reactions were reported (Listing 11 Analysis: IPIG).

4.7.2.12. Potential Breakthrough Hemolysis

4.7.2.12.1. IPIG PNH Registry Dataset

As of the data cutoff date (13 Jan 2025), no events of potential breakthrough hemolysis were reported (Post-text Table 8.2 Analysis: IPIG).

4.8. Medical History at Ultomiris Initiation

4.8.1. Alexion PNH Registry Dataset

Bone Marrow Disorder (BMD)

Out of 517 Ultomiris-treated participants with analyzable data, 229 (44.3%) had a history of BMD. These included 125 (42.2%) out of 296 analyzable participants with prior Soliris treatment, 76 (48.7%) out of 156 analyzable participants without prior Soliris treatment, and 28 (43.1%) out of 65 analyzable participants with unknown prior Soliris treatment.

A total of 169 (73.8%) Ultomiris-treated participants had BMD ongoing at Ultomiris initiation. This included 85 (68.0%) participants with prior Soliris treatment, 62 (81.6%) participants without prior Soliris treatment and 22 (78.6%) participants with unknown prior Soliris treatment.

A total of 60 (26.2%) Ultomiris-treated participants had BMD resolved prior to Ultomiris initiation. This included 40 (32.0%) participants with prior Soliris treatment,

14 (18.4%) participants without prior Soliris treatment, and 6 (21.4%) participants with unknown prior Soliris treatment (Post-text Table 8 Analysis: Ravuema202501).

Aplastic or Hypoplastic Anemia

Out of 515 Ultomiris-treated participants with analyzable data, 193 (37.5%) had a history of aplastic or hypoplastic anemia. These included 102 (34.7%) out of 294 analyzable participants with prior Soliris treatment, 68 (43.6%) out of 156 analyzable participants without prior Soliris treatment, and 23 (35.4%) out of 65 analyzable participants with unknown prior Soliris treatment. A total of 143 (74.1%) Ultomiris-treated participants had aplastic or hypoplastic anemia ongoing at Ultomiris initiation. This included 71 (69.6%) participants with prior Soliris treatment, 55 (80.9%) participants without prior Soliris treatment and 17 (73.9%) participants with unknown prior Soliris treatment. A total of 50 (25.9%) Ultomiris-treated participants had aplastic or hypoplastic anemia resolved prior to Ultomiris initiation. This included 31 (30.4%) participants with prior Soliris treatment, 13 (19.1%) participants without prior Soliris treatment, and 6 (26.1%) participants with unknown prior Soliris treatment (Post-text Table 8 Analysis: Ravuema202501).

Myelodysplastic Syndrome (MDS)

Out of 509 Ultomiris-treated participants with analyzable data, 23 (4.5%) had a history of MDS. These included 12 (4.1%) out of 292 analyzable participants with prior Soliris treatment, 7 (4.6%) out of 153 analyzable participants without prior Soliris treatment and 4 (6.3%) out of 64 analyzable participants with unknown prior Soliris treatment had a history of MDS. A total of 19 (82.6%) Ultomiris-treated participants had MDS ongoing at Ultomiris initiation. This included 9 (75.0%) participants with prior Soliris treatment and 6 (85.7%) participants without prior Soliris treatment and 4 (100.0%) participants with unknown prior Soliris treatment.

A total of 4 (17.4%) Ultomiris-treated participants had MDS resolved prior to Ultomiris initiation. This included 3 (25.0%) participants with prior Soliris treatment and 1 (14.3%) participant without prior Soliris treatment (Post-text Table 8 Analysis: Ravuema202501).

Major Adverse Vascular Event (MAVE)

Out of 521 Ultomiris-treated participants with analyzable data, 147 (28.2%) participants had a history of MAVE. These included 83 (28.0%) out of 296 participants with prior Soliris treatment, 43 (27.2%) out of 158 participants without prior Soliris treatment and 21 (31.3%) out of 67 participants with unknown prior Soliris treatment (Post-text Table 8 Analysis: Ravuema202501).

Thrombotic Event (TE)

Out of 519 Ultomiris-treated participants with analyzable data, 119 (22.9%) participants had a history of TEs. These included 66 (22.4%) out of 295 participants with prior Soliris treatment, 35 (22.3%) out of 157 participants without prior Soliris treatment and 18 (26.9%) out of 67 participants with unknown prior Soliris treatment (Post-text Table 8 Analysis: Ravuema202501).

Non-Thrombotic Major Adverse Vascular Event (Non-TE MAVE)

Out of 518 Ultomiris-treated participants with analyzable data, 43 (8.3%) participants had a history of non-TE MAVE. These included 25 (8.5%) out of 294 participants with prior Soliris

treatment 13 (8.3%) out of 157 participants without prior Soliris treatment and 5 (7.5%) out of 67 participants with unknown prior Soliris treatment (Post-text Table 8 Analysis: Ravuema202501).

Impaired Renal Function (IRF)

Out of 512 Ultomiris-treated participants with analyzable data, 76 (14.8%) participants had a history of IRF. These included 46 (15.7%) out of 293 participants with prior Soliris treatment, 22 (14.3%) out of 154 participants without prior Soliris treatment and 8 (12.3%) out of 65 participants with unknown prior Soliris treatment (Post-text Table 8 Analysis: Ravuema202501).

Impaired Hepatic Function (IHF)

Out of 512 Ultomiris-treated participants with analyzable data, 21 (4.1%) participants had a history of IHF. These included 17 (5.8%) out of 293 participants with prior Soliris treatment, 1 (0.6%) out of 154 participants without prior Soliris treatment and 3 (4.6%) out of 65 participants with unknown prior Soliris treatment had a history of IHF (Post-text Table 8 Analysis: Ravuema202501).

Pulmonary Hypertension

Out of 512 Ultomiris-treated participants with analyzable data, 26 (5.1%) participants had a history of pulmonary hypertension. These included 17 (5.8%) out of 293 participants with prior Soliris treatment, 5 (3.2%) out of 154 participants without prior Soliris treatment and 4 (6.2%) out of 65 participants with unknown prior Soliris treatment (Post-text Table 8 Analysis: Ravuema202501).

Malignancy

Out of 520 Ultomiris-treated participants with analyzable data, 66 (12.7%) participants had a history of malignancy. These included 31 (10.5%) out of 296 participants with prior Soliris treatment, 27 (17.2%) out of 157 participants without prior Soliris treatment and 8 (11.9%) out of 67 participants with unknown prior Soliris treatment (Post-text Table 8 Analysis: Ravuema202501).

Infection

Out of 514 Ultomiris-treated participants with analyzable data, 107 (20.8%) participants had a history of infection. These included 52 (17.7%) out of 294 participants with prior Soliris treatment, 41 (26.6%) out of 154 participants without prior Soliris treatment and 14 (21.2%) out of 66 participants with unknown prior Soliris treatment (Post-text Table 8 Analysis: Ravuema202501).

Pregnancy

Out of 147 female Ultomiris-treated participants with available data, history of pregnancy was reported for 122 (83.0%) participants. These included 75 (89.3%) out of 84 female participants with prior Soliris treatment, 27 (64.3%) out of 42 female participants without prior Soliris treatment and 20 (95.2%) out of 21 female participants with unknown prior Soliris treatment. Pregnancy was not reported in female partners of male participants (Post-text Table 8 Analysis: Ravuema202501).

4.8.2. IPIG PNH Registry Dataset

The medical history prior to Ultomiris initiation of the 56 participants who transitioned from the Alexion PNH Registry to the IPIG PNH Registry (ie, Alexion PNH Registry study population as described in Section 3.2.1.1) have been previously documented (Section 4.8.1; Post-text Table 8 Analysis: Ravuema202501). In contrast, Post-text Table 8.1 Analysis: IPIG exclusively presents the medical history of the 6 participants who initiated Ultomiris on or after enrollment in the IPIG PNH Registry (ie, IPIG PNH Registry study population as described in Section 3.2.1.2) as of the data cutoff date (13 Jan 2025).

Aplastic or Hypoplastic Anemia

Out of 6 Ultomiris-treated participants with analyzable data, 2 (33.3%) had a history of aplastic or hypoplastic anemia, which included 2 (40.0%) out of 5 analyzable participants without prior Soliris treatment (Post-text Table 8.1 Analysis: IPIG).

COVID-19

Out of 6 Ultomiris-treated participants with available data, 3 (50.0%) participants had a history of COVID-19, which included 1 (100.0%) out of 1 participant with prior Soliris treatment and 2 (40.0%) out of 5 participants without prior Soliris treatment (Post-text Table 8.1 Analysis: IPIG).

4.9. Concomitant Therapy Use at Ultomiris Initiation

4.9.1. Alexion PNH Registry Dataset

RBC transfusions, use of analgesics (both opioid and nonopioid), oral prophylactic antibiotics, immunosuppressant therapy (corticosteroids and cyclosporine or anti-thymocyte globulin [ATG]), and anticoagulation therapy (heparin or warfarin) were assessed within the 6 months prior to Ultomiris initiation and summarized in Post-text Table 9 Analysis: Ravuema202501.

Red Blood Cell Transfusions

Out of 523 Ultomiris-treated participants with analyzable data, 80 (15.3%) participants received RBC transfusions within the 6 months prior to Ultomiris initiation. These included 38 (12.8%) out of 296 participants with prior Soliris treatment, 33 (20.9%) out of 158 participants without prior Soliris treatment, and 9 (13.0%) out of 69 participants with unknown prior Soliris treatment.

Anticoagulation Therapy

Out of 405 Ultomiris-treated participants with analyzable data, 136 (33.6%) participants received anticoagulation therapy with heparin or warfarin within the 6 months prior to Ultomiris initiation. These included 77 (33.6%) out of 229 participants with prior Soliris treatment, 33 (26.6%) out of 124 participants without prior Soliris treatment, and 26 (50.0%) out of 52 participants with unknown prior Soliris treatment.

Immunosuppressant Therapy

Out of 413 Ultomiris-treated participants with analyzable data, 83 (20.1%) participants received immunosuppressant therapy with cyclosporine or ATG within the 6 months prior to Ultomiris initiation. These included 47 (20.7%) out of 227 participants with prior Soliris treatment,

30 (21.3%) out of 141 participants without prior Soliris treatment, and 6 (13.3%) out of 45 participants with unknown prior Soliris treatment.

Out of 398 Ultomiris-treated participants with analyzable data, 72 (18.1%) participants received immunosuppressant therapy with corticosteroids within the 6 months prior to Ultomiris initiation. These included 44 (19.7%) out of 223 participants with prior Soliris treatment, 19 (14.8%) out of 128 participants without prior Soliris treatment, and 9 (19.1%) out of 47 participants with unknown prior Soliris treatment.

Pain Medication

Out of 370 Ultomiris-treated participants with analyzable data, 61 (16.5%) participants received pain medication within the 6 months prior to Ultomiris initiation. These included 39 (19.1%) out of 204 participants with prior Soliris treatment, 10 (8.2%) out of 122 participants without prior Soliris treatment, and 12 (27.3%) out of 44 participants with unknown prior Soliris treatment.

Out of 359 Ultomiris-treated participants with analyzable data, 31 (8.6%) participants received opioid pain medication within the 6 months prior to Ultomiris initiation. These included 20 (10.1%) out of 199 participants with prior Soliris treatment, 4 (3.4%) out of 118 participants without prior Soliris treatment, and 7 (16.7%) out of 42 participants with unknown prior Soliris treatment.

Out of 360 Ultomiris-treated participants with analyzable data, 42 (11.7%) participants received nonopioid pain medication within the 6 months prior to Ultomiris initiation. These included 28 (14.1%) out of 198 participants with prior Soliris treatment, 8 (6.7%) out of 120 participants without prior Soliris treatment, and 6 (14.3%) out of 42 participants with unknown prior Soliris treatment.

Prophylactic Antibiotics

Out of 423 Ultomiris-treated participants with analyzable data, 226 (53.4%) participants received oral prophylactic antibiotics within the 6 months prior to Ultomiris initiation. These included 132 (56.4%) out of 234 participants with prior Soliris treatment, 69 (50.0%) out of 138 participants without prior Soliris treatment, and 25 (49.0%) out of 51 participants with unknown prior Soliris treatment.

4.9.2. IPIG PNH Registry Dataset

The concomitant therapy use at Ultomiris initiation for the 56 participants who transitioned from the Alexion PNH registry to the IPIG PNH Registry (ie, Alexion PNH Registry study population as described in Section 3.2.1.1) have been previously documented (Section 4.9.1, Post-text Table 9 Analysis: Ravuema202501). In contrast, Post-text Table 9 Analysis: IPIG exclusively presents the concomitant therapy use for the 6 participants who initiated Ultomiris on or after enrollment in the IPIG PNH Registry (ie, IPIG PNH Registry study population as described in Section 3.2.1.2) as of the data cutoff date (13 Jan 2025).

Concomitant therapies included anticomplement therapy, antibiotic prophylaxis, anticoagulation therapy, immunosuppressant therapy, iron chelation therapy, thrombopoietin receptor agonists, and vaccination at Ultomiris initiation, which are summarized in Post-text Table 9 Analysis: IPIG.

Anticomplement Therapy

Out of 6 Ultomiris-treated participants with analyzable data, 1 (16.7%) participant received anticomplement therapy with Soliris, which included 1 (100.0%) participant with prior Soliris treatment.

Antibiotic Prophylaxis

Out of 6 Ultomiris-treated participants with analyzable data, 1 (16.7%) participant received antibiotic prophylaxis with penicillin, which included 1 (100.0%) participant with prior Soliris treatment.

Anticoagulation Therapy

Out of 6 Ultomiris-treated participants with analyzable data, 4 (66.7%) participants received anticoagulation therapy with apixaban or heparin-derivative or direct oral anticoagulants or aspirin or warfarin-derivative at Ultomiris initiation. These included 1 (100.0%) out of 1 participant with prior Soliris treatment.

Immunosuppressant Therapy

Out of 6 Ultomiris-treated participants with analyzable data, 2 (33.3%) participants received immunosuppression therapy with cyclosporin or ATG cycle 1 or corticosteroids at Ultomiris initiation. These included 1 (100.0%) out of 1 participant with prior Soliris treatment and 1 (20.0%) out of 5 participants without prior Soliris treatment.

Iron Chelation Therapy

Out of 6 Ultomiris-treated participants with analyzable data, 1 (16.7%) participant received iron chelation therapy with deferasirox, which included 1 (20.0%) out of 5 participants without prior Soliris treatment.

Thrombopoietin Receptor Agonists

Out of 6 Ultomiris-treated participants with analyzable data, 1 (16.7%) participant received iron thrombopoietin receptor agonists with eltrombopag, which included 1 (20.0%) out of 5 participants without prior Soliris treatment.

Vaccination

Out of 6 Ultomiris-treated participants with analyzable data, 3 (50.0%) participants received vaccination with unknown/missing medication class or COVID-19, which included 1 (100.0%) out of 1 participant with prior Soliris treatment and 2 (40%) out of 5 participants without prior Soliris treatment.

4.10. Laboratory Values at Ultomiris Initiation

4.10.1. Alexion PNH Registry Dataset

Laboratory results at Ultomiris initiation were obtained within 6 months prior to Ultomiris initiation and are presented in Table 31. It should be noted that there was a high proportion of missing data for laboratory values due to the observational nature of the Registry.

Table 31: Laboratory Values at Ultomiris Initiation, By Treatment Status (Ultomiris Study Population)

	All Ravulizumab Patients[a] (N=532)	Prior Eculizumab Treatment[b] (N=301)	Without Prior Eculizumab Treatment[c] (N=161)	Prior Eculizumab Treatment Unknown (N=70)
Percent GPI-deficient granulocytes				
n	280	150	94	36
Mean (SD)	76.7 (26.34)	79.0 (26.73)	73.8 (24.65)	74.6 (28.68)
Median (Q1, Q3)	89.1 (61.4, 97.9)	92.8 (67.7, 98.2)	81.3 (58.3, 94.5)	88.8 (60.6, 98.3)
Percent GPI-deficient granulocytes, n (%)				
n	280	150	94	36
<1%	1 (0.4)	1 (0.7)	0 (0.0)	0 (0.0)
≥1% to <10%	3 (1.1)	3 (2.0)	0 (0.0)	0 (0.0)
≥10% to <50%	51 (18.2)	23 (15.3)	21 (22.3)	7 (19.4)
≥50%	225 (80.4)	123 (82.0)	73 (77.7)	29 (80.6)
Percent GPI-deficient erythrocytes				
n	246	134	84	28
Mean (SD)	51.4 (32.15)	59.3 (31.58)	41.3 (29.45)	44.0 (33.40)
Median (Q1, Q3)	47.5 (19.8, 84.3)	61.5 (31.5, 89.9)	30.4 (16.0, 63.0)	30.6 (14.0, 80.3)
Percent GPI-deficient erythrocytes, n (%)				
n	246	134	84	28
<10%	16 (6.5)	7 (5.2)	7 (8.3)	2 (7.1)
≥10%	230 (93.5)	127 (94.8)	77 (91.7)	26 (92.9)
LDH (U/L)				
n	410	228	130	52
Mean (SD)	441.1 (489.46)	327.6 (214.46)	608.8 (716.23)	519.2 (532.52)
Median (Q1, Q3)	273.0 (223.0, 432.0)	264.0 (223.0, 370.5)	301.5 (225.0, 730.0)	307.0 (225.0, 595.0)
LDH ratio (× ULN)				
n	385	216	121	48

Table 31: Laboratory Values at Ultomiris Initiation, By Treatment Status (Ultomiris Study Population)

	All Ravulizumab Patients[a] (N=532)	Prior Eculizumab Treatment[b] (N=301)	Without Prior Eculizumab Treatment[c] (N=161)	Prior Eculizumab Treatment Unknown (N=70)
Mean (SD)	1.8 (2.11)	1.2 (0.89)	2.5 (3.05)	2.2 (2.42)
Median (Q1, Q3)	1.1 (0.9, 1.4)	1.0 (0.9, 1.2)	1.2 (0.9, 2.7)	1.2 (0.9, 2.4)
LDH ratio (× ULN), n (%)				
n	385	216	121	48
<1.5	298 (77.4)	188 (87.0)	77 (63.6)	33 (68.8)
≥1.5	87 (22.6)	28 (13.0)	44 (36.4)	15 (31.3)
Hemoglobin (g/dL)				
n	402	213	131	58
Mean (SD)	10.9 (2.03)	11.1 (2.01)	10.9 (2.08)	10.5 (1.97)
Median (Q1, Q3)	10.8 (9.5, 12.3)	10.9 (9.6, 12.4)	10.8 (9.3, 12.3)	10.6 (9.0, 11.9)
eGFR (mL/min)				
n	420	230	131	59
Mean (SD)	92.5 (25.56)	92.5 (26.27)	93.3 (22.83)	91.0 (28.70)
Median (Q1, Q3)	96.5 (76.7, 111.4)	98.2 (76.7, 113.1)	95.3 (78.6, 111.0)	96.7 (73.1, 107.5)
eGFR (mL/min), n (%)				
n	420	230	131	59
<30	7 (1.7)	5 (2.2)	0 (0.0)	2 (3.4)
30 to <60	49 (11.7)	28 (12.2)	15 (11.5)	6 (10.2)
60 to <90	119 (28.3)	65 (28.3)	40 (30.5)	14 (23.7)
≥90	245 (58.3)	132 (57.4)	76 (58.0)	37 (62.7)
Absolute reticulocytes (× 10^9/L)				
n	349	188	112	49
Mean (SD)	160.3 (83.87)	168.5 (85.41)	145.1 (75.11)	163.8 (93.38)
Median (Q1, Q3)	155.4 (99.4, 209.0)	165.5 (100.1, 226.5)	131.2 (91.8, 185.8)	171.3 (104.0, 209.0)

Note: Data shown are reported in the 6 months prior to the timepoint.

[a] Patients were classified into the Prior Eculizumab Treatment Unknown group due to unknown prior eculizumab treatment history or because of a missing eculizumab discontinuation date.

Table 31: Laboratory Values at Ultomiris Initiation, By Treatment Status (Ultomiris Study Population)

[b] Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. There were 27 patients who discontinued eculizumab between 17 and 28 days of ravulizumab initiation.
[c] Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.
Abbreviations: eGFR = estimated glomerular filtration rate; GPI = glycophosphatidylinositol; LDH = lactate dehydrogenase; N/n = number of patients; Q1 = first quartile; Q3 = third quartile; SD = standard deviation; ULN = upper limit of normal
Source: Adapted from Post-text Table 10 Analysis: Ravuema202501

4.10.2. IPIG PNH Registry Dataset

Laboratory results at Ultomiris initiation were obtained at Ultomiris initiation and are presented in Table 32.

The laboratory results at Ultomiris initiation for the 56 participants who transitioned from the Alexion PNH registry to the IPIG PNH Registry (ie, Alexion PNH Registry study population as described in Section 3.2.1.1) have been previously documented (Section 4.10.1, Table 31). In contrast, Table 32 exclusively presents the laboratory results for the 6 participants who initiated Ultomiris on or after enrollment in the IPIG PNH Registry (ie, IPIG PNH Registry study population as described in Section 3.2.1.2) as of the data cutoff date (13 Jan 2025).

Table 32: Laboratory Values at Ultomiris Initiation, by Treatment Status (IPIG PNH Registry Study Population)

	All Ravulizumab Patients[a] (N=6)	Prior Eculizumab Treatment (N=1)	Without Prior Eculizumab Treatment (N=5)	Prior Eculizumab Treatment Unknown (N=0)
Percent GPI-deficient granulocytes				
n	4	1	3	0
Mean (SD)	63.7 (26.27)	76.2 (---)	59.5 (30.52)	-- (---)
Median (Q1, Q3)	68.2 (44.5, 82.9)	76.2 (76.2, 76.2)	60.3 (28.7, 89.7)	-- (--, --)
Percent GPI-deficient granulocytes, n (%)				
n	4	1	3	0
<1%	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
≥1% to <10%	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
≥10% to <50%	1 (25.0)	0 (0.0)	1 (33.3)	0 (0.0)
≥50%	3 (75.0)	1 (100.0)	2 (66.7)	0 (0.0)
LDH (U/L)				
n	6	1	5	0

Table 32: Laboratory Values at Ultomiris Initiation, by Treatment Status (IPIG PNH Registry Study Population)

	All Ravulizumab Patients[a] (N=6)	Prior Eculizumab Treatment (N=1)	Without Prior Eculizumab Treatment (N=5)	Prior Eculizumab Treatment Unknown (N=0)
Mean (SD)	1007.5 (699.72)	230.0 (---)	1163.0 (656.25)	-- (---)
Median (Q1, Q3)	914.0 (450.0, 1352.0)	230.0 (230.0, 230.0)	985.0 (843.0, 1352.0)	-- (--, --)
LDH ratio (× ULN)				
n	6	1	5	0
Mean (SD)	4.2 (2.80)	1.1 (---)	4.8 (2.62)	-- (---)
Median (Q1, Q3)	3.9 (1.8, 5.5)	1.1 (1.1, 1.1)	4.0 (3.8, 5.5)	-- (--, --)
LDH ratio (× ULN), n (%)				
n	6	1	5	0
<1.5	1 (16.7)	1 (100.0)	0 (0.0)	0 (0.0)
>=1.5	5 (83.3)	0 (0.0)	5 (100.0)	0 (0.0)
Hemoglobin (g/dL)				
n	6	1	5	0
Mean (SD)	9.8 (1.44)	12.2 (---)	9.3 (0.92)	-- (---)
Median (Q1, Q3)	9.7 (9.0, 10.3)	12.2 (12.2, 12.2)	9.6 (9.0, 9.8)	-- (--, --)
eGFR (mL/min/1.73 m²)				
n	6	1	5	0
Mean (SD)	79.3 (11.48)	90.0 (---)	77.2 (11.43)	-- (---)
Median (Q1, Q3)	82.5 (72.0, 89.0)	90.0 (90.0, 90.0)	81.0 (72.0, 84.0)	-- (--, --)
eGFR (mL/min/1.73 m²), n (%)				
n	6	1	5	0
<30	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
30 to <60	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
60 to <90	5 (83.3)	0 (0.0)	5 (100.0)	0 (0.0)
≥90	1 (16.7)	1 (100.0)	0 (0.0)	0 (0.0)

Table 32: Laboratory Values at Ultomiris Initiation, by Treatment Status (IPIG PNH Registry Study Population)

	All Ravulizumab Patients[a] (N=6)	Prior Eculizumab Treatment (N=1)	Without Prior Eculizumab Treatment (N=5)	Prior Eculizumab Treatment Unknown (N=0)
Absolute reticulocytes (× 10^9/L)				
n	6	1	5	0
Mean (SD)	196.3 (135.38)	224.9 (---)	190.6 (150.55)	-- (---)
Median (Q1, Q3)	176.5 (97.0, 229.0)	224.9 (224.9, 224.9)	128.0 (97.0, 229.0)	-- (--, --)

Notes: Data shown are reported in the 6 months prior to the timepoint.
[a] Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation. Patients were classified into the Prior Eculizumab Treatment Unknown group due to unknown prior eculizumab treatment history or because of a missing eculizumab discontinuation date.
Abbreviations: eGFR = estimated glomerular filtration rate; GPI = glycophosphatidylinositol; LDH = lactate dehydrogenase; n/N = number of patients; Q1 = first quartile; Q3 = third quartile; SD = standard deviation; ULN = upper limit of normal; WBC = white blood cells.
Source: Adapted from Post-text Table 10 Analysis: IPIG

5. SUMMARY AND DISCUSSION

Alexion has reported on the analyses of safety events captured in the Alexion PNH Registry since 2021. The results of this analysis should be considered alongside prior data and conclusions from the 2021 and 2023 biennial interim analysis reports and Ultomiris Periodic Safety Update Reports (PSURs) since 2019. This review includes data from a total of 5976 participants (cumulative) enrolled in the Alexion PNH Registry until 06 Jan 2025 with 1245 participants within the Alexion PNH Registry study population. A total of 532 participants were treated with Ultomiris and contributed 1155.4 person-years of exposure. Thirty participants were considered as frequent treatment switchers, which refers to participants who switched between Soliris and Ultomiris treatment more than once during their participation in the Alexion PNH Registry. In sensitivity analysis, cumulatively, 916 of 5976 participants were included in the study population with clone size ≥ 1%. Of these, 392 participants were treated with Ultomiris. Analyses of the data were performed as described in the SAP, version 1.0 dated 15 Apr 2025 (Appendix B). The participants were stratified by prior treatment status into the following treatment groups: “All Ultomiris Participants” including “Prior Soliris Treatment”, “Without Prior Soliris Treatment”, and “Prior Soliris Treatment Unknown”.

Cumulatively as of the data cutoff date of 06 Jan 2025, the majority of Ultomiris-treated participants were White (73.0%) and male (51.7%) with a mean age of 45.2 years at enrollment. The mean age of the participants at Ultomiris initiation was 52.1 years. The majority of participants (67.1%) received a first dose of 2700 mg Ultomiris. A total of 87.6% of participants discontinued from the Alexion PNH Registry; the reasons provided included death, enrolled in a clinical study of PNH treatment, participant choice, treated by another physician, received BMT, and other reasons. Other reasons for discontinuation (primarily due to site closure), were reported for 45.1% of the discontinued participants.

A total of 20 (3.8%) deaths were reported among 532 Ultomiris-treated participants. This included 9 (3.0%) out of 301 participants with prior Soliris treatment, 10 (6.2%) out of 161 participants without prior Soliris treatment, and 1 (1.4%) out of 70 participants with unknown prior Soliris treatment.

In Ultomiris-treated participants, 229 (44.3%) out of 517 participants had a history of BMD, 193 (37.5%) of 515 participants had a history of aplastic or hypoplastic anemia, 23 (4.5%) of 509 participants had a history of MDS, 66 (12.7%) of 520 participants had a history of malignancy and 107 (20.8%) of 514 participants had a history of infection. Additionally, 147 (28.2%) of 521 participants had a history of MAVE, 119 (22.9%) of 519 participants had a history of TE, 43 (8.3%) of 518 participants had a history of non-TE MAVE, 76 (14.8%) of 512 participants had a history of IRF, 21 (4.1%) of 512 participants had a history of IHF, and 26 (5.1%) of 512 participants had a history of pulmonary hypertension. Of the 147 female Ultomiris-treated participants with available data, history of pregnancy data was reported for 122 (83.0%) participants.

A total of 80 (15.3%) of 523 participants received RBC transfusions, 136 (33.6%) of 405 participants received anticoagulation therapy with heparin or warfarin, 83 (20.1%) of 413 participants received immunosuppressant therapy with cyclosporine or ATG, 72 (18.1%) of 398 participants received immunosuppressant therapy with corticosteroids, 61 (16.5%) of 370 participants received pain medication, 31 (8.6%) of 359 participants received opioid pain

medication, 42 (11.7%) of 360 participants received nonopioid pain medication, and 226 (53.4%) of 423 participants received oral prophylactic antibiotics. All concomitant therapy was received within the 6 months prior to Ultomiris initiation.

Laboratory results were obtained within the 6 months prior to Ultomiris initiation. It is to be noted that there was a high proportion of missing data for laboratory values due to the observational nature of the Alexion PNH Registry, thereby limiting the assessment and conclusions for laboratory values. In Ultomiris-treated participants, mean LDH was 441.1 U/L, mean hemoglobin was 10.9 g/dL, mean eGFR was 92.5 mL/min, mean absolute reticulocyte count was 160.3×10^9/L, mean percent GPI-deficient erythrocyte count was 51.4, and mean percent GPI-deficient granulocyte count was 76.7.

There were 0 cases of meningococcal infection during Ultomiris treatment. Safety events were stratified by the exposure period detailed in Section 3.2.3.1 for Alexion PNH Registry. The cumulative adjusted event rate for malignancy and hematologic malignancies respectively was 0.9 (95% CI: 0.6, 1.5) and 0.4 (95%CI: 0.2, 0.8) for participants while treated with Ultomiris and 1.0 (95% CI: 0.7, 1.4) and 0.5 (95% CI: 0.3, 0.8) for Soliris-only treated participants. The cumulative adjusted rate of infection was 5.1 (95% CI: 3.8, 6.8) and 5.7 (4.8, 6.7) for participants during their Ultomiris-treated time and for Soliris-only participants respectively. Event rates observed during Ultomiris-treated time remained consistent with previous interim analyses and comparable to those documented in the Soliris only treated patient population. The same observation was noted with respect to MAVE, TEs, non-TE MAVE, IRFs, IHFs, pulmonary hypertensions, BMTs, and infusion reactions in participants treated with Ultomiris.

As of the data cutoff date of 13 Jan 2025, a total of 123 participants were enrolled in the IPIG PNH Registry inclusive of 81 participants who were also present in the Alexion PNH Registry. A total of 62 participants were treated with Ultomiris (ie, Ultomiris study population) including 56 participants who were also present in the Alexion PNH Registry (ie, Alexion PNH Registry study population) and 6 participants without prior participation in the Alexion PNH Registry (ie, IPIG PNH Registry study population). There were no frequent treatment switchers in the IPIG PNH Registry. Analyses of the data were performed as described in the SAP, version 1.0 dated 15 Apr 2025 (Appendix B). In this analysis, safety events were stratified by the exposure period detailed in Section 3.2.3.2 for IPIG PNH Registry.

Demographics included data from IPIG PNH Registry study population (6 participants). The mean age at enrollment in the IPIG PNH Registry was 48.3 years, mean age at PNH disease start was 44.7 years, and mean age at Ultomiris initiation was 48.5 years for all 6 Ultomiris-treated participants.

At the last registry follow-up date, 1 (1.6%) death was reported in 62 Ultomiris-treated participants, including 1 (2.1%) out of 47 participants with prior Soliris treatment. No participant died out of 14 participants without prior Soliris treatment and 1 participant with unknown prior Soliris treatment. The mean duration from enrollment to last Registry follow-up was 0.4 years for all Ultomiris-treated participants.

Four SAEs were reported in 4 participants: acute cardiac failure (1 participant), which led to death; prostate cancer (1 participant), outcome of which was reported as not resolved; and pyrexia and worsening of gallstone disease (1 participant each), outcomes of which were reported as resolved. No events of TE or non-TE MAVE were reported. MAVE (acute cardiac

failure) was reported in 1 participant treated with Ultomiris, which had fatal outcome. Malignancy (prostate cancer) was reported in 1 participant, which was reported as not resolved. No infections, BMT, pregnancy cases, IRF, IHF, pulmonary hypertension, infusion reactions, or potential breakthrough hemolysis were reported.

Medical history included data from IPIG PNH Registry study population: out of 6 Ultomiris-treated participants with analyzable data, 2 (33.3%) had a history of aplastic or hypoplastic anemia and 3 (50.0%) participants had a history of COVID-19. Concomitant therapy included anticomplement therapy, antibiotic prophylaxis, anticoagulation therapy, immunosuppressant therapy, iron chelation therapy, thrombopoietin receptor agonists, and vaccination. In Ultomiris-treated participants at Ultomiris initiation, mean LDH was 1007.5 U/L, mean hemoglobin was 9.8 g/dL, mean eGFR was 79.3 mL/min/1.73 m^2, mean absolute reticulocyte count was 196.3 × 10^9/L, and mean percent GPI-deficient granulocyte count was 63.7.

Based on this analysis of data collected in the Alexion PNH Registry for Ultomiris up to 06 Jan 2025for those participants who were treated with Ultomiris, the experience was similar with that of Soliris and no additional safety concerns were observed when compared with the known safety profile of Ultomiris.

The safety profile characterized in the analysis report inclusive of both Alexion and IPIG PNH Registry data is consistent with the 2 previous analyses and data from the most recent PSUR (data lock point [DLP] 31 Dec 2024).

5.1. Data and Analysis Limitations and Strengths

There are several important strengths of the analyses provided as well as the Alexion and IPIG PNH Registries as data sources. This registry-based Studies M07-001 and ALX-PNH-501 provide real-world, observational data inclusive of a broad population of participants with PNH. In turn, findings from this registry-based study are more generalizable to real world patients as compared to data from clinical studies with more stringent inclusion/exclusion criteria and prescribed visits. When interpreting the results between the various treatment groups it is important to consider the possibility of surveillance bias wherein participants with prior Soliris treatment may have presented more often for their infusions or for regular follow-up visits than participants without prior Soliris treatment. Therefore, the event reports among the participants with prior Soliris treatment may be more complete than those of participants without prior Soliris treatment. The registries collect follow-up data via sites updating the study database at 6-month intervals to reflect the participants' status during the prior 6 months. This is done in lieu of requiring a fixed visit schedule for participants. The registries do not collect the number of times a participant was seen by the site or by other healthcare providers; however, the direction of the surveillance bias is likely to result in greater confidence in the completeness of data for the participants with prior Soliris treatment.

Inherent with the observational nature of data collection in a registry, the accuracy and completeness of data can vary. Though efforts are made to increase data completeness and ensure the validity of key outcomes, missing data may lead to bias, the direction of which is uncertain. Specific to data from the IPIG PNH Registry, the number of participants and length of follow-up is limited; however, when the data are taken into account in conjunction with data from the Alexion PNH Registry, this limitation is minimized. Further, the closure of the Alexion

PNH Registry coincident with the timing of this analysis precluded further investigation of site-level verifiable data. Specifically, it limited the ability to comprehensively assess prior complement inhibitor exposure in patients classified as inhibitor-naïve who subsequently developed malignancies following the initiation of Ultomiris.

5.2. Conclusions

The Alexion PNH Registry was a large observational study of participants with PNH, with all participants who received Ultomiris treatment including participants who received prior Soliris treatment, who did not receive prior Soliris treatment, and participants with unknown prior Soliris treatment status.

The analysis of safety data collected in the Alexion PNH Registry from 06 Jan 2023 until 06 Jan 2025 did not identify any notable changes from the prior Alexion PNH Registry analysis (ie, 13 Apr 2021 to 03 Apr 2023). The malignancy rate was low cumulatively, and taking into account the limited information available, no significant concern was identified from the available malignancy data. No *Neisseria spp (N meningitidis or N gonorrhoeae)*, *Haemophilus influenza*e, or *Aspergillus spp* infections were reported during the Analysis Period. The rates of infection, MAVE, TE MAVE, IRF, IHF, and pulmonary hypertension were lower among participants while treated with Ultomiris as compared with participants with untreated person-time. The nature, frequency, and severity of AEs reported in this analysis are consistent with the known safety profile of Ultomiris, and there is no change to the positive benefit-risk balance of Ultomiris in this population of participants with PNH.

The analysis of clinical and safety data collected in the IPIG PNH Registry until the data cutoff of 13 Jan 2025 revealed no new information and showed no new safety signal.

This third and proposed final interim analysis report for Ultomiris presents data from both the Alexion PNH Registry and participants enrolled in the Alexion Silo of the IPIG PNH Registry. Study ALX-PNH-501, which is an “IPIG PNH Registry-based Study” utilizes data from the IPIG Registry and is the successor to the Alexion PNH Registry. The results remain consistent with over 6 years of registry data analyzed and presented to the agency. Further, the conclusions are consistent with the most recent Ultomiris safety aggregate report (PSUR – DLP 31 Dec 2024). The MAH considers that this Postauthorization Measure is fulfilled and proposes that data from the IPIG PNH Registry continue to be collected as part of routine pharmacovigilance, and presented within PSURs.

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APPENDIX A. TABLES AND LISTINGS

Alexion PNH Registry (Analysis: Ravuema202501)

IPIG PNH Registry (Analysis: IPIG)

APPENDIX B. STATISTICAL ANALYSIS PLAN

Statistical Analysis Plan (SAP) – Version 1.0 dated 15 Apr 2025.

Table 1.1
Study Population, Cumulative
Alexion PNH Registry

	N
Patients ever enrolled in registry as of 06JAN2025	5976
Patients in study population[a]	1245
All ravulizumab patients	532
Prior eculizumab treatment[b]	301
Without prior eculizumab treatment[c]	161
Patients never treated with eculizumab before ravulizumab initiation	59
Eculizumab was discontinued at least 28 days prior to ravulizumab initiation	102
Prior eculizumab treatment unknown[d]	70
Treated with eculizumab only	713
Patients with untreated person time[e]	252
Frequent treatment switchers[f]	30

Notes: (a) Study population includes patients ever enrolled in the registry as of 06JAN2025 who have non-missing and valid enrollment date, date of birth, sex. In addition, the study population only includes subjects treated with ravulizumab or treated with eculizumab only.
(b) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. There were 27 patients who discontinued eculizumab between 17 and 28 days of ravulizumab initiation.
(c) Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.
(d) Patients were classified into the Prior Eculizumab Treatment Unknown group due to unknown prior eculizumab treatment history or because of a missing eculizumab discontinuation date.
(e) Patients with untreated person time are never treated with any anti-complement therapies on and prior to enrollment and may receive eculizumab, ravulizumab, or other anti-complement therapies after enrollment. They contribute information between registry enrollment and last untreated follow-up date.
(f) Frequent treatment switchers refer to patients switched between eculizumab and ravulizumab treatment more than once in the registry. These patients will not be included in the analysis.

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Table 1.2
Study Population, During the Analysis Period[a]
Alexion PNH Registry

	N
Patients actively enrolled in registry between 06JAN2023 and 06JAN2025	1765
Patients in study population[b]	597
All ravulizumab patients	493
Prior eculizumab treatment[c]	278
Without prior eculizumab treatment[d]	152
Patients never treated with eculizumab before ravulizumab initiation	58
Eculizumab was discontinued at least 28 days prior to ravulizumab initiation	94
Prior eculizumab treatment unknown[e]	63
Treated with eculizumab only	104
Patients with untreated person time[f]	239
Frequent treatment switchers[g]	25

Notes: (a) The analysis period is from 06JAN2023 to 06JAN2025.
(b) Study population includes patients actively enrolled in the registry between 06JAN2023 and 06JAN2025 who have non-missing and valid enrollment date, date of birth, sex. In addition, the study population only includes subjects treated with ravulizumab or treated with eculizumab only.
(c) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. There were 24 patients who discontinued eculizumab between 17 and 28 days of ravulizumab initiation.
(d) Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.
(e) Patients were classified into the Prior Eculizumab Treatment Unknown group due to unknown prior eculizumab treatment history or because of a missing eculizumab discontinuation date.
(f) Patients with untreated person time are never treated with any anti-complement therapies on and prior to enrollment and may receive eculizumab, ravulizumab, or other anti-complement therapies after enrollment. They contribute information between registry enrollment and last untreated follow-up date.
(g) Frequent treatment switchers refer to patients switched between eculizumab and ravulizumab treatment more than once in the registry. These patients will not be included in the analysis.
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Table 1.3
Sensitivity Analysis - Study Population, Cumulative
Alexion PNH Registry

	N
Patients ever enrolled in registry as of 06JAN2025	5976
Patients in study population with clone size >= 1%[a]	916
All ravulizumab patients	392
Prior eculizumab treatment[b]	224
Without prior eculizumab treatment[c]	120
Patients never treated with eculizumab before ravulizumab initiation	49
Eculizumab was discontinued at least 28 days prior to ravulizumab initiation	71
Prior eculizumab treatment unknown[d]	48
Treated with eculizumab only	524
Patients with untreated person time[e]	200
Frequent treatment switchers[f]	30

Notes: (a) Study population includes patients ever enrolled in the registry as of 06JAN2025 who have non-missing and valid enrollment date, date of birth, sex. In addition, the study population only includes subjects treated with ravulizumab or treated with eculizumab only.
(b) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. There were 17 patients who discontinued eculizumab between 17 and 28 days of ravulizumab initiation.
(c) Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.
(d) Patients were classified into the Prior Eculizumab Treatment Unknown group due to unknown prior eculizumab treatment history or because of a missing eculizumab discontinuation date.
(e) Patients with untreated person time are never treated with any anti-complement therapies on and prior to enrollment and may receive eculizumab, ravulizumab, or other anti-complement therapies after enrollment. They contribute information between registry enrollment and last untreated follow-up date.
(f) Frequent treatment switchers refer to patients switched between eculizumab and ravulizumab treatment more than once in the registry. These patients will not be included in the analysis.

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Table 2.1
Patient Demographics, Cumulative and by Treatment Status
Ravulizumab Study Population

	All Ravulizumab Patients[b] (N=532)	Prior Eculizumab Treatment[c] (N=301)	Without Prior Eculizumab Treatment[d] (N=161)	Prior Eculizumab Treatment Unknown (N=70)
Gender, n (%)				
n	532	301	161	70
Female	257 (48.3)	147 (48.8)	77 (47.8)	33 (47.1)
Male	275 (51.7)	154 (51.2)	84 (52.2)	37 (52.9)
Ethnicity, n (%)				
n	531	300	161	70
Not Hispanic/Latino	518 (97.6)	295 (98.3)	154 (95.7)	69 (98.6)
Hispanic/Latino	13 (2.4)	5 (1.7)	7 (4.3)	1 (1.4)
Race, n (%)				
n	530	299	161	70
Black or African descent	22 (4.2)	12 (4.0)	5 (3.1)	5 (7.1)
Asian	109 (20.6)	71 (23.7)	33 (20.5)	5 (7.1)
Native/Aboriginal	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Pacific Islander	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

Note: Q1 = first quartile; Q3 = third quartile; SD = standard deviation.
(a) PNH disease start is defined as the earliest date among date of PNH diagnosis, date of first PNH symptom, and date of lab test with reported granulocyte clone > 0.01%.
(b) Patients were classified into the Prior Eculizumab Treatment Unknown group due to unknown prior eculizumab treatment history or because of a missing eculizumab discontinuation date.
(c) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. There were 27 patients who discontinued eculizumab between 17 and 28 days of ravulizumab initiation.
(d) Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.

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Table 2.1
Patient Demographics, Cumulative and by Treatment Status
Ravulizumab Study Population

	All Ravulizumab Patients[b] (N=532)	Prior Eculizumab Treatment[c] (N=301)	Without Prior Eculizumab Treatment[d] (N=161)	Prior Eculizumab Treatment Unknown (N=70)
White or Caucasian	387 (73.0)	212 (70.9)	118 (73.3)	57 (81.4)
Other (unlisted or multiple races)	12 (2.3)	4 (1.3)	5 (3.1)	3 (4.3)
Age at enrollment (years)				
n	532	301	161	70
Mean (SD)	45.2 (16.98)	44.0 (16.78)	47.7 (17.03)	44.3 (17.33)
Median (Q1, Q3)	43.6 (31.8, 59.7)	43.0 (30.7, 56.4)	47.8 (33.7, 62.7)	42.3 (30.9, 60.2)
Age group at enrollment, n (%)				
n	532	301	161	70
<2 years	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
2 to <12 years	1 (0.2)	1 (0.3)	0 (0.0)	0 (0.0)
12 to <18 years	10 (1.9)	7 (2.3)	2 (1.2)	1 (1.4)
18 to <30 years	101 (19.0)	63 (20.9)	23 (14.3)	15 (21.4)
30 to <50 years	220 (41.4)	126 (41.9)	68 (42.2)	26 (37.1)
50 to <65 years	112 (21.1)	59 (19.6)	37 (23.0)	16 (22.9)

Note: Q1 = first quartile; Q3 = third quartile; SD = standard deviation.
(a) PNH disease start is defined as the earliest date among date of PNH diagnosis, date of first PNH symptom, and date of lab test with reported granulocyte clone > 0.01%.
(b) Patients were classified into the Prior Eculizumab Treatment Unknown group due to unknown prior eculizumab treatment history or because of a missing eculizumab discontinuation date.
(c) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. There were 27 patients who discontinued eculizumab between 17 and 28 days of ravulizumab initiation.
(d) Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.

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Table 2.1
Patient Demographics, Cumulative and by Treatment Status
Ravulizumab Study Population

	All Ravulizumab Patients[b] (N=532)	Prior Eculizumab Treatment[c] (N=301)	Without Prior Eculizumab Treatment[d] (N=161)	Prior Eculizumab Treatment Unknown (N=70)
65+ years	88 (16.5)	45 (15.0)	31 (19.3)	12 (17.1)
Age at PNH disease start (years)[a]				
n	532	301	161	70
Mean (SD)	39.2 (17.53)	37.6 (17.07)	42.0 (18.03)	39.5 (17.74)
Median (Q1, Q3)	35.3 (24.7, 52.0)	33.9 (24.1, 50.2)	37.1 (27.0, 58.9)	36.1 (23.7, 54.0)
Age group at PNH disease start, n (%)				
n	532	301	161	70
<2 years	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
2 to <12 years	9 (1.7)	6 (2.0)	1 (0.6)	2 (2.9)
12 to <18 years	28 (5.3)	23 (7.6)	4 (2.5)	1 (1.4)
18 to <30 years	162 (30.5)	93 (30.9)	45 (28.0)	24 (34.3)
30 to <50 years	183 (34.4)	103 (34.2)	60 (37.3)	20 (28.6)
50 to <65 years	92 (17.3)	47 (15.6)	28 (17.4)	17 (24.3)
65+ years	58 (10.9)	29 (9.6)	23 (14.3)	6 (8.6)

Note: Q1 = first quartile; Q3 = third quartile; SD = standard deviation.
(a) PNH disease start is defined as the earliest date among date of PNH diagnosis, date of first PNH symptom, and date of lab test with reported granulocyte clone > 0.01%.
(b) Patients were classified into the Prior Eculizumab Treatment Unknown group due to unknown prior eculizumab treatment history or because of a missing eculizumab discontinuation date.
(c) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. There were 27 patients who discontinued eculizumab between 17 and 28 days of ravulizumab initiation.
(d) Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.

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Table 2.1
Patient Demographics, Cumulative and by Treatment Status
Ravulizumab Study Population

	All Ravulizumab Patients[b] (N=532)	Prior Eculizumab Treatment[c] (N=301)	Without Prior Eculizumab Treatment[d] (N=161)	Prior Eculizumab Treatment Unknown (N=70)
Years from PNH disease start to enrollment				
n	532	301	161	70
Mean (SD)	6.0 (8.02)	6.4 (8.09)	5.7 (8.54)	4.8 (6.29)
Median (Q1, Q3)	2.7 (0.6, 8.1)	3.1 (0.7, 9.4)	2.1 (0.4, 6.8)	2.4 (0.6, 6.7)
Years from PNH disease start to ravulizumab initiation				
n	532	301	161	70
Mean (SD)	12.9 (9.63)	13.7 (9.30)	11.9 (10.57)	11.6 (8.47)
Median (Q1, Q3)	10.9 (6.1, 17.6)	11.7 (7.1, 18.6)	9.7 (4.5, 16.2)	10.8 (6.3, 15.5)
Age at ravulizumab initiation (years)				
n	532	301	161	70
Mean (SD)	52.1 (16.64)	51.3 (16.69)	53.9 (16.29)	51.1 (17.10)
Median (Q1, Q3)	50.4 (39.3, 65.7)	50.1 (39.3, 64.6)	53.9 (40.5, 67.3)	48.4 (36.1, 64.7)
Age group at ravulizumab initiation, n (%)				
n	532	301	161	70

Note: Q1 = first quartile; Q3 = third quartile; SD = standard deviation.
(a) PNH disease start is defined as the earliest date among date of PNH diagnosis, date of first PNH symptom, and date of lab test with reported granulocyte clone > 0.01%.
(b) Patients were classified into the Prior Eculizumab Treatment Unknown group due to unknown prior eculizumab treatment history or because of a missing eculizumab discontinuation date.
(c) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. There were 27 patients who discontinued eculizumab between 17 and 28 days of ravulizumab initiation.
(d) Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.

Source: ADAM.ADSL, ADAM.ADPOP
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Table 2.1
Patient Demographics, Cumulative and by Treatment Status
Ravulizumab Study Population

	All Ravulizumab Patients[b] (N=532)	Prior Eculizumab Treatment[c] (N=301)	Without Prior Eculizumab Treatment[d] (N=161)	Prior Eculizumab Treatment Unknown (N=70)
<2 years	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
2 to <12 years	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
12 to <18 years	1 (0.2)	0 (0.0)	1 (0.6)	0 (0.0)
18 to <30 years	43 (8.1)	27 (9.0)	10 (6.2)	6 (8.6)
30 to <50 years	214 (40.2)	123 (40.9)	60 (37.3)	31 (44.3)
50 to <65 years	133 (25.0)	76 (25.2)	41 (25.5)	16 (22.9)
65+ years	141 (26.5)	75 (24.9)	49 (30.4)	17 (24.3)

Note: Q1 = first quartile; Q3 = third quartile; SD = standard deviation.
(a) PNH disease start is defined as the earliest date among date of PNH diagnosis, date of first PNH symptom, and date of lab test with reported granulocyte clone > 0.01%.
(b) Patients were classified into the Prior Eculizumab Treatment Unknown group due to unknown prior eculizumab treatment history or because of a missing eculizumab discontinuation date.
(c) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. There were 27 patients who discontinued eculizumab between 17 and 28 days of ravulizumab initiation.
(d) Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.

Source: ADAM.ADSL, ADAM.ADPOP
Run Date: 2025-05-14T14:50:31
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ravuema202501/Files/tables/production/programs/t2_demo_cum.sas

Table 2.2
Patient Demographics, During the Analysis Period and by Treatment Status[a]
Ravulizumab Study Population

	All Ravulizumab Patients[c] (N=493)	Prior Eculizumab Treatment[d] (N=278)	Without Prior Eculizumab Treatment[e] (N=152)	Prior Eculizumab Treatment Unknown (N=63)
Gender, n (%)				
n	493	278	152	63
Female	239 (48.5)	133 (47.8)	76 (50.0)	30 (47.6)
Male	254 (51.5)	145 (52.2)	76 (50.0)	33 (52.4)
Ethnicity, n (%)				
n	492	277	152	63
Not Hispanic/Latino	480 (97.6)	273 (98.6)	145 (95.4)	62 (98.4)
Hispanic/Latino	12 (2.4)	4 (1.4)	7 (4.6)	1 (1.6)
Race, n (%)				
n	491	276	152	63
Black or African descent	19 (3.9)	10 (3.6)	4 (2.6)	5 (7.9)
Asian	103 (21.0)	69 (25.0)	30 (19.7)	4 (6.3)
Native/Aboriginal	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Pacific Islander	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

Note: Q1 = first quartile; Q3 = third quartile; SD = standard deviation.
(a) Includes patients actively enrolled in the registry during the analysis period, which covers the time period from 06JAN2023 to 06JAN2025.
(b) PNH disease start is defined as the earliest date among date of PNH diagnosis, date of first PNH symptom, and date of lab test with reported granulocyte clone > 0.01%.
(c) Patients were classified into the Prior Eculizumab Treatment Unknown group due to unknown prior eculizumab treatment history or because of a missing eculizumab discontinuation date.
(d) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. There were 24 patients who discontinued eculizumab between 17 and 28 days of ravulizumab initiation.
(e) Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.

Source: ADAM.ADSL, ADAM.ADPOP
Run Date: 2025-05-14T14:50:41
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ravuema202501/Files/tables/production/programs/t2_demo_dur.sas

Table 2.2
Patient Demographics, During the Analysis Period and by Treatment Status[a]
Ravulizumab Study Population

	All Ravulizumab Patients[c] (N=493)	Prior Eculizumab Treatment[d] (N=278)	Without Prior Eculizumab Treatment[e] (N=152)	Prior Eculizumab Treatment Unknown (N=63)
White or Caucasian	358 (72.9)	193 (69.9)	114 (75.0)	51 (81.0)
Other (unlisted or multiple races)	11 (2.2)	4 (1.4)	4 (2.6)	3 (4.8)
Age at enrollment (years)				
n	493	278	152	63
Mean (SD)	45.2 (16.92)	44.0 (16.76)	47.9 (16.94)	43.8 (17.08)
Median (Q1, Q3)	43.5 (31.9, 59.7)	43.0 (30.7, 56.5)	47.9 (33.8, 62.8)	41.7 (30.3, 59.3)
Age group at enrollment, n (%)				
n	493	278	152	63
<2 years	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
2 to <12 years	1 (0.2)	1 (0.4)	0 (0.0)	0 (0.0)
12 to <18 years	9 (1.8)	6 (2.2)	2 (1.3)	1 (1.6)
18 to <30 years	93 (18.9)	58 (20.9)	21 (13.8)	14 (22.2)
30 to <50 years	205 (41.6)	117 (42.1)	64 (42.1)	24 (38.1)
50 to <65 years	103 (20.9)	55 (19.8)	35 (23.0)	13 (20.6)

Note: Q1 = first quartile; Q3 = third quartile; SD = standard deviation.
(a) Includes patients actively enrolled in the registry during the analysis period, which covers the time period from 06JAN2023 to 06JAN2025.
(b) PNH disease start is defined as the earliest date among date of PNH diagnosis, date of first PNH symptom, and date of lab test with reported granulocyte clone > 0.01%.
(c) Patients were classified into the Prior Eculizumab Treatment Unknown group due to unknown prior eculizumab treatment history or because of a missing eculizumab discontinuation date.
(d) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. There were 24 patients who discontinued eculizumab between 17 and 28 days of ravulizumab initiation.
(e) Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.

Source: ADAM.ADSL, ADAM.ADPOP
Run Date: 2025-05-14T14:50:41
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ravuema202501/Files/tables/production/programs/t2_demo_dur.sas

Table 2.2
Patient Demographics, During the Analysis Period and by Treatment Status[a]
Ravulizumab Study Population

	All Ravulizumab Patients[c] (N=493)	Prior Eculizumab Treatment[d] (N=278)	Without Prior Eculizumab Treatment[e] (N=152)	Prior Eculizumab Treatment Unknown (N=63)
65+ years	82 (16.6)	41 (14.7)	30 (19.7)	11 (17.5)
Age at PNH disease start (years)[b]				
n	493	278	152	63
Mean (SD)	39.1 (17.45)	37.6 (17.06)	42.1 (17.90)	39.1 (17.38)
Median (Q1, Q3)	35.0 (24.9, 51.6)	33.9 (24.0, 49.6)	37.8 (27.0, 59.3)	36.0 (24.9, 54.0)
Age group at PNH disease start, n (%)				
n	493	278	152	63
<2 years	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
2 to <12 years	8 (1.6)	5 (1.8)	1 (0.7)	2 (3.2)
12 to <18 years	27 (5.5)	22 (7.9)	4 (2.6)	1 (1.6)
18 to <30 years	149 (30.2)	86 (30.9)	42 (27.6)	21 (33.3)
30 to <50 years	173 (35.1)	96 (34.5)	57 (37.5)	20 (31.7)
50 to <65 years	83 (16.8)	43 (15.5)	26 (17.1)	14 (22.2)
65+ years	53 (10.8)	26 (9.4)	22 (14.5)	5 (7.9)

Note: Q1 = first quartile; Q3 = third quartile; SD = standard deviation.
(a) Includes patients actively enrolled in the registry during the analysis period, which covers the time period from 06JAN2023 to 06JAN2025.
(b) PNH disease start is defined as the earliest date among date of PNH diagnosis, date of first PNH symptom, and date of lab test with reported granulocyte clone > 0.01%.
(c) Patients were classified into the Prior Eculizumab Treatment Unknown group due to unknown prior eculizumab treatment history or because of a missing eculizumab discontinuation date.
(d) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. There were 24 patients who discontinued eculizumab between 17 and 28 days of ravulizumab initiation.
(e) Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.

Source: ADAM.ADSL, ADAM.ADPOP
Run Date: 2025-05-14T14:50:41
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ravuema202501/Files/tables/production/programs/t2_demo_dur.sas

Table 2.2
Patient Demographics, During the Analysis Period and by Treatment Status[a]
Ravulizumab Study Population

	All Ravulizumab Patients[c] (N=493)	Prior Eculizumab Treatment[d] (N=278)	Without Prior Eculizumab Treatment[e] (N=152)	Prior Eculizumab Treatment Unknown (N=63)
Years from PNH disease start to enrollment				
n	493	278	152	63
Mean (SD)	6.0 (8.12)	6.4 (8.14)	5.8 (8.71)	4.7 (6.37)
Median (Q1, Q3)	2.7 (0.6, 8.1)	3.1 (0.7, 9.5)	2.2 (0.4, 6.6)	2.3 (0.6, 6.7)
Years from PNH disease start to ravulizumab initiation				
n	493	278	152	63
Mean (SD)	13.0 (9.74)	13.8 (9.35)	12.2 (10.72)	11.9 (8.71)
Median (Q1, Q3)	11.2 (6.1, 17.7)	11.8 (7.1, 18.7)	9.9 (4.5, 16.2)	11.1 (6.3, 15.7)
Age at ravulizumab initiation (years)				
n	493	278	152	63
Mean (SD)	52.2 (16.55)	51.3 (16.66)	54.2 (16.15)	51.0 (16.86)
Median (Q1, Q3)	50.4 (39.5, 66.2)	49.6 (39.3, 64.6)	54.7 (40.6, 68.2)	48.1 (36.1, 64.7)
Age group at ravulizumab initiation, n (%)				

Note: Q1 = first quartile; Q3 = third quartile; SD = standard deviation.
(a) Includes patients actively enrolled in the registry during the analysis period, which covers the time period from 06JAN2023 to 06JAN2025.
(b) PNH disease start is defined as the earliest date among date of PNH diagnosis, date of first PNH symptom, and date of lab test with reported granulocyte clone > 0.01%.
(c) Patients were classified into the Prior Eculizumab Treatment Unknown group due to unknown prior eculizumab treatment history or because of a missing eculizumab discontinuation date.
(d) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. There were 24 patients who discontinued eculizumab between 17 and 28 days of ravulizumab initiation.
(e) Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.

Source: ADAM.ADSL, ADAM.ADPOP
Run Date: 2025-05-14T14:50:41
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ravuema202501/Files/tables/production/programs/t2_demo_dur.sas

Table 2.2
Patient Demographics, During the Analysis Period and by Treatment Status[a]
Ravulizumab Study Population

	All Ravulizumab Patients[c] (N=493)	Prior Eculizumab Treatment[d] (N=278)	Without Prior Eculizumab Treatment[e] (N=152)	Prior Eculizumab Treatment Unknown (N=63)
n	493	278	152	63
<2 years	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
2 to <12 years	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
12 to <18 years	1 (0.2)	0 (0.0)	1 (0.7)	0 (0.0)
18 to <30 years	37 (7.5)	23 (8.3)	9 (5.9)	5 (7.9)
30 to <50 years	202 (41.0)	117 (42.1)	56 (36.8)	29 (46.0)
50 to <65 years	121 (24.5)	69 (24.8)	38 (25.0)	14 (22.2)
65+ years	132 (26.8)	69 (24.8)	48 (31.6)	15 (23.8)

Note: Q1 = first quartile; Q3 = third quartile; SD = standard deviation.
(a) Includes patients actively enrolled in the registry during the analysis period, which covers the time period from 06JAN2023 to 06JAN2025.
(b) PNH disease start is defined as the earliest date among date of PNH diagnosis, date of first PNH symptom, and date of lab test with reported granulocyte clone > 0.01%.
(c) Patients were classified into the Prior Eculizumab Treatment Unknown group due to unknown prior eculizumab treatment history or because of a missing eculizumab discontinuation date.
(d) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. There were 24 patients who discontinued eculizumab between 17 and 28 days of ravulizumab initiation.
(e) Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.

Source: ADAM.ADSL, ADAM.ADPOP
Run Date: 2025-05-14T14:50:41
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ravuema202501/Files/tables/production/programs/t2_demo_dur.sas

Table 3.1
Patient Disposition at Last Registry Follow-Up Date, Cumulative and by Treatment Status
Ravulizumab Study Population

	All Ravulizumab Patients[a] (N=532)	Prior Eculizumab Treatment[b] (N=301)	Without Prior Eculizumab Treatment[c] (N=161)	Prior Eculizumab Treatment Unknown (N=70)
Registry discontinuation, n (%)				
n	532	301	161	70
No	66 (12.4)	57 (18.9)	8 (5.0)	1 (1.4)
Yes	466 (87.6)	244 (81.1)	153 (95.0)	69 (98.6)
Reported reason for registry discontinuation, n (%)				
n	466	244	153	69
Patient choice	4 (0.9)	1 (0.4)	3 (2.0)	0 (0.0)
Patient received a bone marrow transplant	3 (0.6)	1 (0.4)	1 (0.7)	1 (1.4)
Patient is being treated by another physician	2 (0.4)	1 (0.4)	1 (0.7)	0 (0.0)
Patient enrolled in a clinical trial of PNH treatment	19 (4.1)	15 (6.1)	3 (2.0)	1 (1.4)
Patient died	20 (4.3)	9 (3.7)	10 (6.5)	1 (1.4)
Enrollment in the IPIG PNH Registry	207 (44.4)	124 (50.8)	53 (34.6)	30 (43.5)
Other	210 (45.1)	93 (38.1)	81 (52.9)	36 (52.2)
Unknown	1 (0.2)	0 (0.0)	1 (0.7)	0 (0.0)

Notes:
(a) Patients were classified into the Prior Eculizumab Treatment Unknown group due to unknown prior eculizumab treatment history or because of a missing eculizumab discontinuation date.
(b) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. There were 27 patients who discontinued eculizumab between 17 and 28 days of ravulizumab initiation.
(c) Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.

Source: ADAM.ADSL, ADAM.ADPOP
Run Date: 2025-05-14T14:50:49
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ravuema202501/Files/tables/production/programs/t3_disp_cum.sas

Table 3.2
Patient Disposition at Last Registry Follow-Up Date, During the Analysis Period and by Treatment Status[a]
Ravulizumab Study Population

	All Ravulizumab Patients[b] (N=493)	Prior Eculizumab Treatment[c] (N=278)	Without Prior Eculizumab Treatment[d] (N=152)	Prior Eculizumab Treatment Unknown (N=63)
Registry discontinuation, n (%)				
n	493	278	152	63
No	63 (12.8)	54 (19.4)	8 (5.3)	1 (1.6)
Yes	430 (87.2)	224 (80.6)	144 (94.7)	62 (98.4)
Reported reason for registry discontinuation, n (%)				
n	430	224	144	62
Patient choice	1 (0.2)	1 (0.4)	0 (0.0)	0 (0.0)
Patient received a bone marrow transplant	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Patient is being treated by another physician	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Patient enrolled in a clinical trial of PNH treatment	12 (2.8)	10 (4.5)	2 (1.4)	0 (0.0)
Patient died	12 (2.8)	4 (1.8)	8 (5.6)	0 (0.0)
Enrollment in the IPIG PNH Registry	207 (48.1)	124 (55.4)	53 (36.8)	30 (48.4)

Notes:
(a) Includes patients actively enrolled in the registry during the analysis period, which covers the time period from 06JAN2023 to 06JAN2025.
(b) Patients were classified into the Prior Eculizumab Treatment Unknown group due to unknown prior eculizumab treatment history or because of a missing eculizumab discontinuation date.
(c) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. There were 24 patients who discontinued eculizumab between 17 and 28 days of ravulizumab initiation.
(d) Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.

Source: ADAM.ADSL, ADAM.ADPOP
Run Date: 2025-05-14T14:50:58
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ravuema202501/Files/tables/production/programs/t3_disp_dur.sas

Table 3.2
Patient Disposition at Last Registry Follow-Up Date, During the Analysis Period and by Treatment Status[a]
Ravulizumab Study Population

	All Ravulizumab Patients[b] (N=493)	Prior Eculizumab Treatment[c] (N=278)	Without Prior Eculizumab Treatment[d] (N=152)	Prior Eculizumab Treatment Unknown (N=63)
Other	197 (45.8)	85 (37.9)	80 (55.6)	32 (51.6)
Unknown	1 (0.2)	0 (0.0)	1 (0.7)	0 (0.0)

Notes:
(a) Includes patients actively enrolled in the registry during the analysis period, which covers the time period from 06JAN2023 to 06JAN2025.
(b) Patients were classified into the Prior Eculizumab Treatment Unknown group due to unknown prior eculizumab treatment history or because of a missing eculizumab discontinuation date.
(c) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. There were 24 patients who discontinued eculizumab between 17 and 28 days of ravulizumab initiation.
(d) Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.

Source: ADAM.ADSL, ADAM.ADPOP
Run Date: 2025-05-14T14:50:58
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ravuema202501/Files/tables/production/programs/t3_disp_dur.sas

Table 4.1
Ultomiris Treatment Discontinuation, Cumulative
Ravulizumab Study Population

	Treated with Ravulizumab (N=532)
Discontinuation of ravulizumab, n (%)	
n	532
No record of discontinuation	470 (88.3)
Discontinuation of ravulizumab	62 (11.7)
Discontinuation, death	10 (16.1)
Discontinuation, adverse event	1 (1.6)
Discontinuation, lack of efficacy	9 (14.5)
Discontinuation, physician decision	10 (16.1)
Discontinuation, switch to other anti-complement treatment	15 (24.2)
Discontinuation, patient choice	3 (4.8)
Discontinuation, cost or access consideration	1 (1.6)
Discontinuation, switch to eculizumab IV	5 (8.1)
Discontinuation, unknown reason	8 (12.9)

Source: ADAM.ADSL, ADAM.ADEX, ADAM.ADPOP
Run Date: 2025-05-14T14:51:06
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ravuema202501/Files/tables/production/programs/t4_ravudisc_cum.sas

Table 4.2
Ultomiris Treatment Discontinuation, During the Analysis Period[a]
Ravulizumab Study Population

	Treated with Ravulizumab (N=493)
Discontinuation of ravulizumab, n (%)	
n	493
No record of discontinuation	447 (90.7)
Discontinuation of ravulizumab	46 (9.3)
Discontinuation, death	6 (13.0)
Discontinuation, adverse event	1 (2.2)
Discontinuation, lack of efficacy	7 (15.2)
Discontinuation, physician decision	7 (15.2)
Discontinuation, switch to other anti-complement treatment	14 (30.4)
Discontinuation, patient choice	2 (4.3)
Discontinuation, cost or access consideration	0 (0.0)
Discontinuation, switch to eculizumab IV	2 (4.3)
Discontinuation, unknown reason	7 (15.2)

Note:
(a) Includes patients actively enrolled in the registry during the analysis period, which covers the time period from 06JAN2023 to 06JAN2025.

Source: ADAM.ADSL, ADAM.ADEX, ADAM.ADPOP
Run Date: 2025-05-14T14:51:16
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ravuema202501/Files/tables/production/programs/t4_ravudisc_dur.sas

Table 5.1
Ultomiris Treatment Information, Cumulative
Ravulizumab Study Population

	Treated with Ravulizumab (N=532)
Meningococcal vaccination prior to ravulizumab start, n (%)	
n	481
No	0 (0.0)
Yes	481 (100.0)
Weight (kg) at initiation of ravulizumab	
All patients, n	364
Mean (SD)	75.3 (18.60)
Median (Q1, Q3)	73.5 (62.0, 85.0)
< 40kg, n (%)	0 (0.0)
≥ 40kg, n (%)	364 (100.0)
First dose of ravulizumab, n	502
2400mg, n (%)	103 (20.5)
2700mg, n (%)	337 (67.1)
3000mg, n (%)	54 (10.8)
Other, n (%)	8 (1.6)
Subsequent doses of ravulizumab, n	505
All doses <3000mg/8 weeks, n (%)	1 (0.2)

Note: Q1 = first quartile; Q3 = third quartile; SD = standard deviation.

Source: ADAM.ADSL, ADAM.ADEX, ADAM.ADPOP
Run Date: 2025-05-14T14:51:26
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ravuema202501/Files/tables/production/programs/t5_ravuinfo_cum.sas

Table 5.1
Ultomiris Treatment Information, Cumulative
Ravulizumab Study Population

	Treated with Ravulizumab (N=532)
All doses ≥3000 to <3300mg/8 weeks, n (%)	88 (17.4)
All doses ≥3300 to <3600mg/8 weeks, n (%)	294 (58.2)
All doses =3600mg/8 weeks, n (%)	41 (8.1)
All doses >3600mg/8 weeks, n (%)	7 (1.4)
Other/Unknown, n (%)	74 (14.7)
Last dose of ravulizumab, n	505
3000mg, n (%)	106 (21.0)
3300mg, n (%)	337 (66.7)
3600mg, n (%)	50 (9.9)
Other, n (%)	12 (2.4)

Note: Q1 = first quartile; Q3 = third quartile; SD = standard deviation.

Source: ADAM.ADSL, ADAM.ADEX, ADAM.ADPOP
Run Date: 2025-05-14T14:51:26
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ravuema202501/Files/tables/production/programs/t5_ravuinfo_cum.sas

Table 5.2
Ultomiris Treatment Information, During the Analysis Period[a]
Ravulizumab Study Population

	Treated with Ravulizumab (N=493)
Meningococcal vaccination prior to ravulizumab start, n (%)	
n	442
No	0 (0.0)
Yes	442 (100.0)
Weight (kg) at initiation of ravulizumab	
All patients, n	340
Mean (SD)	75.0 (18.58)
Median (Q1, Q3)	73.0 (61.9, 84.9)
< 40kg, n (%)	0 (0.0)
≥ 40kg, n (%)	340 (100.0)
First dose of ravulizumab, n	468
2400mg, n (%)	96 (20.5)
2700mg, n (%)	316 (67.5)
3000mg, n (%)	49 (10.5)
Other, n (%)	7 (1.5)
Subsequent doses of ravulizumab, n	470

Note: Q1 = first quartile; Q3 = third quartile; SD = standard deviation.
(a) Includes patients actively enrolled in the registry during the analysis period, which covers the time period from 06JAN2023 to 06JAN2025.

Source: ADAM.ADSL, ADAM.ADEX, ADAM.ADPOP
Run Date: 2025-05-14T14:51:35
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ravuema202501/Files/tables/production/programs/t5_ravuinfo_dur.sas

Table 5.2
Ultomiris Treatment Information, During the Analysis Period[a]
Ravulizumab Study Population

	Treated with Ravulizumab (N=493)
All doses <3000mg/8 weeks, n (%)	1 (0.2)
All doses ≥3000 to <3300mg/8 weeks, n (%)	82 (17.4)
All doses ≥3300 to <3600mg/8 weeks, n (%)	279 (59.4)
All doses =3600mg/8 weeks, n (%)	36 (7.7)
All doses >3600mg/8 weeks, n (%)	7 (1.5)
Other/Unknown, n (%)	65 (13.8)
Last dose of ravulizumab, n	473
3000mg, n (%)	99 (20.9)
3300mg, n (%)	318 (67.2)
3600mg, n (%)	45 (9.5)
Other, n (%)	11 (2.3)

Note: Q1 = first quartile; Q3 = third quartile; SD = standard deviation.
(a) Includes patients actively enrolled in the registry during the analysis period, which covers the time period from 06JAN2023 to 06JAN2025.

Source: ADAM.ADSL, ADAM.ADEX, ADAM.ADPOP
Run Date: 2025-05-14T14:51:35
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ravuema202501/Files/tables/production/programs/t5_ravuinfo_dur.sas

Table 6.1
Patient Durations of Follow-up, Cumulative and by Treatment Status
Ravulizumab Study Population

	All Ravulizumab Patients[a] (N=532)	Prior Eculizumab Treatment[b] (N=301)	Without Prior Eculizumab Treatment[c] (N=161)	Prior Eculizumab Treatment Unknown (N=70)
Years from enrollment to last registry follow-up				
n	532	301	161	70
Mean (SD)	9.4 (4.19)	10.1 (3.70)	8.0 (4.67)	9.2 (4.31)
Median (Min, Max)	9.6 (0.0, 19.5)	10.4 (1.0, 19.5)	8.3 (0.0, 17.3)	10.4 (0.4, 17.5)
Years of ravulizumab treatment follow-up				
n	529	300	160	69
Mean (SD)	2.2 (1.37)	2.6 (1.27)	1.6 (1.20)	1.9 (1.55)
Median (Min, Max)	2.3 (0.0, 5.3)	2.6 (0.0, 5.3)	1.5 (0.0, 5.1)	1.8 (0.0, 5.0)

Note: SD = standard deviation.
(a) Patients were classified into the Prior Eculizumab Treatment Unknown group due to unknown prior eculizumab treatment history or because of a missing eculizumab discontinuation date.
(b) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. There were 27 patients who discontinued eculizumab between 17 and 28 days of ravulizumab initiation.
(c) Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.

Source: ADAM.ADSL, ADAM.ADPOP
Run Date: 2025-05-14T14:51:47
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ravuema202501/Files/tables/production/programs/t6_dura_cum.sas

Table 6.2
Patient Durations of Follow-up, During the Analysis Period and by Treatment Status[a]
Ravulizumab Study Population

	All Ravulizumab Patients[b] (N=493)	Prior Eculizumab Treatment[c] (N=278)	Without Prior Eculizumab Treatment[d] (N=152)	Prior Eculizumab Treatment Unknown (N=63)
Years of follow-up during the analysis period				
n	493	278	152	63
Mean (SD)	1.2 (0.35)	1.2 (0.35)	1.2 (0.31)	1.2 (0.39)
Median (Min, Max)	1.3 (0.0, 1.9)	1.2 (0.1, 1.9)	1.3 (0.0, 1.9)	1.4 (0.0, 1.9)
Years of ravulizumab treatment during the analysis period				
n	454	259	143	52
Mean (SD)	1.1 (0.42)	1.2 (0.40)	1.0 (0.40)	1.1 (0.51)
Median (Min, Max)	1.2 (0.0, 1.9)	1.2 (0.0, 1.9)	1.2 (0.0, 1.7)	1.3 (0.0, 1.7)

Note: SD = standard deviation.
(a) Includes patients actively enrolled in the registry during the analysis period, which covers the time period from 06JAN2023 to 06JAN2025.
(b) Patients were classified into the Prior Eculizumab Treatment Unknown group due to unknown prior eculizumab treatment history or because of a missing eculizumab discontinuation date.
(c) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. There were 24 patients who discontinued eculizumab between 17 and 28 days of ravulizumab initiation.
(d) Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.

Source: ADAM.ADSL, ADAM.ADPOP
Run Date: 2025-05-14T14:51:59
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ravuema202501/Files/tables/production/programs/t6_dura_dur.sas

Table 7.1
Vital Status at Last Registry Follow-Up Date, Cumulative and by Treatment Status
Ravulizumab Study Population

	All Ravulizumab Patients[a] (N=532)	Prior Eculizumab Treatment[b] (N=301)	Without Prior Eculizumab Treatment[c] (N=161)	Prior Eculizumab Treatment Unknown (N=70)
Vital status, n (%)				
n	532	301	161	70
Alive	512 (96.2)	292 (97.0)	151 (93.8)	69 (98.6)
Dead	20 (3.8)	9 (3.0)	10 (6.2)	1 (1.4)
Reported cause of death by system organ class				
Blood and lymphatic system disorders, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Cardiac disorders, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Gastrointestinal disorders, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
General disorders and administration site conditions, n (%)	4 (20.0)	1 (11.1)	3 (30.0)	0 (0.0)
Hepatobiliary disorders, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Immune system disorders, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Infections and infestations, n (%)	3 (15.0)	0 (0.0)	3 (30.0)	0 (0.0)
Injury, poisoning and procedural complications, n (%)	1 (5.0)	0 (0.0)	1 (10.0)	0 (0.0)

Note: The percentages are the percent of all death reported in the registry.
(a) Patients were classified into the Prior Eculizumab Treatment Unknown group due to unknown prior eculizumab treatment history or because of a missing eculizumab discontinuation date.
(b) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. There were 27 patients who discontinued eculizumab between 17 and 28 days of ravulizumab initiation.
(c) Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.

Source: ADAM.ADSL, ADAM.ADPOP
Run Date: 2025-05-14T14:52:08
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ravuema202501/Files/tables/production/programs/t7_death_cum.sas

Table 7.1
Vital Status at Last Registry Follow-Up Date, Cumulative and by Treatment Status
Ravulizumab Study Population

	All Ravulizumab Patients[a] (N=532)	Prior Eculizumab Treatment[b] (N=301)	Without Prior Eculizumab Treatment[c] (N=161)	Prior Eculizumab Treatment Unknown (N=70)
Lung infection, n (%)	1 (5.0)	1 (11.1)	0 (0.0)	0 (0.0)
Neoplasms benign, malignant and unspecified (incl cysts and polyps), n (%)	5 (25.0)	2 (22.2)	2 (20.0)	1 (100.0)
Nervous system disorders, n (%)	2 (10.0)	1 (11.1)	1 (10.0)	0 (0.0)
Psychiatric disorders, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Renal and urinary disorders, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Respiratory, thoracic and mediastinal disorders, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Vascular disorder, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

Note: The percentages are the percent of all death reported in the registry.
(a) Patients were classified into the Prior Eculizumab Treatment Unknown group due to unknown prior eculizumab treatment history or because of a missing eculizumab discontinuation date.
(b) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. There were 27 patients who discontinued eculizumab between 17 and 28 days of ravulizumab initiation.
(c) Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.

Source: ADAM.ADSL, ADAM.ADPOP
Run Date: 2025-05-14T14:52:08
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ravuema202501/Files/tables/production/programs/t7_death_cum.sas

Table 7.2
Vital Status at Last Registry Follow-Up Date, During the Analysis Period and by Treatment Status[a]
Ravulizumab Study Population

	All Ravulizumab Patients[b] (N=493)	Prior Eculizumab Treatment[c] (N=278)	Without Prior Eculizumab Treatment[d] (N=152)	Prior Eculizumab Treatment Unknown (N=63)
Vital status, n (%)				
n	493	278	152	63
Alive	481 (97.6)	274 (98.6)	144 (94.7)	63 (100.0)
Dead	12 (2.4)	4 (1.4)	8 (5.3)	0 (0.0)
Reported cause of death by system organ class				
Blood and lymphatic system disorders, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Cardiac disorders, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Gastrointestinal disorders, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
General disorders and administration site conditions, n (%)	3 (25.0)	0 (0.0)	3 (37.5)	0 (0.0)
Hepatobiliary disorders, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Immune system disorders, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Infections and infestations, n (%)	2 (16.7)	0 (0.0)	2 (25.0)	0 (0.0)

Note: The percentages are the percent of all death reported in the registry.
(a) Includes patients actively enrolled in the registry during the analysis period, which covers the time period from 06JAN2023 to 06JAN2025.
(b) Patients were classified into the Prior Eculizumab Treatment Unknown group due to unknown prior eculizumab treatment history or because of a missing eculizumab discontinuation date.
(c) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. There were 24 patients who discontinued eculizumab between 17 and 28 days of ravulizumab initiation.
(d) Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.

Source: ADAM.ADSL, ADAM.ADPOP
Run Date: 2025-05-14T14:52:18
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ravuema202501/Files/tables/production/programs/t7_death_dur.sas

Table 7.2
Vital Status at Last Registry Follow-Up Date, During the Analysis Period and by Treatment Status[a]
Ravulizumab Study Population

	All Ravulizumab Patients[b] (N=493)	Prior Eculizumab Treatment[c] (N=278)	Without Prior Eculizumab Treatment[d] (N=152)	Prior Eculizumab Treatment Unknown (N=63)
Injury, poisoning and procedural complications, n (%)	1 (8.3)	0 (0.0)	1 (12.5)	0 (0.0)
Lung infection, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Neoplasms benign, malignant and unspecified (incl cysts and polyps), n (%)	3 (25.0)	1 (25.0)	2 (25.0)	0 (0.0)
Nervous system disorders, n (%)	1 (8.3)	1 (25.0)	0 (0.0)	0 (0.0)
Psychiatric disorders, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Renal and urinary disorders, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Respiratory, thoracic and mediastinal disorders, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Vascular disorder, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

Note: The percentages are the percent of all death reported in the registry.
(a) Includes patients actively enrolled in the registry during the analysis period, which covers the time period from 06JAN2023 to 06JAN2025.
(b) Patients were classified into the Prior Eculizumab Treatment Unknown group due to unknown prior eculizumab treatment history or because of a missing eculizumab discontinuation date.
(c) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. There were 24 patients who discontinued eculizumab between 17 and 28 days of ravulizumab initiation.
(d) Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.

Source: ADAM.ADSL, ADAM.ADPOP
Run Date: 2025-05-14T14:52:18
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ravuema202501/Files/tables/production/programs/t7_death_dur.sas

Table 8
History of Medical Events at Ultomiris Initiation, by Treatment Status
Ravulizumab Study Population

	All Ravulizumab Patients[a] (N=532)	Prior Eculizumab Treatment[b] (N=301)	Without Prior Eculizumab Treatment[c] (N=161)	Prior Eculizumab Treatment Unknown (N=70)
History of bone marrow disorder, n (%)				
n	517	296	156	65
No	288 (55.7)	171 (57.8)	80 (51.3)	37 (56.9)
Yes	229 (44.3)	125 (42.2)	76 (48.7)	28 (43.1)
Ongoing at ravulizumab initiation	169 (73.8)	85 (68.0)	62 (81.6)	22 (78.6)
Resolved prior to ravulizumab initiation	60 (26.2)	40 (32.0)	14 (18.4)	6 (21.4)
History of bone marrow disorder – aplastic or hypoplastic anemia, n (%)				
n	515	294	156	65
No	322 (62.5)	192 (65.3)	88 (56.4)	42 (64.6)
Yes	193 (37.5)	102 (34.7)	68 (43.6)	23 (35.4)
Ongoing at ravulizumab initiation	143 (74.1)	71 (69.6)	55 (80.9)	17 (73.9)
Resolved prior to ravulizumab initiation	50 (25.9)	31 (30.4)	13 (19.1)	6 (26.1)
History of bone marrow disorder – MDS, n (%)				

Note: MAVE = major adverse vascular event; MDS = myelodysplastic syndromes; TE = thrombotic event.
(a) Patients were classified into the Prior Eculizumab Treatment Unknown group due to unknown prior eculizumab treatment history or because of a missing eculizumab discontinuation date.
(b) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. There were 27 patients who discontinued eculizumab between 17 and 28 days of ravulizumab initiation. Medical history reported at the time of eculizumab initiation.
(c) Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation. Medical history reported at the time of eculizumab initiation.

Source: ADAM.ADSL, ADAM.ADPOP, ADAM.ADMESUM
Run Date: 2025-05-14T14:52:27
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ravuema202501/Files/tables/production/programs/t8_medhis.sas

Table 8
History of Medical Events at Ultomiris Initiation, by Treatment Status
Ravulizumab Study Population

	All Ravulizumab Patients[a] (N=532)	Prior Eculizumab Treatment[b] (N=301)	Without Prior Eculizumab Treatment[c] (N=161)	Prior Eculizumab Treatment Unknown (N=70)
n	509	292	153	64
No	486 (95.5)	280 (95.9)	146 (95.4)	60 (93.8)
Yes	23 (4.5)	12 (4.1)	7 (4.6)	4 (6.3)
Ongoing at ravulizumab initiation	19 (82.6)	9 (75.0)	6 (85.7)	4 (100.0)
Resolved prior to ravulizumab initiation	4 (17.4)	3 (25.0)	1 (14.3)	0 (0.0)
History of bone marrow disorder – other, n (%)				
n	509	293	152	64
No	479 (94.1)	275 (93.9)	143 (94.1)	61 (95.3)
Yes	30 (5.9)	18 (6.1)	9 (5.9)	3 (4.7)
Ongoing at ravulizumab initiation	17 (56.7)	9 (50.0)	5 (55.6)	3 (100.0)
Resolved prior to ravulizumab initiation	13 (43.3)	9 (50.0)	4 (44.4)	0 (0.0)
History of MAVE, n (%)				
n	521	296	158	67
No	374 (71.8)	213 (72.0)	115 (72.8)	46 (68.7)

Note: MAVE = major adverse vascular event; MDS = myelodysplastic syndromes; TE = thrombotic event.
(a) Patients were classified into the Prior Eculizumab Treatment Unknown group due to unknown prior eculizumab treatment history or because of a missing eculizumab discontinuation date.
(b) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. There were 27 patients who discontinued eculizumab between 17 and 28 days of ravulizumab initiation. Medical history reported at the time of eculizumab initiation.
(c) Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation. Medical history reported at the time of eculizumab initiation.

Source: ADAM.ADSL, ADAM.ADPOP, ADAM.ADMESUM
Run Date: 2025-05-14T14:52:27
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ravuema202501/Files/tables/production/programs/t8_medhis.sas

Table 8
History of Medical Events at Ultomiris Initiation, by Treatment Status
Ravulizumab Study Population

	All Ravulizumab Patients[a] (N=532)	Prior Eculizumab Treatment[b] (N=301)	Without Prior Eculizumab Treatment[c] (N=161)	Prior Eculizumab Treatment Unknown (N=70)
Yes	147 (28.2)	83 (28.0)	43 (27.2)	21 (31.3)
History of TE, n (%)				
n	519	295	157	67
No	400 (77.1)	229 (77.6)	122 (77.7)	49 (73.1)
Yes	119 (22.9)	66 (22.4)	35 (22.3)	18 (26.9)
History of non-TE MAVE, n (%)				
n	518	294	157	67
No	475 (91.7)	269 (91.5)	144 (91.7)	62 (92.5)
Yes	43 (8.3)	25 (8.5)	13 (8.3)	5 (7.5)
History of impaired renal function, n (%)				
n	512	293	154	65
No	436 (85.2)	247 (84.3)	132 (85.7)	57 (87.7)
Yes	76 (14.8)	46 (15.7)	22 (14.3)	8 (12.3)

Note: MAVE = major adverse vascular event; MDS = myelodysplastic syndromes; TE = thrombotic event.
(a) Patients were classified into the Prior Eculizumab Treatment Unknown group due to unknown prior eculizumab treatment history or because of a missing eculizumab discontinuation date.
(b) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. There were 27 patients who discontinued eculizumab between 17 and 28 days of ravulizumab initiation. Medical history reported at the time of eculizumab initiation.
(c) Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation. Medical history reported at the time of eculizumab initiation.

Source: ADAM.ADSL, ADAM.ADPOP, ADAM.ADMESUM
Run Date: 2025-05-14T14:52:27
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ravuema202501/Files/tables/production/programs/t8_medhis.sas

Table 8
History of Medical Events at Ultomiris Initiation, by Treatment Status
Ravulizumab Study Population

	All Ravulizumab Patients[a] (N=532)	Prior Eculizumab Treatment[b] (N=301)	Without Prior Eculizumab Treatment[c] (N=161)	Prior Eculizumab Treatment Unknown (N=70)
History of impaired hepatic function, n (%)				
n	512	293	154	65
No	491 (95.9)	276 (94.2)	153 (99.4)	62 (95.4)
Yes	21 (4.1)	17 (5.8)	1 (0.6)	3 (4.6)
History of pulmonary hypertension, n (%)				
n	512	293	154	65
No	486 (94.9)	276 (94.2)	149 (96.8)	61 (93.8)
Yes	26 (5.1)	17 (5.8)	5 (3.2)	4 (6.2)
History of malignancy, n (%)				
n	520	296	157	67
No	454 (87.3)	265 (89.5)	130 (82.8)	59 (88.1)
Yes	66 (12.7)	31 (10.5)	27 (17.2)	8 (11.9)

Note: MAVE = major adverse vascular event; MDS = myelodysplastic syndromes; TE = thrombotic event.
(a) Patients were classified into the Prior Eculizumab Treatment Unknown group due to unknown prior eculizumab treatment history or because of a missing eculizumab discontinuation date.
(b) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. There were 27 patients who discontinued eculizumab between 17 and 28 days of ravulizumab initiation. Medical history reported at the time of eculizumab initiation.
(c) Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation. Medical history reported at the time of eculizumab initiation.

Source: ADAM.ADSL, ADAM.ADPOP, ADAM.ADMESUM
Run Date: 2025-05-14T14:52:27
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ravuema202501/Files/tables/production/programs/t8_medhis.sas

Table 8
History of Medical Events at Ultomiris Initiation, by Treatment Status
Ravulizumab Study Population

	All Ravulizumab Patients[a] (N=532)	Prior Eculizumab Treatment[b] (N=301)	Without Prior Eculizumab Treatment[c] (N=161)	Prior Eculizumab Treatment Unknown (N=70)
History of infection, n (%)				
n	514	294	154	66
No	407 (79.2)	242 (82.3)	113 (73.4)	52 (78.8)
Yes	107 (20.8)	52 (17.7)	41 (26.6)	14 (21.2)
History of pregnancy (female only), n (%)				
n	147	84	42	21
No	25 (17.0)	9 (10.7)	15 (35.7)	1 (4.8)
Yes	122 (83.0)	75 (89.3)	27 (64.3)	20 (95.2)
History of patient's partner pregnancy (male only), n (%)				
n	0	0	0	0
No	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Yes	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

Note: MAVE = major adverse vascular event; MDS = myelodysplastic syndromes; TE = thrombotic event.
(a) Patients were classified into the Prior Eculizumab Treatment Unknown group due to unknown prior eculizumab treatment history or because of a missing eculizumab discontinuation date.
(b) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. There were 27 patients who discontinued eculizumab between 17 and 28 days of ravulizumab initiation. Medical history reported at the time of eculizumab initiation.
(c) Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation. Medical history reported at the time of eculizumab initiation.

Source: ADAM.ADSL, ADAM.ADPOP, ADAM.ADMESUM
Run Date: 2025-05-14T14:52:27
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ravuema202501/Files/tables/production/programs/t8_medhis.sas

Table 9
History of Concomitant Medication Use at Ultomiris Initiation, by Treatment Status
Ravulizumab Study Population

	All Ravulizumab Patients[a] (N=532)	Prior Eculizumab Treatment[b] (N=301)	Without Prior Eculizumab Treatment[c] (N=161)	Prior Eculizumab Treatment Unknown (N=70)
RBC transfusions, n (%)				
n	523	296	158	69
No	443 (84.7)	258 (87.2)	125 (79.1)	60 (87.0)
Yes	80 (15.3)	38 (12.8)	33 (20.9)	9 (13.0)
Anticoagulation therapy - heparin or warfarin, n (%)				
n	405	229	124	52
No	269 (66.4)	152 (66.4)	91 (73.4)	26 (50.0)
Yes	136 (33.6)	77 (33.6)	33 (26.6)	26 (50.0)
Immunosuppressant therapy - cyclosporine or ATG, n (%)				
n	413	227	141	45
No	330 (79.9)	180 (79.3)	111 (78.7)	39 (86.7)
Yes	83 (20.1)	47 (20.7)	30 (21.3)	6 (13.3)
Immunosuppressant therapy - corticosteroids, n (%)				
n	398	223	128	47

Note: ATG = anti-thymocyte globulin; RBC = red blood cell.
Data shown are reported in the 6 months prior to the timepoint.
(a) Patients were classified into the Prior Eculizumab Treatment Unknown group due to unknown prior eculizumab treatment history or because of a missing eculizumab discontinuation date.
(b) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. There were 27 patients who discontinued eculizumab between 17 and 28 days of ravulizumab initiation.
(c) Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.

Source: ADAM.ADSL, ADAM.ADPOP, ADAM.ADCMSUM, ADAM.ADRBCSUM
Run Date: 2025-05-14T14:52:30
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ravuema202501/Files/tables/production/programs/t9_cmhis.sas

Table 9
History of Concomitant Medication Use at Ultomiris Initiation, by Treatment Status
Ravulizumab Study Population

	All Ravulizumab Patients[a] (N=532)	Prior Eculizumab Treatment[b] (N=301)	Without Prior Eculizumab Treatment[c] (N=161)	Prior Eculizumab Treatment Unknown (N=70)
No	326 (81.9)	179 (80.3)	109 (85.2)	38 (80.9)
Yes	72 (18.1)	44 (19.7)	19 (14.8)	9 (19.1)
Any pain medication, n (%)				
n	370	204	122	44
No	309 (83.5)	165 (80.9)	112 (91.8)	32 (72.7)
Yes	61 (16.5)	39 (19.1)	10 (8.2)	12 (27.3)
Any opioids pain medication, n (%)				
n	359	199	118	42
No	328 (91.4)	179 (89.9)	114 (96.6)	35 (83.3)
Yes	31 (8.6)	20 (10.1)	4 (3.4)	7 (16.7)
Any non-opioids pain medication, n (%)				
n	360	198	120	42
No	318 (88.3)	170 (85.9)	112 (93.3)	36 (85.7)
Yes	42 (11.7)	28 (14.1)	8 (6.7)	6 (14.3)

Note: ATG = anti-thymocyte globulin; RBC = red blood cell.
Data shown are reported in the 6 months prior to the timepoint.
(a) Patients were classified into the Prior Eculizumab Treatment Unknown group due to unknown prior eculizumab treatment history or because of a missing eculizumab discontinuation date.
(b) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. There were 27 patients who discontinued eculizumab between 17 and 28 days of ravulizumab initiation.
(c) Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.

Source: ADAM.ADSL, ADAM.ADPOP, ADAM.ADCMSUM, ADAM.ADRBCSUM
Run Date: 2025-05-14T14:52:30
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ravuema202501/Files/tables/production/programs/t9_cmhis.sas

Table 9
History of Concomitant Medication Use at Ultomiris Initiation, by Treatment Status
Ravulizumab Study Population

	All Ravulizumab Patients[a] (N=532)	Prior Eculizumab Treatment[b] (N=301)	Without Prior Eculizumab Treatment[c] (N=161)	Prior Eculizumab Treatment Unknown (N=70)
Any oral prophylactic antibiotics, n (%)				
n	423	234	138	51
No	197 (46.6)	102 (43.6)	69 (50.0)	26 (51.0)
Yes	226 (53.4)	132 (56.4)	69 (50.0)	25 (49.0)

Note: ATG = anti-thymocyte globulin; RBC = red blood cell.
Data shown are reported in the 6 months prior to the timepoint.
(a) Patients were classified into the Prior Eculizumab Treatment Unknown group due to unknown prior eculizumab treatment history or because of a missing eculizumab discontinuation date.
(b) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. There were 27 patients who discontinued eculizumab between 17 and 28 days of ravulizumab initiation.
(c) Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.

Source: ADAM.ADSL, ADAM.ADPOP, ADAM.ADCMSUM, ADAM.ADRBCSUM
Run Date: 2025-05-14T14:52:30
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ravuema202501/Files/tables/production/programs/t9_cmhis.sas

Table 10
Laboratory Values at Ultomiris Initiation, by Treatment Status
Ravulizumab Study Population

	All Ravulizumab Patients[a] (N=532)	Prior Eculizumab Treatment[b] (N=301)	Without Prior Eculizumab Treatment[c] (N=161)	Prior Eculizumab Treatment Unknown (N=70)
Percent GPI-deficient granulocytes				
n	280	150	94	36
Mean (SD)	76.7 (26.34)	79.0 (26.73)	73.8 (24.65)	74.6 (28.68)
Median (Q1, Q3)	89.1 (61.4, 97.9)	92.8 (67.7, 98.2)	81.3 (58.3, 94.5)	88.8 (60.6, 98.3)
Percent GPI-deficient granulocytes, n (%)				
n	280	150	94	36
<1%	1 (0.4)	1 (0.7)	0 (0.0)	0 (0.0)
≥1% to <10%	3 (1.1)	3 (2.0)	0 (0.0)	0 (0.0)
≥10% to <50%	51 (18.2)	23 (15.3)	21 (22.3)	7 (19.4)
≥50%	225 (80.4)	123 (82.0)	73 (77.7)	29 (80.6)

Note: eGFR = estimated glomerular filtration rate; GPI = glycophosphatidylinositol; LDH = lactate dehydrogenase; Q1 = first quartile; Q3 = third quartile; SD = standard deviation; ULN = upper limit of normal; RBC = red blood cells; WBC = white blood cells.
Data shown are reported in the 6 months prior to the timepoint
(a) Patients were classified into the Prior Eculizumab Treatment Unknown group due to unknown prior eculizumab treatment history or because of a missing eculizumab discontinuation date.
(b) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. There were 27 patients who discontinued eculizumab between 17 and 28 days of ravulizumab initiation.
(c) Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.

Source: ADAM.ADSL, ADAM.ADLBSUM, ADAM.ADPOP
Run Date: 2025-05-14T14:52:58
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ravuema202501/Files/tables/production/programs/t10_labhis.sas

Table 10
Laboratory Values at Ultomiris Initiation, by Treatment Status
Ravulizumab Study Population

	All Ravulizumab Patients[a] (N=532)	Prior Eculizumab Treatment[b] (N=301)	Without Prior Eculizumab Treatment[c] (N=161)	Prior Eculizumab Treatment Unknown (N=70)
Percent GPI-deficient erythrocytes				
n	246	134	84	28
Mean (SD)	51.4 (32.15)	59.3 (31.58)	41.3 (29.45)	44.0 (33.40)
Median (Q1, Q3)	47.5 (19.8, 84.3)	61.5 (31.5, 89.9)	30.4 (16.0, 63.0)	30.6 (14.0, 80.3)
Percent GPI-deficient erythrocytes, n (%)				
n	246	134	84	28
<10%	16 (6.5)	7 (5.2)	7 (8.3)	2 (7.1)
≥10%	230 (93.5)	127 (94.8)	77 (91.7)	26 (92.9)
LDH (U/L)				
n	410	228	130	52

Note: eGFR = estimated glomerular filtration rate; GPI = glycophosphatidylinositol; LDH = lactate dehydrogenase; Q1 = first quartile; Q3 = third quartile; SD = standard deviation; ULN = upper limit of normal; RBC = red blood cells; WBC = white blood cells.
Data shown are reported in the 6 months prior to the timepoint
(a) Patients were classified into the Prior Eculizumab Treatment Unknown group due to unknown prior eculizumab treatment history or because of a missing eculizumab discontinuation date.
(b) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. There were 27 patients who discontinued eculizumab between 17 and 28 days of ravulizumab initiation.
(c) Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.

Source: ADAM.ADSL, ADAM.ADLBSUM, ADAM.ADPOP
Run Date: 2025-05-14T14:52:58
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ravuema202501/Files/tables/production/programs/t10_labhis.sas

Table 10
Laboratory Values at Ultomiris Initiation, by Treatment Status
Ravulizumab Study Population

	All Ravulizumab Patients[a] (N=532)	Prior Eculizumab Treatment[b] (N=301)	Without Prior Eculizumab Treatment[c] (N=161)	Prior Eculizumab Treatment Unknown (N=70)
Mean (SD)	441.1 (489.46)	327.6 (214.46)	608.8 (716.23)	519.2 (532.52)
Median (Q1, Q3)	273.0 (223.0, 432.0)	264.0 (223.0, 370.5)	301.5 (225.0, 730.0)	307.0 (225.0, 595.0)
LDH ratio (x ULN)				
n	385	216	121	48
Mean (SD)	1.8 (2.11)	1.2 (0.89)	2.5 (3.05)	2.2 (2.42)
Median (Q1, Q3)	1.1 (0.9, 1.4)	1.0 (0.9, 1.2)	1.2 (0.9, 2.7)	1.2 (0.9, 2.4)
LDH ratio (x ULN), n (%)				
n	385	216	121	48
<1.5	298 (77.4)	188 (87.0)	77 (63.6)	33 (68.8)
≥1.5	87 (22.6)	28 (13.0)	44 (36.4)	15 (31.3)

Note: eGFR = estimated glomerular filtration rate; GPI = glycophosphatidylinositol; LDH = lactate dehydrogenase; Q1 = first quartile; Q3 = third quartile; SD = standard deviation; ULN = upper limit of normal; RBC = red blood cells; WBC = white blood cells.
Data shown are reported in the 6 months prior to the timepoint
(a) Patients were classified into the Prior Eculizumab Treatment Unknown group due to unknown prior eculizumab treatment history or because of a missing eculizumab discontinuation date.
(b) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. There were 27 patients who discontinued eculizumab between 17 and 28 days of ravulizumab initiation.
(c) Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.

Source: ADAM.ADSL, ADAM.ADLBSUM, ADAM.ADPOP
Run Date: 2025-05-14T14:52:58
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ravuema202501/Files/tables/production/programs/t10_labhis.sas

Table 10
Laboratory Values at Ultomiris Initiation, by Treatment Status
Ravulizumab Study Population

	All Ravulizumab Patients[a] (N=532)	Prior Eculizumab Treatment[b] (N=301)	Without Prior Eculizumab Treatment[c] (N=161)	Prior Eculizumab Treatment Unknown (N=70)
Hemoglobin (g/dL)				
n	402	213	131	58
Mean (SD)	10.9 (2.03)	11.1 (2.01)	10.9 (2.08)	10.5 (1.97)
Median (Q1, Q3)	10.8 (9.5, 12.3)	10.9 (9.6, 12.4)	10.8 (9.3, 12.3)	10.6 (9.0, 11.9)
Haptoglobin (umol/L)				
n	42	24	15	3
Mean (SD)	0.4 (0.41)	0.4 (0.44)	0.4 (0.38)	0.2 (0.06)
Median (Q1, Q3)	0.3 (0.1, 0.7)	0.4 (0.1, 0.7)	0.2 (0.1, 0.6)	0.1 (0.1, 0.2)
Platelets ($x10^9$/L)				
n	449	249	139	61
Mean (SD)	146.2 (65.67)	151.7 (65.04)	135.8 (61.15)	147.3 (75.74)

Note: eGFR = estimated glomerular filtration rate; GPI = glycophosphatidylinositol; LDH = lactate dehydrogenase; Q1 = first quartile; Q3 = third quartile; SD = standard deviation; ULN = upper limit of normal; RBC = red blood cells; WBC = white blood cells.
Data shown are reported in the 6 months prior to the timepoint
(a) Patients were classified into the Prior Eculizumab Treatment Unknown group due to unknown prior eculizumab treatment history or because of a missing eculizumab discontinuation date.
(b) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. There were 27 patients who discontinued eculizumab between 17 and 28 days of ravulizumab initiation.
(c) Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.

Source: ADAM.ADSL, ADAM.ADLBSUM, ADAM.ADPOP
Run Date: 2025-05-14T14:52:58
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ravuema202501/Files/tables/production/programs/t10_labhis.sas

Table 10
Laboratory Values at Ultomiris Initiation, by Treatment Status
Ravulizumab Study Population

	All Ravulizumab Patients[a] (N=532)	Prior Eculizumab Treatment[b] (N=301)	Without Prior Eculizumab Treatment[c] (N=161)	Prior Eculizumab Treatment Unknown (N=70)
Median (Q1, Q3)	139.0 (104.0, 185.0)	145.0 (112.0, 190.0)	129.0 (100.0, 172.0)	125.0 (101.0, 185.0)
Serum creatinine (umol/L)				
n	421	230	132	59
Mean (SD)	78.3 (34.03)	78.8 (30.61)	73.9 (21.99)	86.4 (59.02)
Median (Q1, Q3)	70.7 (61.0, 88.4)	72.2 (61.0, 88.4)	70.4 (59.6, 84.9)	73.0 (61.9, 91.0)
eGFR (mL/min)				
n	420	230	131	59
Mean (SD)	92.5 (25.56)	92.5 (26.27)	93.3 (22.83)	91.0 (28.70)
Median (Q1, Q3)	96.5 (76.7, 111.4)	98.2 (76.7, 113.1)	95.3 (78.6, 111.0)	96.7 (73.1, 107.5)
eGFR (mL/min), n (%)				

Note: eGFR = estimated glomerular filtration rate; GPI = glycophosphatidylinositol; LDH = lactate dehydrogenase; Q1 = first quartile; Q3 = third quartile; SD = standard deviation; ULN = upper limit of normal; RBC = red blood cells; WBC = white blood cells.
Data shown are reported in the 6 months prior to the timepoint
(a) Patients were classified into the Prior Eculizumab Treatment Unknown group due to unknown prior eculizumab treatment history or because of a missing eculizumab discontinuation date.
(b) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. There were 27 patients who discontinued eculizumab between 17 and 28 days of ravulizumab initiation.
(c) Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.

Source: ADAM.ADSL, ADAM.ADLBSUM, ADAM.ADPOP
Run Date: 2025-05-14T14:52:58
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ravuema202501/Files/tables/production/programs/t10_labhis.sas

Table 10
Laboratory Values at Ultomiris Initiation, by Treatment Status
Ravulizumab Study Population

	All Ravulizumab Patients[a] (N=532)	Prior Eculizumab Treatment[b] (N=301)	Without Prior Eculizumab Treatment[c] (N=161)	Prior Eculizumab Treatment Unknown (N=70)
n	420	230	131	59
<30	7 (1.7)	5 (2.2)	0 (0.0)	2 (3.4)
30 to <60	49 (11.7)	28 (12.2)	15 (11.5)	6 (10.2)
60 to <90	119 (28.3)	65 (28.3)	40 (30.5)	14 (23.7)
≥90	245 (58.3)	132 (57.4)	76 (58.0)	37 (62.7)
Absolute neutrophils (/uL)				
n	429	237	135	57
Mean (SD)	2238.7 (1250.95)	2209.0 (1199.74)	2253.0 (1177.67)	2328.1 (1601.01)
Median (Q1, Q3)	2040.0 (1470.0, 2800.0)	2040.0 (1460.0, 2840.0)	2040.0 (1460.0, 2700.0)	2090.0 (1540.0, 2700.0)
Absolute reticulocytes (x10^9/L)				
n	349	188	112	49

Note: eGFR = estimated glomerular filtration rate; GPI = glycophosphatidylinositol; LDH = lactate dehydrogenase; Q1 = first quartile; Q3 = third quartile; SD = standard deviation; ULN = upper limit of normal; RBC = red blood cells; WBC = white blood cells.
Data shown are reported in the 6 months prior to the timepoint
(a) Patients were classified into the Prior Eculizumab Treatment Unknown group due to unknown prior eculizumab treatment history or because of a missing eculizumab discontinuation date.
(b) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. There were 27 patients who discontinued eculizumab between 17 and 28 days of ravulizumab initiation.
(c) Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.

Source: ADAM.ADSL, ADAM.ADLBSUM, ADAM.ADPOP
Run Date: 2025-05-14T14:52:58
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ravuema202501/Files/tables/production/programs/t10_labhis.sas

Table 10
Laboratory Values at Ultomiris Initiation, by Treatment Status
Ravulizumab Study Population

	All Ravulizumab Patients[a] (N=532)	Prior Eculizumab Treatment[b] (N=301)	Without Prior Eculizumab Treatment[c] (N=161)	Prior Eculizumab Treatment Unknown (N=70)
Mean (SD)	160.3 (83.87)	168.5 (85.41)	145.1 (75.11)	163.8 (93.38)
Median (Q1, Q3)	155.4 (99.4, 209.0)	165.5 (100.1, 226.5)	131.2 (91.8, 185.8)	171.3 (104.0, 209.0)
Total RBC ($x10^{12}$/L)				
n	429	234	136	59
Mean (SD)	3.2 (0.67)	3.2 (0.65)	3.2 (0.65)	3.1 (0.83)
Median (Q1, Q3)	3.1 (2.7, 3.6)	3.1 (2.7, 3.7)	3.2 (2.8, 3.7)	3.0 (2.5, 3.5)
Total WBC ($x10^{9}$/L)				
n	447	248	138	61
Mean (SD)	3.9 (1.65)	3.9 (1.62)	4.0 (1.52)	3.9 (2.03)
Median (Q1, Q3)	3.7 (3.0, 4.7)	3.7 (3.0, 4.8)	3.7 (3.1, 4.7)	3.7 (3.0, 4.7)

Note: eGFR = estimated glomerular filtration rate; GPI = glycophosphatidylinositol; LDH = lactate dehydrogenase; Q1 = first quartile; Q3 = third quartile; SD = standard deviation; ULN = upper limit of normal; RBC = red blood cells; WBC = white blood cells.
Data shown are reported in the 6 months prior to the timepoint
(a) Patients were classified into the Prior Eculizumab Treatment Unknown group due to unknown prior eculizumab treatment history or because of a missing eculizumab discontinuation date.
(b) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. There were 27 patients who discontinued eculizumab between 17 and 28 days of ravulizumab initiation.
(c) Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.

Source: ADAM.ADSL, ADAM.ADLBSUM, ADAM.ADPOP
Run Date: 2025-05-14T14:52:58
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ravuema202501/Files/tables/production/programs/t10_labhis.sas

Table 11.1
Rates of Major Adverse Vascular Events, Cumulative and by Exposure Period
Study Population

	Patients with Untreated Person Time (N=252)	Treated with Eculizumab (Prior to Ravulizumab Switch) (N=301)	Treated with Ravulizumab (N=532)	Treated with Eculizumab Only (N=713)
All patients				
Total patients at risk	252	299	525	711
Number of patients with events	22	19	5	31
Incidence (percent of population at risk, %)	8.7	6.4	1.0	4.4
Number of events	26	19	6	36
Person-years	609.7	2181.6	1155.4	3258.0
Rate per 100 person-years	4.3	0.9	0.5	1.1
Estimated rate per 100 person-years[a]	4.3	0.9	0.5	1.1
95% CI	(2.9, 6.3)	(0.6, 1.4)	(0.2, 1.2)	(0.8, 1.5)

Notes: CI = confidence interval.
(a) Poisson regression estimate of incidence density.

Source: ADAM.ADSL, ADAM.ADPOP, ADAM.ADTTE
Run Date: 2025-05-14T14:53:36
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ravuema202501/Files/tables/production/programs/t11_mave_cum.sas

Table 11.1.1
Rates of Thrombotic Events, Cumulative and by Exposure Period
Study Population

	Patients with Untreated Person Time (N=252)	Treated with Eculizumab (Prior to Ravulizumab Switch) (N=301)	Treated with Ravulizumab (N=532)	Treated with Eculizumab Only (N=713)
All patients				
Total patients at risk	252	299	525	711
Number of patients with events	16	15	3	19
Incidence (percent of population at risk, %)	6.3	5.0	0.6	2.7
Number of events	18	15	4	21
Person-years	609.7	2181.6	1155.4	3258.0
Rate per 100 person-years	3.0	0.7	0.3	0.6
Estimated rate per 100 person-years[a]	3.0	0.7	0.3	0.6
95% CI	(1.9, 4.7)	(0.4, 1.1)	(0.1, 0.9)	(0.4, 1.0)

Notes: CI = confidence interval.
(a) Poisson regression estimate of incidence density.

Source: ADAM.ADSL, ADAM.ADPOP, ADAM.ADTTE
Run Date: 2025-05-14T14:53:07
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ravuema202501/Files/tables/production/programs/t11_1_te_cum.sas

Table 11.1.2
Adjusted Rates of Thrombotic Events, Cumulative and by Exposure Period
Study Population

	Patients with Untreated Person Time (N=252)	Treated with Eculizumab (Prior to Ravulizumab Switch) (N=301)	Treated with Ravulizumab (N=532)	Treated with Eculizumab Only (N=713)
All patients				
Total patients at risk	252	299	525	711
Number of patients with events	16	15	3	19
Incidence (percent of population at risk, %)	6.3	5.0	0.6	2.7
Number of events	18	15	4	21
Person-years	609.7	2181.6	1155.4	3258.0
Rate per 100 person-years	3.0	0.7	0.3	0.6
Adjusted rate per 100 person-years[a]	4.2	0.7	0.5	0.7
95% CI	(2.4, 7.1)	(0.3, 1.3)	(0.2, 1.4)	(0.4, 1.2)

Notes: CI = confidence interval.
(a) Poisson regression estimate of incidence density. The adjusted multivariable regression model includes the following covariates: age at baseline, gender, LDH at baseline, and history of MAVEs at baseline.
(b) Baseline is defined as the enrollment date for 'patients with untreated person time' and the ravulizumab treatment initiation date for patients in 'treated with ravulizumab' group. For patients included in the group of 'treated with eculizumab (prior to ravulizumab switch)' and 'treated with eculizumab only', baseline is the eculizumab treatment initiation date.

Source: ADAM.ADSL, ADAM.ADPOP, ADAM.ADMESUM, ADAM.ADLBSUM
Run Date: 2025-05-14T14:53:00
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ravuema202501/Files/tables/production/programs/t11_1_te_cum_adj.sas

Table 11.1.3
Rates of Thrombotic Events, During the Analysis Period and by Exposure Period[a]
Study Population

	Patients with Untreated Person Time (N=239)	Treated with Eculizumab (Prior to Ravulizumab Switch) (N=278)	Treated with Ravulizumab (N=493)	Treated with Eculizumab Only (N=104)
All patients				
Total patients at risk	23	14	452	78
Number of patients with events	1	0	1	0
Incidence (percent of population at risk, %)	4.3	0.0	0.2	0.0
Number of events	1	0	2	0
Person-years	9.7	5.6	500.0	86.2
Rate per 100 person-years	10.3	0.0	0.4	0.0
Estimated rate per 100 person-years[b]	10.3	n/a	0.4	n/a
95% CI	(1.5, 73.4)	(n/a)	(0.1, 1.6)	(n/a)

Notes: CI = confidence interval.
(a) The analysis period is from 06JAN2023 to 06JAN2025.
(b) Poisson regression estimate of incidence density.

Source: ADAM.ADSL, ADAM.ADPOP, ADAM.ADTTE
Run Date: 2025-05-14T14:53:09
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ravuema202501/Files/tables/production/programs/t11_1_te_dur.sas

Table 11.1.4
Sensitivity Analysis - Rates of Thrombotic Events, Cumulative and by Exposure Period
Study Population with clone size >= 1%

	Patients with Untreated Person Time (N=200)	Treated with Eculizumab (Prior to Ravulizumab Switch) (N=224)	Treated with Ravulizumab (N=392)	Treated with Eculizumab Only (N=524)
All patients				
Total patients at risk	200	223	387	523
Number of patients with events	12	8	2	12
Incidence (percent of population at risk, %)	6.0	3.6	0.5	2.3
Number of events	14	8	2	13
Person-years	450.2	1478.6	834.9	2358.4
Rate per 100 person-years	3.1	0.5	0.2	0.6
Estimated rate per 100 person-years[a]	3.1	0.5	0.2	0.6
95% CI	(1.8, 5.3)	(0.3, 1.1)	(0.1, 1.0)	(0.3, 0.9)

Notes: CI = confidence interval.
(a) Poisson regression estimate of incidence density.

Source: ADAM.ADSL, ADAM.ADPOP, ADAM.ADTTE, ADAM.ADLBSUM
Run Date: 2025-05-14T14:53:04
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ravuema202501/Files/tables/production/programs/t11_1_te_cum_sen.sas

Table 11.2
Adjusted Rates of Major Adverse Vascular Events, Cumulative and by Exposure Period[a]
Study Population

	Patients with Untreated Person Time (N=252)	Treated with Eculizumab (Prior to Ravulizumab Switch) (N=301)	Treated with Ravulizumab (N=532)	Treated with Eculizumab Only (N=713)
All patients				
Total patients at risk	252	299	525	711
Number of patients with events	22	19	5	31
Incidence (percent of population at risk, %)	8.7	6.4	1.0	4.4
Number of events	26	19	6	36
Person-years	609.7	2181.6	1155.4	3258.0
Rate per 100 person-years	4.3	0.9	0.5	1.1
Adjusted rate per 100 person-years[a]	5.9	0.8	0.8	1.1
95% CI	(3.7, 9.2)	(0.4, 1.5)	(0.4, 1.9)	(0.7, 1.6)

Note: CI = confidence interval.
(a) Poisson regression estimate of incidence density. The adjusted multivariable regression model includes the following covariates: age at baseline, gender, LDH at baseline, and history of MAVEs at baseline.
(b) Baseline is defined as the enrollment date for 'patients with untreated person time' and the ravulizumab treatment initiation date for patients in 'treated with ravulizumab' group. For patients included in the group of 'treated with eculizumab (prior to ravulizumab switch)' and 'treated with eculizumab only', baseline is the eculizumab treatment initiation date.

Source: ADAM.ADSL, ADAM.ADPOP, ADAM.ADMESUM, ADAM.ADLBSUM
Run Date: 2025-05-14T14:53:19
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ravuema202501/Files/tables/production/programs/t11_mave_cum_adj.sas

Table 11.2.1
Rates of Non-Thrombotic Major Adverse Vascular Events, Cumulative and by Exposure Period
Study Population

	Patients with Untreated Person Time (N=252)	Treated with Eculizumab (Prior to Ravulizumab Switch) (N=301)	Treated with Ravulizumab (N=532)	Treated with Eculizumab Only (N=713)
All patients				
Total patients at risk	252	299	525	711
Number of patients with events	7	4	2	13
Incidence (percent of population at risk, %)	2.8	1.3	0.4	1.8
Number of events	8	4	2	15
Person-years	609.7	2181.6	1155.4	3258.0
Rate per 100 person-years	1.3	0.2	0.2	0.5
Estimated rate per 100 person-years[a]	1.3	0.2	0.2	0.5
95% CI	(0.7, 2.6)	(0.1, 0.5)	(0.0, 0.7)	(0.3, 0.8)

Notes: CI = confidence interval.
(a) Poisson regression estimate of incidence density.

Source: ADAM.ADSL, ADAM.ADPOP, ADAM.ADTTE
Run Date: 2025-05-14T14:53:16
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ravuema202501/Files/tables/production/programs/t11_2_nontemave_cum.sas

Table 11.2.2
Adjusted Rates of Non-Thrombotic Major Adverse Vascular Events, Cumulative and by Exposure Period
Study Population

	Patients with Untreated Person Time (N=252)	Treated with Eculizumab (Prior to Ravulizumab Switch) (N=301)	Treated with Ravulizumab (N=532)	Treated with Eculizumab Only (N=713)
All patients				
Total patients at risk	252	299	525	711
Number of patients with events	7	4	2	13
Incidence (percent of population at risk, %)	2.8	1.3	0.4	1.8
Number of events	8	4	2	15
Person-years	609.7	2181.6	1155.4	3258.0
Rate per 100 person-years	1.3	0.2	0.2	0.5
Adjusted rate per 100 person-years[a]	1.7	0.1	0.3	0.4
95% CI	(0.7, 3.9)	(0.0, 0.5)	(0.1, 1.3)	(0.2, 0.7)

Notes: CI = confidence interval.
(a) Poisson regression estimate of incidence density. The adjusted multivariable regression model includes the following covariates: age at baseline, gender, LDH at baseline, and history of MAVEs at baseline.
(b) Baseline is defined as the enrollment date for 'patients with untreated person time' and the ravulizumab treatment initiation date for patients in 'treated with ravulizumab' group. For patients included in the group of 'treated with eculizumab (prior to ravulizumab switch)' and 'treated with eculizumab only', baseline is the eculizumab treatment initiation date.

Source: ADAM.ADSL, ADAM.ADPOP, ADAM.ADMESUM, ADAM.ADLBSUM
Run Date: 2025-05-14T14:53:11
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ravuema202501/Files/tables/production/programs/t11_2_nontemave_cum_adj.sas

Table 11.2.3
Rates of Non-Thrombotic Major Adverse Vascular Events, During the Analysis Period and by Exposure Period[a]
Study Population

	Patients with Untreated Person Time (N=239)	Treated with Eculizumab (Prior to Ravulizumab Switch) (N=278)	Treated with Ravulizumab (N=493)	Treated with Eculizumab Only (N=104)
All patients				
Total patients at risk	23	14	452	78
Number of patients with events	0	0	1	1
Incidence (percent of population at risk, %)	0.0	0.0	0.2	1.3
Number of events	0	0	1	1
Person-years	9.7	5.6	500.0	86.2
Rate per 100 person-years	0.0	0.0	0.2	1.2
Estimated rate per 100 person-years[b]	n/a	n/a	0.2	1.2
95% CI	(n/a)	(n/a)	(0.0, 1.4)	(0.2, 8.2)

Notes: CI = confidence interval.
(a) The analysis period is from 06JAN2023 to 06JAN2025.
(b) Poisson regression estimate of incidence density.

Source: ADAM.ADSL, ADAM.ADPOP, ADAM.ADTTE
Run Date: 2025-05-14T14:53:18
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ravuema202501/Files/tables/production/programs/t11_2_nontemave_dur.sas

Table 11.3
Rates of Major Adverse Vascular Events, During the Analysis Period and by Exposure Period[a]
Study Population

	Patients with Untreated Person Time (N=239)	Treated with Eculizumab (Prior to Ravulizumab Switch) (N=278)	Treated with Ravulizumab (N=493)	Treated with Eculizumab Only (N=104)
All patients				
Total patients at risk	23	14	452	78
Number of patients with events	1	0	2	1
Incidence (percent of population at risk, %)	4.3	0.0	0.4	1.3
Number of events	1	0	3	1
Person-years	9.7	5.6	500.0	86.2
Rate per 100 person-years	10.3	0.0	0.6	1.2
Estimated rate per 100 person-years[b]	10.3	n/a	0.6	1.2
95% CI	(1.5, 73.4)	(n/a)	(0.2, 1.9)	(0.2, 8.2)

Notes: CI = confidence interval.
(a) The analysis period is from 06JAN2023 to 06JAN2025.
(b) Poisson regression estimate of incidence density.

Source: ADAM.ADSL, ADAM.ADPOP, ADAM.ADTTE
Run Date: 2025-05-14T14:53:39
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ravuema202501/Files/tables/production/programs/t11_mave_dur.sas

Table 11.4
Sensitivity Analysis - Rates of Major Adverse Vascular Events, Cumulative and by Exposure Period
Study Population with clone size >= 1%

	Patients with Untreated Person Time (N=200)	Treated with Eculizumab (Prior to Ravulizumab Switch) (N=224)	Treated with Ravulizumab (N=392)	Treated with Eculizumab Only (N=524)
All patients				
Total patients at risk	200	223	387	523
Number of patients with events	18	12	2	20
Incidence (percent of population at risk, %)	9.0	5.4	0.5	3.8
Number of events	22	12	2	23
Person-years	450.2	1478.6	834.9	2358.4
Rate per 100 person-years	4.9	0.8	0.2	1.0
Estimated rate per 100 person-years[a]	4.9	0.8	0.2	1.0
95% CI	(3.2, 7.4)	(0.5, 1.4)	(0.1, 1.0)	(0.6, 1.5)

Notes: CI = confidence interval.
(a) Poisson regression estimate of incidence density.

Source: ADAM.ADSL, ADAM.ADPOP, ADAM.ADTTE, ADAM.ADLBSUM
Run Date: 2025-05-14T14:53:29
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ravuema202501/Files/tables/production/programs/t11_mave_cum_sen.sas

Table 12.1
Rates of Malignancy, Cumulative and by Exposure Period
Study Population

	Patients with Untreated Person Time (N=252)	Treated with Eculizumab (Prior to Ravulizumab Switch) (N=301)	Treated with Ravulizumab (N=532)	Treated with Eculizumab Only (N=713)
All patients				
All reported malignancy				
Total patients at risk	252	299	525	711
Number of patients with events	4	17	19	40
Incidence (percent of population at risk, %)	1.6	5.7	3.6	5.6
Number of events	4	19	21	45
Person-years	609.7	2181.6	1155.4	3258.0
Rate per 100 person-years	0.7	0.9	1.8	1.4
Estimated rate per 100 person-years[a]	0.7	0.9	1.8	1.4
95% CI	(0.2, 1.7)	(0.6, 1.4)	(1.2, 2.8)	(1.0, 1.8)
All confirmed malignancy				
Total patients at risk	252	299	525	711
Number of patients with events	3	16	19	40
Incidence (percent of population at risk, %)	1.2	5.4	3.6	5.6
Number of events	3	18	21	45
Person-years	609.7	2181.6	1155.4	3258.0
Rate per 100 person-years	0.5	0.8	1.8	1.4

Notes: CI = confidence interval.
(a) Poisson regression estimate of incidence density.

Source: ADAM.ADSL, ADAM.ADPOP, ADAM.ADTTE
Run Date: 2025-05-14T14:54:12
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ravuema202501/Files/tables/production/programs/t12_mal_cum.sas

Table 12.1
Rates of Malignancy, Cumulative and by Exposure Period
Study Population

	Patients with Untreated Person Time (N=252)	Treated with Eculizumab (Prior to Ravulizumab Switch) (N=301)	Treated with Ravulizumab (N=532)	Treated with Eculizumab Only (N=713)
Estimated rate per 100 person-years[a]	0.5	0.8	1.8	1.4
95% CI	(0.2, 1.5)	(0.5, 1.3)	(1.2, 2.8)	(1.0, 1.8)

Notes: CI = confidence interval.
(a) Poisson regression estimate of incidence density.

Source: ADAM.ADSL, ADAM.ADPOP, ADAM.ADTTE
Run Date: 2025-05-14T14:54:12
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ravuema202501/Files/tables/production/programs/t12_mal_cum.sas

Table 12.1.1
Rates of Malignancy - Hematologic, Cumulative and by Exposure Group
Study Population

	Patients with Untreated Person Time (N=252)	Treated with Eculizumab (Prior to Ravulizumab Switch) (N=301)	Treated with Ravulizumab (N=532)	Treated with Eculizumab Only (N=713)
All patients				
All reported hematologic malignancy				
Total patients at risk	252	299	525	711
Number of patients with events	0	3	6	19
Incidence (percent of population at risk, %)	0.0	1.0	1.1	2.7
Number of events	0	3	7	22
Person-years	609.7	2181.6	1155.4	3258.0
Rate per 100 person-years	0.0	0.1	0.6	0.7
Estimated rate per 100 person-years[a]	n/a	0.1	0.6	0.7
95% CI	(n/a)	(0.0, 0.4)	(0.3, 1.3)	(0.4, 1.0)
All confirmed primary hematologic malignancy				
Total patients at risk	252	299	525	711
Number of patients with events	0	3	6	19
Incidence (percent of population at risk, %)	0.0	1.0	1.1	2.7
Number of events	0	3	7	22
Person-years	609.7	2181.6	1155.4	3258.0
Rate per 100 person-years	0.0	0.1	0.6	0.7

Notes: CI = confidence interval; MDS = myelodysplastic syndromes.
(a) Poisson regression estimate of incidence density.

Source: ADAM.ADSL, ADAM.ADPOP, ADAM.ADTTE
Run Date: 2025-05-14T14:53:48
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ravuema202501/Files/tables/production/programs/t12_hema_cum.sas

Table 12.1.1
Rates of Malignancy - Hematologic, Cumulative and by Exposure Group
Study Population

	Patients with Untreated Person Time (N=252)	Treated with Eculizumab (Prior to Ravulizumab Switch) (N=301)	Treated with Ravulizumab (N=532)	Treated with Eculizumab Only (N=713)
Estimated rate per 100 person-years[a]	n/a	0.1	0.6	0.7
95% CI	(n/a)	(0.0, 0.4)	(0.3, 1.3)	(0.4, 1.0)
Myeloma				
Total patients at risk	252	299	525	711
Number of patients with events	0	0	0	0
Incidence (percent of population at risk, %)	0.0	0.0	0.0	0.0
Number of events	0	0	0	0
Person-years	609.7	2181.6	1155.4	3258.0
Rate per 100 person-years	0.0	0.0	0.0	0.0
Estimated rate per 100 person-years[a]	n/a	n/a	n/a	n/a
95% CI	(n/a)	(n/a)	(n/a)	(n/a)
Leukemia				
Total patients at risk	252	299	525	711
Number of patients with events	0	0	1	8
Incidence (percent of population at risk, %)	0.0	0.0	0.2	1.1
Number of events	0	0	1	9

Notes: CI = confidence interval; MDS = myelodysplastic syndromes.
(a) Poisson regression estimate of incidence density.

Source: ADAM.ADSL, ADAM.ADPOP, ADAM.ADTTE
Run Date: 2025-05-14T14:53:48
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ravuema202501/Files/tables/production/programs/t12_hema_cum.sas

Table 12.1.1
Rates of Malignancy - Hematologic, Cumulative and by Exposure Group
Study Population

	Patients with Untreated Person Time (N=252)	Treated with Eculizumab (Prior to Ravulizumab Switch) (N=301)	Treated with Ravulizumab (N=532)	Treated with Eculizumab Only (N=713)
Person-years	609.7	2181.6	1155.4	3258.0
Rate per 100 person-years	0.0	0.0	0.1	0.3
Estimated rate per 100 person-years[a]	n/a	n/a	0.1	0.3
95% CI	(n/a)	(n/a)	(0.0, 0.6)	(0.1, 0.5)
Lymphoma				
Total patients at risk	252	299	525	711
Number of patients with events	0	2	1	0
Incidence (percent of population at risk, %)	0.0	0.7	0.2	0.0
Number of events	0	2	1	0
Person-years	609.7	2181.6	1155.4	3258.0
Rate per 100 person-years	0.0	0.1	0.1	0.0
Estimated rate per 100 person-years[a]	n/a	0.1	0.1	n/a
95% CI	(n/a)	(0.0, 0.4)	(0.0, 0.6)	(n/a)
MDS				
Total patients at risk	252	299	525	711
Number of patients with events	0	1	4	11

Notes: CI = confidence interval; MDS = myelodysplastic syndromes.
(a) Poisson regression estimate of incidence density.

Source: ADAM.ADSL, ADAM.ADPOP, ADAM.ADTTE
Run Date: 2025-05-14T14:53:48
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ravuema202501/Files/tables/production/programs/t12_hema_cum.sas

Table 12.1.1
Rates of Malignancy - Hematologic, Cumulative and by Exposure Group
Study Population

	Patients with Untreated Person Time (N=252)	Treated with Eculizumab (Prior to Ravulizumab Switch) (N=301)	Treated with Ravulizumab (N=532)	Treated with Eculizumab Only (N=713)
Incidence (percent of population at risk, %)	0.0	0.3	0.8	1.5
Number of events	0	1	5	13
Person-years	609.7	2181.6	1155.4	3258.0
Rate per 100 person-years	0.0	0.0	0.4	0.4
Estimated rate per 100 person-years[a]	n/a	0.0	0.4	0.4
95% CI	(n/a)	(0.0, 0.3)	(0.2, 1.0)	(0.2, 0.7)
Other				
Total patients at risk	252	299	525	711
Number of patients with events	0	0	0	0
Incidence (percent of population at risk, %)	0.0	0.0	0.0	0.0
Number of events	0	0	0	0
Person-years	609.7	2181.6	1155.4	3258.0
Rate per 100 person-years	0.0	0.0	0.0	0.0
Estimated rate per 100 person-years[a]	n/a	n/a	n/a	n/a
95% CI	(n/a)	(n/a)	(n/a)	(n/a)

Notes: CI = confidence interval; MDS = myelodysplastic syndromes.
(a) Poisson regression estimate of incidence density.

Source: ADAM.ADSL, ADAM.ADPOP, ADAM.ADTTE
Run Date: 2025-05-14T14:53:48
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ravuema202501/Files/tables/production/programs/t12_hema_cum.sas

Table 12.1.2
Adjusted rates of Malignancy - Hematologic, Cumulative and by Exposure Group
Study Population

	Patients with Untreated Person Time (N=252)	Treated with Eculizumab (Prior to Ravulizumab Switch) (N=301)	Treated with Ravulizumab (N=532)	Treated with Eculizumab Only (N=713)
All patients				
All reported hematologic malignancy				
Total patients at risk	252	299	525	711
Number of patients with events	0	3	6	19
Incidence (percent of population at risk, %)	0.0	1.0	1.1	2.7
Number of events	0	3	7	22
Person-years	609.7	2181.6	1155.4	3258.0
Rate per 100 person-years	0.0	0.1	0.6	0.7
Adjusted rate per 100 person-years[a]	0.0	0.1	0.4	0.5
95% CI	(0.0, 0.0)	(0.0, 0.4)	(0.2, 0.8)	(0.3, 0.8)
All confirmed primary hematologic malignancy				
Total patients at risk	252	299	525	711
Number of patients with events	0	3	6	19
Incidence (percent of population at risk, %)	0.0	1.0	1.1	2.7
Number of events	0	3	7	22

Notes: CI = confidence interval; MDS = myelodysplastic syndromes.
(a) Poisson regression estimate of incidence density. The adjusted multivariable regression model includes the following covariates: age at baseline, gender, and history of BMD at baseline.
(b) Baseline is defined as the enrollment date for 'patients with untreated person time' and the ravulizumab treatment initiation date for patients in 'treated with ravulizumab' group. For patients included in the group of 'treated with eculizumab (prior to ravulizumab switch)' and 'treated with eculizumab only', baseline is the eculizumab treatment initiation date.

Source: ADAM.ADSL, ADAM.ADPOP, ADAM.ADMESUM, ADAM.ADTTE
Run Date: 2025-05-14T14:53:41
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ravuema202501/Files/tables/production/programs/t12_hema_cum_adj.sas

Table 12.1.2
Adjusted rates of Malignancy - Hematologic, Cumulative and by Exposure Group
Study Population

	Patients with Untreated Person Time (N=252)	Treated with Eculizumab (Prior to Ravulizumab Switch) (N=301)	Treated with Ravulizumab (N=532)	Treated with Eculizumab Only (N=713)
Person-years	609.7	2181.6	1155.4	3258.0
Rate per 100 person-years	0.0	0.1	0.6	0.7
Adjusted rate per 100 person-years[a]	0.0	0.1	0.4	0.5
95% CI	(0.0, 0.0)	(0.0, 0.4)	(0.2, 0.8)	(0.3, 0.8)
Myeloma				
Total patients at risk	252	299	525	711
Number of patients with events	0	0	0	0
Incidence (percent of population at risk, %)	0.0	0.0	0.0	0.0
Number of events	0	0	0	0
Person-years	609.7	2181.6	1155.4	3258.0
Rate per 100 person-years	0.0	0.0	0.0	0.0
Adjusted rate per 100 person-years[a]	n/a	n/a	n/a	n/a
95% CI	(n/a)	(n/a)	(n/a)	(n/a)
Leukemia				

Notes: CI = confidence interval; MDS = myelodysplastic syndromes.
(a) Poisson regression estimate of incidence density. The adjusted multivariable regression model includes the following covariates: age at baseline, gender, and history of BMD at baseline.
(b) Baseline is defined as the enrollment date for 'patients with untreated person time' and the ravulizumab treatment initiation date for patients in 'treated with ravulizumab' group. For patients included in the group of 'treated with eculizumab (prior to ravulizumab switch)' and 'treated with eculizumab only', baseline is the eculizumab treatment initiation date.

Source: ADAM.ADSL, ADAM.ADPOP, ADAM.ADMESUM, ADAM.ADTTE
Run Date: 2025-05-14T14:53:41
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ravuema202501/Files/tables/production/programs/t12_hema_cum_adj.sas

Table 12.1.2
Adjusted rates of Malignancy - Hematologic, Cumulative and by Exposure Group
Study Population

	Patients with Untreated Person Time (N=252)	Treated with Eculizumab (Prior to Ravulizumab Switch) (N=301)	Treated with Ravulizumab (N=532)	Treated with Eculizumab Only (N=713)
Total patients at risk	252	299	525	711
Number of patients with events	0	0	1	8
Incidence (percent of population at risk, %)	0.0	0.0	0.2	1.1
Number of events	0	0	1	9
Person-years	609.7	2181.6	1155.4	3258.0
Rate per 100 person-years	0.0	0.0	0.1	0.3
Adjusted rate per 100 person-years[a]	n/a	n/a	n/a	n/a
95% CI	(n/a)	(n/a)	(n/a)	(n/a)
Lymphoma				
Total patients at risk	252	299	525	711
Number of patients with events	0	2	1	0
Incidence (percent of population at risk, %)	0.0	0.7	0.2	0.0
Number of events	0	2	1	0
Person-years	609.7	2181.6	1155.4	3258.0
Rate per 100 person-years	0.0	0.1	0.1	0.0

Notes: CI = confidence interval; MDS = myelodysplastic syndromes.
(a) Poisson regression estimate of incidence density. The adjusted multivariable regression model includes the following covariates: age at baseline, gender, and history of BMD at baseline.
(b) Baseline is defined as the enrollment date for 'patients with untreated person time' and the ravulizumab treatment initiation date for patients in 'treated with ravulizumab' group. For patients included in the group of 'treated with eculizumab (prior to ravulizumab switch)' and 'treated with eculizumab only', baseline is the eculizumab treatment initiation date.

Source: ADAM.ADSL, ADAM.ADPOP, ADAM.ADMESUM, ADAM.ADTTE
Run Date: 2025-05-14T14:53:41
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ravuema202501/Files/tables/production/programs/t12_hema_cum_adj.sas

Table 12.1.2
Adjusted rates of Malignancy - Hematologic, Cumulative and by Exposure Group
Study Population

	Patients with Untreated Person Time (N=252)	Treated with Eculizumab (Prior to Ravulizumab Switch) (N=301)	Treated with Ravulizumab (N=532)	Treated with Eculizumab Only (N=713)
Adjusted rate per 100 person-years[a]	n/a	n/a	n/a	n/a
95% CI	(n/a)	(n/a)	(n/a)	(n/a)
MDS				
Total patients at risk	252	299	525	711
Number of patients with events	0	1	4	11
Incidence (percent of population at risk, %)	0.0	0.3	0.8	1.5
Number of events	0	1	5	13
Person-years	609.7	2181.6	1155.4	3258.0
Rate per 100 person-years	0.0	0.0	0.4	0.4
Adjusted rate per 100 person-years[a]	0.0	0.0	0.2	0.3
95% CI	(0.0, 0.0)	(0.0, 0.3)	(0.1, 0.6)	(0.1, 0.5)
Other				
Total patients at risk	252	299	525	711
Number of patients with events	0	0	0	0

Notes: CI = confidence interval; MDS = myelodysplastic syndromes.
(a) Poisson regression estimate of incidence density. The adjusted multivariable regression model includes the following covariates: age at baseline, gender, and history of BMD at baseline.
(b) Baseline is defined as the enrollment date for 'patients with untreated person time' and the ravulizumab treatment initiation date for patients in 'treated with ravulizumab' group. For patients included in the group of 'treated with eculizumab (prior to ravulizumab switch)' and 'treated with eculizumab only', baseline is the eculizumab treatment initiation date.

Source: ADAM.ADSL, ADAM.ADPOP, ADAM.ADMESUM, ADAM.ADTTE
Run Date: 2025-05-14T14:53:41
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ravuema202501/Files/tables/production/programs/t12_hema_cum_adj.sas

Table 12.1.2
Adjusted rates of Malignancy - Hematologic, Cumulative and by Exposure Group
Study Population

	Patients with Untreated Person Time (N=252)	Treated with Eculizumab (Prior to Ravulizumab Switch) (N=301)	Treated with Ravulizumab (N=532)	Treated with Eculizumab Only (N=713)
Incidence (percent of population at risk, %)	0.0	0.0	0.0	0.0
Number of events	0	0	0	0
Person-years	609.7	2181.6	1155.4	3258.0
Rate per 100 person-years	0.0	0.0	0.0	0.0
Adjusted rate per 100 person-years[a]	n/a	n/a	n/a	n/a
95% CI	(n/a)	(n/a)	(n/a)	(n/a)

Notes: CI = confidence interval; MDS = myelodysplastic syndromes.
(a) Poisson regression estimate of incidence density. The adjusted multivariable regression model includes the following covariates: age at baseline, gender, and history of BMD at baseline.
(b) Baseline is defined as the enrollment date for 'patients with untreated person time' and the ravulizumab treatment initiation date for patients in 'treated with ravulizumab' group. For patients included in the group of 'treated with eculizumab (prior to ravulizumab switch)' and 'treated with eculizumab only', baseline is the eculizumab treatment initiation date.

Source: ADAM.ADSL, ADAM.ADPOP, ADAM.ADMESUM, ADAM.ADTTE
Run Date: 2025-05-14T14:53:41
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ravuema202501/Files/tables/production/programs/t12_hema_cum_adj.sas

Table 12.1.3
Rates of Malignancy - Hematologic, During the Analysis Period and by Exposure Group[a]
Study Population

	Patients with Untreated Person Time (N=239)	Treated with Eculizumab (Prior to Ravulizumab Switch) (N=278)	Treated with Ravulizumab (N=493)	Treated with Eculizumab Only (N=104)
All patients				
All reported hematologic malignancy				
Total patients at risk	23	14	452	78
Number of patients with events	0	0	2	0
Incidence (percent of population at risk, %)	0.0	0.0	0.4	0.0
Number of events	0	0	2	0
Person-years	9.7	5.6	500.0	86.2
Rate per 100 person-years	0.0	0.0	0.4	0.0
Estimated rate per 100 person-years[b]	n/a	n/a	0.4	n/a
95% CI	(n/a)	(n/a)	(0.1, 1.6)	(n/a)
All confirmed primary hematologic malignancy				
Total patients at risk	23	14	452	78
Number of patients with events	0	0	2	0
Incidence (percent of population at risk, %)	0.0	0.0	0.4	0.0
Number of events	0	0	2	0
Person-years	9.7	5.6	500.0	86.2
Rate per 100 person-years	0.0	0.0	0.4	0.0

Notes: CI = confidence interval; MDS = myelodysplastic syndromes.
(a) The analysis period is from 06JAN2023 to 06JAN2025.
(b) Poisson regression estimate of incidence density.

Source: ADAM.ADSL, ADAM.ADPOP, ADAM.ADTTE
Run Date: 2025-05-14T14:53:53
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ravuema202501/Files/tables/production/programs/t12_hema_dur.sas

Table 12.1.3
Rates of Malignancy - Hematologic, During the Analysis Period and by Exposure Group[a]
Study Population

	Patients with Untreated Person Time (N=239)	Treated with Eculizumab (Prior to Ravulizumab Switch) (N=278)	Treated with Ravulizumab (N=493)	Treated with Eculizumab Only (N=104)
Estimated rate per 100 person-years[b]	n/a	n/a	0.4	n/a
95% CI	(n/a)	(n/a)	(0.1, 1.6)	(n/a)
Myeloma				
Total patients at risk	23	14	452	78
Number of patients with events	0	0	0	0
Incidence (percent of population at risk, %)	0.0	0.0	0.0	0.0
Number of events	0	0	0	0
Person-years	9.7	5.6	500.0	86.2
Rate per 100 person-years	0.0	0.0	0.0	0.0
Estimated rate per 100 person-years[b]	n/a	n/a	n/a	n/a
95% CI	(n/a)	(n/a)	(n/a)	(n/a)
Leukemia				
Total patients at risk	23	14	452	78
Number of patients with events	0	0	0	0
Incidence (percent of population at risk, %)	0.0	0.0	0.0	0.0

Notes: CI = confidence interval; MDS = myelodysplastic syndromes.
(a) The analysis period is from 06JAN2023 to 06JAN2025.
(b) Poisson regression estimate of incidence density.

Source: ADAM.ADSL, ADAM.ADPOP, ADAM.ADTTE
Run Date: 2025-05-14T14:53:53
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ravuema202501/Files/tables/production/programs/t12_hema_dur.sas

Table 12.1.3
Rates of Malignancy - Hematologic, During the Analysis Period and by Exposure Group[a]
Study Population

	Patients with Untreated Person Time (N=239)	Treated with Eculizumab (Prior to Ravulizumab Switch) (N=278)	Treated with Ravulizumab (N=493)	Treated with Eculizumab Only (N=104)
Number of events	0	0	0	0
Person-years	9.7	5.6	500.0	86.2
Rate per 100 person-years	0.0	0.0	0.0	0.0
Estimated rate per 100 person-years[b]	n/a	n/a	n/a	n/a
95% CI	(n/a)	(n/a)	(n/a)	(n/a)
Lymphoma				
Total patients at risk	23	14	452	78
Number of patients with events	0	0	0	0
Incidence (percent of population at risk, %)	0.0	0.0	0.0	0.0
Number of events	0	0	0	0
Person-years	9.7	5.6	500.0	86.2
Rate per 100 person-years	0.0	0.0	0.0	0.0
Estimated rate per 100 person-years[b]	n/a	n/a	n/a	n/a
95% CI	(n/a)	(n/a)	(n/a)	(n/a)
MDS				

Notes: CI = confidence interval; MDS = myelodysplastic syndromes.
(a) The analysis period is from 06JAN2023 to 06JAN2025.
(b) Poisson regression estimate of incidence density.

Source: ADAM.ADSL, ADAM.ADPOP, ADAM.ADTTE
Run Date: 2025-05-14T14:53:53
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ravuema202501/Files/tables/production/programs/t12_hema_dur.sas

Table 12.1.3
Rates of Malignancy - Hematologic, During the Analysis Period and by Exposure Group[a]
Study Population

	Patients with Untreated Person Time (N=239)	Treated with Eculizumab (Prior to Ravulizumab Switch) (N=278)	Treated with Ravulizumab (N=493)	Treated with Eculizumab Only (N=104)
Total patients at risk	23	14	452	78
Number of patients with events	0	0	2	0
Incidence (percent of population at risk, %)	0.0	0.0	0.4	0.0
Number of events	0	0	2	0
Person-years	9.7	5.6	500.0	86.2
Rate per 100 person-years	0.0	0.0	0.4	0.0
Estimated rate per 100 person-years[b]	n/a	n/a	0.4	n/a
95% CI	(n/a)	(n/a)	(0.1, 1.6)	(n/a)
Other				
Total patients at risk	23	14	452	78
Number of patients with events	0	0	0	0
Incidence (percent of population at risk, %)	0.0	0.0	0.0	0.0
Number of events	0	0	0	0
Person-years	9.7	5.6	500.0	86.2
Rate per 100 person-years	0.0	0.0	0.0	0.0

Notes: CI = confidence interval; MDS = myelodysplastic syndromes.
(a) The analysis period is from 06JAN2023 to 06JAN2025.
(b) Poisson regression estimate of incidence density.

Source: ADAM.ADSL, ADAM.ADPOP, ADAM.ADTTE
Run Date: 2025-05-14T14:53:53
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ravuema202501/Files/tables/production/programs/t12_hema_dur.sas

Table 12.1.3
Rates of Malignancy - Hematologic, During the Analysis Period and by Exposure Group[a]
Study Population

	Patients with Untreated Person Time (N=239)	Treated with Eculizumab (Prior to Ravulizumab Switch) (N=278)	Treated with Ravulizumab (N=493)	Treated with Eculizumab Only (N=104)
Estimated rate per 100 person-years[b]	n/a	n/a	n/a	n/a
95% CI	(n/a)	(n/a)	(n/a)	(n/a)

Notes: CI = confidence interval; MDS = myelodysplastic syndromes.
(a) The analysis period is from 06JAN2023 to 06JAN2025.
(b) Poisson regression estimate of incidence density.

Source: ADAM.ADSL, ADAM.ADPOP, ADAM.ADTTE
Run Date: 2025-05-14T14:53:53
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ravuema202501/Files/tables/production/programs/t12_hema_dur.sas

Table 12.2
Adjusted Rates of Malignancy, Cumulative and by Exposure Period
Study Population

	Patients with Untreated Person Time (N=252)	Treated with Eculizumab (Prior to Ravulizumab Switch) (N=301)	Treated with Ravulizumab (N=532)	Treated with Eculizumab Only (N=713)
All patients				
All reported malignancy				
Total patients at risk	252	299	525	711
Number of patients with events	4	17	19	40
Incidence (percent of population at risk, %)	1.6	5.7	3.6	5.6
Number of events	4	19	21	45
Person-years	609.7	2181.6	1155.4	3258.0
Rate per 100 person-years	0.7	0.9	1.8	1.4
Adjusted rate per 100 person-years[a]	0.5	0.7	0.9	1.0
95% CI	(0.2, 1.3)	(0.4, 1.1)	(0.6, 1.5)	(0.7, 1.4)
All confirmed malignancy				
Total patients at risk	252	299	525	711
Number of patients with events	3	16	19	40
Incidence (percent of population at risk, %)	1.2	5.4	3.6	5.6
Number of events	3	18	21	45

Notes: CI = confidence interval.
(a) Poisson regression estimate of incidence density. The adjusted multivariable regression model includes the following covariates: age at baseline, gender, and history of BMD at baseline.
(b) Baseline is defined as the enrollment date for 'patients with untreated person time' and the ravulizumab treatment initiation date for patients in 'treated with ravulizumab' group. For patients included in the group of 'treated with eculizumab (prior to ravulizumab switch)' and 'treated with eculizumab only', baseline is the eculizumab treatment initiation date.

Source: ADAM.ADSL, ADAM.ADPOP, ADAM.ADMESUM, ADAM.ADTTE
Run Date: 2025-05-14T14:53:58
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ravuema202501/Files/tables/production/programs/t12_mal_cum_adj.sas

Table 12.2
Adjusted Rates of Malignancy, Cumulative and by Exposure Period
Study Population

	Patients with Untreated Person Time (N=252)	Treated with Eculizumab (Prior to Ravulizumab Switch) (N=301)	Treated with Ravulizumab (N=532)	Treated with Eculizumab Only (N=713)
Person-years	609.7	2181.6	1155.4	3258.0
Rate per 100 person-years	0.5	0.8	1.8	1.4
Adjusted rate per 100 person-years[a]	0.3	0.6	0.9	0.9
95% CI	(0.1, 1.1)	(0.4, 1.0)	(0.5, 1.5)	(0.7, 1.3)

Notes: CI = confidence interval.
(a) Poisson regression estimate of incidence density. The adjusted multivariable regression model includes the following covariates: age at baseline, gender, and history of BMD at baseline.
(b) Baseline is defined as the enrollment date for 'patients with untreated person time' and the ravulizumab treatment initiation date for patients in 'treated with ravulizumab' group. For patients included in the group of 'treated with eculizumab (prior to ravulizumab switch)' and 'treated with eculizumab only', baseline is the eculizumab treatment initiation date.

Source: ADAM.ADSL, ADAM.ADPOP, ADAM.ADMESUM, ADAM.ADTTE
Run Date: 2025-05-14T14:53:58
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ravuema202501/Files/tables/production/programs/t12_mal_cum_adj.sas

Table 12.2.1
Rates of Malignancy by Duration between Initiation of Ravulizumab and Malignancy Onset, Cumulative
Ravulizumab Treated Patients –Prior Eculizumab Treatment

System Organ Class Preferred Term	# of Patients with Events	# of Patients at Risk	Incidence (Percent of Population at Risk, %)	# of Events	Person-Years	Incidence Rate Per 100 Person-years
0-1 years between initiation of ravulizumab and malignancy onset						
All reported malignancy	7	300	2.3	7	274.9	2.5
All confirmed malignancy	7	300	2.3	7	274.9	2.5
All confirmed primary hematologic malignancy	2	300	0.7	2	274.9	0.7
Myeloma	0	300	0.0	0	274.9	0.0
Leukemia	0	300	0.0	0	274.9	0.0
Lymphoma	1	300	0.3	1	274.9	0.4
MDS	1	300	0.3	1	274.9	0.4
Other	0	300	0.0	0	274.9	0.0
1-2 years between initiation of ravulizumab and malignancy onset						
All reported malignancy	2	258	0.8	2	240.0	0.8
All confirmed malignancy	2	258	0.8	2	240.0	0.8
All confirmed primary hematologic malignancy	0	258	0.0	0	240.0	0.0
Myeloma	0	258	0.0	0	240.0	0.0

Note: MDS = myelodysplastic syndromes; NMSC = non-malignant skin cancer.

Source: ADAM.ADSL, ADAM.ADPOP, ADAM.ADMEIN
Run Date: 2025-05-14T14:54:31
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ravuema202501/Files/tables/production/programs/t12_mal_dur_cum_prior.sas

Table 12.2.1
Rates of Malignancy by Duration between Initiation of Ravulizumab and Malignancy Onset, Cumulative
Ravulizumab Treated Patients –Prior Eculizumab Treatment

System Organ Class Preferred Term	# of Patients with Events	# of Patients at Risk	Incidence (Percent of Population at Risk, %)	# of Events	Person-Years	Incidence Rate Per 100 Person-years
Leukemia	0	258	0.0	0	240.0	0.0
Lymphoma	0	258	0.0	0	240.0	0.0
MDS	0	258	0.0	0	240.0	0.0
Other	0	258	0.0	0	240.0	0.0
2-5 years between initiation of ravulizumab and malignancy onset						
All reported malignancy	2	214	0.9	2	259.2	0.8
All confirmed malignancy	2	214	0.9	2	259.2	0.8
All confirmed primary hematologic malignancy	1	214	0.5	1	259.2	0.4
Myeloma	0	214	0.0	0	259.2	0.0
Leukemia	0	214	0.0	0	259.2	0.0
Lymphoma	0	214	0.0	0	259.2	0.0
MDS	1	214	0.5	1	259.2	0.4
Other	0	214	0.0	0	259.2	0.0

Note: MDS = myelodysplastic syndromes; NMSC = non-malignant skin cancer.

Source: ADAM.ADSL, ADAM.ADPOP, ADAM.ADMEIN
Run Date: 2025-05-14T14:54:31
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ravuema202501/Files/tables/production/programs/t12_mal_dur_cum_prior.sas

Table 12.2.1
Rates of Malignancy by Duration between Initiation of Ravulizumab and Malignancy Onset, Cumulative
Ravulizumab Treated Patients –Prior Eculizumab Treatment

System Organ Class Preferred Term	# of Patients with Events	# of Patients at Risk	Incidence (Percent of Population at Risk, %)	# of Events	Person-Years	Incidence Rate Per 100 Person-years
5-8 years between initiation of ravulizumab and malignancy onset						
All reported malignancy	0	4	0.0	0	0.9	0.0
All confirmed malignancy	0	4	0.0	0	0.9	0.0
All confirmed primary hematologic malignancy	0	4	0.0	0	0.9	0.0
Myeloma	0	4	0.0	0	0.9	0.0
Leukemia	0	4	0.0	0	0.9	0.0
Lymphoma	0	4	0.0	0	0.9	0.0
MDS	0	4	0.0	0	0.9	0.0
Other	0	4	0.0	0	0.9	0.0
> 8 years between initiation of ravulizumab and malignancy onset						
All reported malignancy	0	0	0.0	0	0.0	0.0
All confirmed malignancy	0	0	0.0	0	0.0	0.0
All confirmed primary hematologic malignancy	0	0	0.0	0	0.0	0.0
Myeloma	0	0	0.0	0	0.0	0.0

Note: MDS = myelodysplastic syndromes; NMSC = non-malignant skin cancer.

Source: ADAM.ADSL, ADAM.ADPOP, ADAM.ADMEIN
Run Date: 2025-05-14T14:54:31
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ravuema202501/Files/tables/production/programs/t12_mal_dur_cum_prior.sas

Table 12.2.1
Rates of Malignancy by Duration between Initiation of Ravulizumab and Malignancy Onset, Cumulative
Ravulizumab Treated Patients –Prior Eculizumab Treatment

System Organ Class Preferred Term	# of Patients with Events	# of Patients at Risk	Incidence (Percent of Population at Risk, %)	# of Events	Person-Years	Incidence Rate Per 100 Person-years
Leukemia	0	0	0.0	0	0.0	0.0
Lymphoma	0	0	0.0	0	0.0	0.0
MDS	0	0	0.0	0	0.0	0.0
Other	0	0	0.0	0	0.0	0.0

Note: MDS = myelodysplastic syndromes; NMSC = non-malignant skin cancer.

Source: ADAM.ADSL, ADAM.ADPOP, ADAM.ADMEIN
Run Date: 2025-05-14T14:54:31
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ravuema202501/Files/tables/production/programs/t12_mal_dur_cum_prior.sas

Table 12.2.2
Rates of Malignancy by Duration between Initiation of Ravulizumab and Malignancy Onset, Cumulative
Ravulizumab Treated Patients – Eculizumab Naive

System Organ Class Preferred Term	# of Patients with Events	# of Patients at Risk	Incidence (Percent of Population at Risk, %)	# of Events	Person-Years	Incidence Rate Per 100 Person-years
0-1 years between initiation of ravulizumab and malignancy onset						
All reported malignancy	5	160	3.1	6	128.2	4.7
All confirmed malignancy	5	160	3.1	6	128.2	4.7
All confirmed primary hematologic malignancy	1	160	0.6	1	128.2	0.8
Myeloma	0	160	0.0	0	128.2	0.0
Leukemia	0	160	0.0	0	128.2	0.0
Lymphoma	0	160	0.0	0	128.2	0.0
MDS	1	160	0.6	1	128.2	0.8
Other	0	160	0.0	0	128.2	0.0
1-2 years between initiation of ravulizumab and malignancy onset						
All reported malignancy	1	97	1.0	1	78.1	1.3
All confirmed malignancy	1	97	1.0	1	78.1	1.3
All confirmed primary hematologic malignancy	1	97	1.0	1	78.1	1.3
Myeloma	0	97	0.0	0	78.1	0.0

Note: MDS = myelodysplastic syndromes; NMSC = non-malignant skin cancer.

Source: ADAM.ADSL, ADAM.ADPOP, ADAM.ADMEIN
Run Date: 2025-05-14T14:54:23
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ravuema202501/Files/tables/production/programs/t12_mal_dur_cum_naive.sas

Table 12.2.2
Rates of Malignancy by Duration between Initiation of Ravulizumab and Malignancy Onset, Cumulative
Ravulizumab Treated Patients – Eculizumab Naive

System Organ Class Preferred Term	# of Patients with Events	# of Patients at Risk	Incidence (Percent of Population at Risk, %)	# of Events	Person-Years	Incidence Rate Per 100 Person-years
Leukemia	0	97	0.0	0	78.1	0.0
Lymphoma	0	97	0.0	0	78.1	0.0
MDS	1	97	1.0	1	78.1	1.3
Other	0	97	0.0	0	78.1	0.0
2-5 years between initiation of ravulizumab and malignancy onset						
All reported malignancy	0	48	0.0	0	51.6	0.0
All confirmed malignancy	0	48	0.0	0	51.6	0.0
All confirmed primary hematologic malignancy	0	48	0.0	0	51.6	0.0
Myeloma	0	48	0.0	0	51.6	0.0
Leukemia	0	48	0.0	0	51.6	0.0
Lymphoma	0	48	0.0	0	51.6	0.0
MDS	0	48	0.0	0	51.6	0.0
Other	0	48	0.0	0	51.6	0.0

Note: MDS = myelodysplastic syndromes; NMSC = non-malignant skin cancer.

Source: ADAM.ADSL, ADAM.ADPOP, ADAM.ADMEIN
Run Date: 2025-05-14T14:54:23
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ravuema202501/Files/tables/production/programs/t12_mal_dur_cum_naive.sas

Table 12.2.2
Rates of Malignancy by Duration between Initiation of Ravulizumab and Malignancy Onset, Cumulative
Ravulizumab Treated Patients – Eculizumab Naive

System Organ Class Preferred Term	# of Patients with Events	# of Patients at Risk	Incidence (Percent of Population at Risk, %)	# of Events	Person-Years	Incidence Rate Per 100 Person-years
5-8 years between initiation of ravulizumab and malignancy onset						
All reported malignancy	0	2	0.0	0	0.1	0.0
All confirmed malignancy	0	2	0.0	0	0.1	0.0
All confirmed primary hematologic malignancy	0	2	0.0	0	0.1	0.0
Myeloma	0	2	0.0	0	0.1	0.0
Leukemia	0	2	0.0	0	0.1	0.0
Lymphoma	0	2	0.0	0	0.1	0.0
MDS	0	2	0.0	0	0.1	0.0
Other	0	2	0.0	0	0.1	0.0
> 8 years between initiation of ravulizumab and malignancy onset						
All reported malignancy	0	0	0.0	0	0.0	0.0
All confirmed malignancy	0	0	0.0	0	0.0	0.0
All confirmed primary hematologic malignancy	0	0	0.0	0	0.0	0.0
Myeloma	0	0	0.0	0	0.0	0.0

Note: MDS = myelodysplastic syndromes; NMSC = non-malignant skin cancer.

Source: ADAM.ADSL, ADAM.ADPOP, ADAM.ADMEIN
Run Date: 2025-05-14T14:54:23
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ravuema202501/Files/tables/production/programs/t12_mal_dur_cum_naive.sas

Table 12.2.2
Rates of Malignancy by Duration between Initiation of Ravulizumab and Malignancy Onset, Cumulative
Ravulizumab Treated Patients – Eculizumab Naive

System Organ Class Preferred Term	# of Patients with Events	# of Patients at Risk	Incidence (Percent of Population at Risk, %)	# of Events	Person-Years	Incidence Rate Per 100 Person-years
Leukemia	0	0	0.0	0	0.0	0.0
Lymphoma	0	0	0.0	0	0.0	0.0
MDS	0	0	0.0	0	0.0	0.0
Other	0	0	0.0	0	0.0	0.0

Note: MDS = myelodysplastic syndromes; NMSC = non-malignant skin cancer.

Source: ADAM.ADSL, ADAM.ADPOP, ADAM.ADMEIN
Run Date: 2025-05-14T14:54:23
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ravuema202501/Files/tables/production/programs/t12_mal_dur_cum_naive.sas

Table 12.3
Rates of Malignancy, During the Analysis Period and by Exposure Period[a]
Study Population

	Patients with Untreated Person Time (N=239)	Treated with Eculizumab (Prior to Ravulizumab Switch) (N=278)	Treated with Ravulizumab (N=493)	Treated with Eculizumab Only (N=104)
All patients				
All reported malignancy				
Total patients at risk	23	14	452	78
Number of patients with events	1	0	6	3
Incidence (percent of population at risk, %)	4.3	0.0	1.3	3.8
Number of events	1	0	7	3
Person-years	9.7	5.6	500.0	86.2
Rate per 100 person-years	10.3	0.0	1.4	3.5
Estimated rate per 100 person-years[b]	10.3	n/a	1.4	3.5
95% CI	(1.5, 73.4)	(n/a)	(0.7, 2.9)	(1.1, 10.8)
All confirmed malignancy				
Total patients at risk	23	14	452	78
Number of patients with events	1	0	6	3
Incidence (percent of population at risk, %)	4.3	0.0	1.3	3.8
Number of events	1	0	7	3
Person-years	9.7	5.6	500.0	86.2
Rate per 100 person-years	10.3	0.0	1.4	3.5

Notes: CI = confidence interval.
(a) The analysis period is from 06JAN2023 to 06JAN2025.
(b) Poisson regression estimate of incidence density.

Source: ADAM.ADSL, ADAM.ADPOP, ADAM.ADTTE
Run Date: 2025-05-14T14:54:32
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ravuema202501/Files/tables/production/programs/t12_mal_dur.sas

Table 12.3
Rates of Malignancy, During the Analysis Period and by Exposure Period[a]
Study Population

	Patients with Untreated Person Time (N=239)	Treated with Eculizumab (Prior to Ravulizumab Switch) (N=278)	Treated with Ravulizumab (N=493)	Treated with Eculizumab Only (N=104)
Estimated rate per 100 person-years[b]	10.3	n/a	1.4	3.5
95% CI	(1.5, 73.4)	(n/a)	(0.7, 2.9)	(1.1, 10.8)

Notes: CI = confidence interval.
(a) The analysis period is from 06JAN2023 to 06JAN2025.
(b) Poisson regression estimate of incidence density.

Source: ADAM.ADSL, ADAM.ADPOP, ADAM.ADTTE
Run Date: 2025-05-14T14:54:32
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ravuema202501/Files/tables/production/programs/t12_mal_dur.sas

Table 12.4
Sensitivity Analysis - Rates of Malignancy, Cumulative and by Exposure Period
Study Population with clone size >= 1%

	Patients with Untreated Person Time (N=200)	Treated with Eculizumab (Prior to Ravulizumab Switch) (N=224)	Treated with Ravulizumab (N=392)	Treated with Eculizumab Only (N=524)
All patients				
All reported malignancy				
Total patients at risk	200	223	387	523
Number of patients with events	4	12	12	28
Incidence (percent of population at risk, %)	2.0	5.4	3.1	5.4
Number of events	4	14	14	32
Person-years	450.2	1478.6	834.9	2358.4
Rate per 100 person-years	0.9	0.9	1.7	1.4
Estimated rate per 100 person-years[a]	0.9	0.9	1.7	1.4
95% CI	(0.3, 2.4)	(0.6, 1.6)	(1.0, 2.8)	(1.0, 1.9)
All confirmed malignancy				
Total patients at risk	200	223	387	523
Number of patients with events	3	12	12	28
Incidence (percent of population at risk, %)	1.5	5.4	3.1	5.4
Number of events	3	14	14	32
Person-years	450.2	1478.6	834.9	2358.4
Rate per 100 person-years	0.7	0.9	1.7	1.4

Notes: CI = confidence interval.
(a) Poisson regression estimate of incidence density.

Source: ADAM.ADSL, ADAM.ADPOP, ADAM.ADTTE, ADAM.ADLBSUM
Run Date: 2025-05-14T14:54:08
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ravuema202501/Files/tables/production/programs/t12_mal_cum_sen.sas

Table 12.4
Sensitivity Analysis - Rates of Malignancy, Cumulative and by Exposure Period
Study Population with clone size >= 1%

	Patients with Untreated Person Time (N=200)	Treated with Eculizumab (Prior to Ravulizumab Switch) (N=224)	Treated with Ravulizumab (N=392)	Treated with Eculizumab Only (N=524)
Estimated rate per 100 person-years[a]	0.7	0.9	1.7	1.4
95% CI	(0.2, 2.1)	(0.6, 1.6)	(1.0, 2.8)	(1.0, 1.9)

Notes: CI = confidence interval.
(a) Poisson regression estimate of incidence density.

Source: ADAM.ADSL, ADAM.ADPOP, ADAM.ADTTE, ADAM.ADLBSUM
Run Date: 2025-05-14T14:54:08
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ravuema202501/Files/tables/production/programs/t12_mal_cum_sen.sas

Table 12.5
Malignancy, Cumulative and by Exposure Period
Study Population

	Patients with Untreated Person Time (N=252)	Treated with Eculizumab (Prior to Ravulizumab Switch) (N=301)	Treated with Ravulizumab (N=532)	Treated with Eculizumab Only (N=713)
All reported malignancy, n	4	19	21	45
All confirmed malignancy, n (%)	3 (75.0)	18 (94.7)	21 (100.0)	45 (100.0)
All reported solid tumor, n (%)	3 (75.0)	15 (78.9)	14 (66.7)	23 (51.1)
All confirmed primary solid tumor, n (%)	3 (75.0)	15 (78.9)	14 (66.7)	22 (48.9)
Colorectal, n (%)	0 (0.0)	1 (5.3)	2 (9.5)	4 (8.9)
Breast, n (%)	0 (0.0)	6 (31.6)	1 (4.8)	1 (2.2)
Melanoma, n (%)	0 (0.0)	0 (0.0)	1 (4.8)	1 (2.2)
Prostate, n (%)	1 (25.0)	1 (5.3)	1 (4.8)	1 (2.2)
Thyroid, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	1 (2.2)
Renal, n (%)	0 (0.0)	1 (5.3)	0 (0.0)	1 (2.2)
Lung, n (%)	0 (0.0)	0 (0.0)	1 (4.8)	1 (2.2)
Cervical, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Liver and biliary, n (%)	0 (0.0)	2 (10.5)	1 (4.8)	0 (0.0)
Gastric, n (%)	2 (50.0)	1 (5.3)	1 (4.8)	2 (4.4)
Ovary, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	3 (6.7)
NMSC, n (%)	0 (0.0)	2 (10.5)	2 (9.5)	3 (6.7)
Head and neck, n (%)	0 (0.0)	1 (5.3)	0 (0.0)	0 (0.0)

Note: MDS = myelodysplastic syndromes; NMSC = non-malignant skin cancer.
The percentage is the percent of total number of malignancies reported for each exposure group.

Source: ADAM.ADSL, ADAM.ADPOP, ADAM.ADTTE
Run Date: 2025-05-14T14:54:34
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ravuema202501/Files/tables/production/programs/t12_mal_cum_nonrates.sas

Table 12.5
Malignancy, Cumulative and by Exposure Period
Study Population

	Patients with Untreated Person Time (N=252)	Treated with Eculizumab (Prior to Ravulizumab Switch) (N=301)	Treated with Ravulizumab (N=532)	Treated with Eculizumab Only (N=713)
Other, n (%)	0 (0.0)	0 (0.0)	2 (9.5)	4 (8.9)
All reported hematologic malignancy, n (%)	0 (0.0)	3 (15.8)	7 (33.3)	22 (48.9)
All confirmed primary hematologic malignancy, n (%)	0 (0.0)	3 (15.8)	7 (33.3)	22 (48.9)
Myeloma, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Leukemia, n (%)	0 (0.0)	0 (0.0)	1 (4.8)	9 (20.0)
Lymphoma, n (%)	0 (0.0)	2 (10.5)	1 (4.8)	0 (0.0)
MDS, n (%)	0 (0.0)	1 (5.3)	5 (23.8)	13 (28.9)
Other, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

Note: MDS = myelodysplastic syndromes; NMSC = non-malignant skin cancer.
The percentage is the percent of total number of malignancies reported for each exposure group.

Source: ADAM.ADSL, ADAM.ADPOP, ADAM.ADTTE
Run Date: 2025-05-14T14:54:34
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ravuema202501/Files/tables/production/programs/t12_mal_cum_nonrates.sas

Table 12.6
Malignancy, During the Analysis Period and by Exposure Period
Study Population

	Patients with Untreated Person Time (N=239)	Treated with Eculizumab (Prior to Ravulizumab Switch) (N=278)	Treated with Ravulizumab (N=493)	Treated with Eculizumab Only (N=104)
All reported malignancy, n	1	0	7	3
All confirmed malignancy, n (%)	1 (100.0)	0 (0.0)	7 (100.0)	3 (100.0)
All reported solid tumor, n (%)	1 (100.0)	0 (0.0)	5 (71.4)	3 (100.0)
All confirmed primary solid tumor, n (%)	1 (100.0)	0 (0.0)	5 (71.4)	3 (100.0)
Colorectal, n (%)	0 (0.0)	0 (0.0)	2 (28.6)	1 (33.3)
Breast, n (%)	0 (0.0)	0 (0.0)	1 (14.3)	0 (0.0)
Melanoma, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Prostate, n (%)	0 (0.0)	0 (0.0)	1 (14.3)	0 (0.0)
Thyroid, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Renal, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Lung, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Cervical, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Liver and biliary, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Gastric, n (%)	1 (100.0)	0 (0.0)	0 (0.0)	0 (0.0)
Ovary, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	1 (33.3)
NMSC, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	1 (33.3)
Head and neck, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

Note: MDS = myelodysplastic syndromes; NMSC = non-malignant skin cancer.
The percentage is the percent of total number of malignancies reported for each exposure group.

Source: ADAM.ADSL, ADAM.ADPOP, ADAM.ADTTE
Run Date: 2025-05-14T14:54:44
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ravuema202501/Files/tables/production/programs/t12_mal_dur_nonrates.sas

Table 12.6
Malignancy, During the Analysis Period and by Exposure Period
Study Population

	Patients with Untreated Person Time (N=239)	Treated with Eculizumab (Prior to Ravulizumab Switch) (N=278)	Treated with Ravulizumab (N=493)	Treated with Eculizumab Only (N=104)
Other, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
All reported hematologic malignancy, n (%)	0 (0.0)	0 (0.0)	2 (28.6)	0 (0.0)
All confirmed primary hematologic malignancy, n (%)	0 (0.0)	0 (0.0)	2 (28.6)	0 (0.0)
Myeloma, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Leukemia, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Lymphoma, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
MDS, n (%)	0 (0.0)	0 (0.0)	2 (28.6)	0 (0.0)
Other, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

Note: MDS = myelodysplastic syndromes; NMSC = non-malignant skin cancer.
The percentage is the percent of total number of malignancies reported for each exposure group.

Source: ADAM.ADSL, ADAM.ADPOP, ADAM.ADTTE
Run Date: 2025-05-14T14:54:44
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ravuema202501/Files/tables/production/programs/t12_mal_dur_nonrates.sas

Table 13.1
Infection, Cumulative and by Exposure Period
Study Population

	Patients with Untreated Person Time (N=252)	Treated with Eculizumab (Prior to Ravulizumab Switch) (N=301)	Treated with Ravulizumab (N=532)	Treated with Eculizumab Only (N=713)
Infections reported, n	34	64	58	195
Neisseria, n (%)	0 (0.0)	4 (6.3)	1 (1.7)	7 (3.6)
Meningococcal, n (%)	0 (0.0)	3 (4.7)	0 (0.0)	6 (3.1)
Suspected meningococcal, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Gonorrhea, n (%)	0 (0.0)	0 (0.0)	1 (1.7)	1 (0.5)
Other, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Unknown, n (%)	0 (0.0)	1 (1.6)	0 (0.0)	0 (0.0)
Encapsulated bacteria[a], n (%)	1 (2.9)	0 (0.0)	0 (0.0)	5 (2.6)
Streptococcus Pneumonia, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)
Haemophilus influenza, n (%)	1 (2.9)	0 (0.0)	0 (0.0)	4 (2.1)
Aspergillus, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	2 (1.0)
Other infection, n (%)	33 (97.1)	59 (92.2)	55 (94.8)	179 (91.8)
Other organism, n (%)	19 (55.9)	28 (43.8)	38 (65.5)	64 (32.8)
Unknown organism, n (%)	14 (41.2)	31 (48.4)	17 (29.3)	115 (59.0)

Note: The percentage is the percent of total number of infections reported for each exposure group.
(a) Streptococcus pneumonia, Haemophilus influenza only.

Source: ADAM.ADSL, ADAM.ADPOP, ADAM.ADTTE
Run Date: 2025-05-14T14:54:50
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ravuema202501/Files/tables/production/programs/t13_infe_cum.sas

Table 13.2
Infection, During the Analysis Period and by Exposure Period[a]
Study Population

	Patients with Untreated Person Time (N=239)	Treated with Eculizumab (Prior to Ravulizumab Switch) (N=278)	Treated with Ravulizumab (N=493)	Treated with Eculizumab Only (N=104)
Infections reported, n	2	0	29	6
Neisseria, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Meningococcal, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Suspected meningococcal, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Gonorrhea, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Other, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Unknown, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Encapsulated bacteria[b], n (%)	0 (0.0)	0 (0.0)	0 (0.0)	1 (16.7)
Streptococcus Pneumonia, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	1 (16.7)
Haemophilus influenza, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Aspergillus, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Other infection, n (%)	2 (100.0)	0 (0.0)	29 (100.0)	4 (66.7)
Other organism, n (%)	2 (100.0)	0 (0.0)	19 (65.5)	1 (16.7)
Unknown organism, n (%)	0 (0.0)	0 (0.0)	10 (34.5)	3 (50.0)

Note: The percentage is the percent of total number of infections reported for each exposure group.
(a) The analysis period is from 06JAN2023 to 06JAN2025.
(b) Streptococcus pneumonia, Haemophilus influenza only.

Source: ADAM.ADSL, ADAM.ADPOP, ADAM.ADTTE
Run Date: 2025-05-14T14:54:54
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ravuema202501/Files/tables/production/programs/t13_infe_dur.sas

Table 14.1
Rates of Infection, Cumulative and by Exposure Period
Study Population

	Patients with Untreated Person Time (N=252)	Treated with Eculizumab (Prior to Ravulizumab Switch) (N=301)	Treated with Ravulizumab (N=532)	Treated with Eculizumab Only (N=713)
All patients				
Total patients at risk	252	299	525	711
Number of patients with events	20	42	46	113
Incidence (percent of population at risk, %)	7.9	14.0	8.8	15.9
Number of events	34	64	58	195
Person-years	609.7	2181.6	1155.4	3258.0
Rate per 100 person-years	5.6	2.9	5.0	6.0
Estimated rate per 100 person-years[a]	5.6	2.9	5.0	6.0
95% CI	(4.0, 7.8)	(2.3, 3.7)	(3.9, 6.5)	(5.2, 6.9)

Notes: CI = confidence interval.
(a) Poisson regression estimate of incidence density.

Source: ADAM.ADSL, ADAM.ADPOP, ADAM.ADTTE
Run Date: 2025-05-14T14:55:05
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ravuema202501/Files/tables/production/programs/t14_rinf_cum.sas

Table 14.2
Adjusted Rates of Infection, Cumulative and by Exposure
Study Population

	Patients with Untreated Person Time (N=252)	Treated with Eculizumab (Prior to Ravulizumab Switch) (N=301)	Treated with Ravulizumab (N=532)	Treated with Eculizumab Only (N=713)
All patients				
Total patients at risk	252	299	525	711
Number of patients with events	20	42	46	113
Incidence (percent of population at risk, %)	7.9	14.0	8.8	15.9
Number of events	34	64	58	195
Person-years	609.7	2181.6	1155.4	3258.0
Rate per 100 person-years	5.6	2.9	5.0	6.0
Adjusted rate per 100 person-years[a]	5.4	3.0	5.1	5.7
95% CI	(3.8, 7.8)	(2.3, 3.9)	(3.8, 6.8)	(4.8, 6.7)

Notes: CI = confidence interval.
(a) Poisson regression estimate of incidence density. The adjusted multivariable regression model includes the following covariates: age at baseline, gender, history of aplastic anemia at baseline, and use of immunosuppressive concomitant mediation at baseline.
(b) Baseline is defined as the enrollment date for 'patients with untreated person time' and the ravulizumab treatment initiation date for patients in 'treated with ravulizumab' group. For patients included in the group of 'treated with eculizumab (prior to ravulizumab switch)' and 'treated with eculizumab only', baseline is the eculizumab treatment initiation date.

Source: ADAM.ADSL, ADAM.ADPOP, ADAM.ADMESUM, ADAM.ADCMSUM
Run Date: 2025-05-14T14:54:58
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ravuema202501/Files/tables/production/programs/t14_rinf_cum_adj.sas

Table 14.3
Rates of Infection, During the Analysis Period and by Exposure Period[a]
Study Population

	Patients with Untreated Person Time (N=239)	Treated with Eculizumab (Prior to Ravulizumab Switch) (N=278)	Treated with Ravulizumab (N=493)	Treated with Eculizumab Only (N=104)
All patients				
Total patients at risk	23	14	452	78
Number of patients with events	2	0	25	6
Incidence (percent of population at risk, %)	8.7	0.0	5.5	7.7
Number of events	2	0	29	6
Person-years	9.7	5.6	500.0	86.2
Rate per 100 person-years	20.7	0.0	5.8	7.0
Estimated rate per 100 person-years[b]	20.7	n/a	5.8	7.0
95% CI	(5.2, 82.7)	(n/a)	(4.0, 8.3)	(3.1, 15.5)

Notes: CI = confidence interval.
(a) The analysis period is from 06JAN2023 to 06JAN2025.
(b) Poisson regression estimate of incidence density.

Source: ADAM.ADSL, ADAM.ADPOP, ADAM.ADTTE
Run Date: 2025-05-14T14:55:07
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ravuema202501/Files/tables/production/programs/t14_rinf_dur.sas

Table 14.4
Sensitivity Analysis -Rates of Infection, Cumulative and by Exposure Period
Study Population with clone size >= 1%

	Patients with Untreated Person Time (N=200)	Treated with Eculizumab (Prior to Ravulizumab Switch) (N=224)	Treated with Ravulizumab (N=392)	Treated with Eculizumab Only (N=524)
All patients				
Total patients at risk	200	223	387	523
Number of patients with events	15	26	30	85
Incidence (percent of population at risk, %)	7.5	11.7	7.8	16.3
Number of events	28	42	40	156
Person-years	450.2	1478.6	834.9	2358.4
Rate per 100 person-years	6.2	2.8	4.8	6.6
Estimated rate per 100 person-years[a]	6.2	2.8	4.8	6.6
95% CI	(4.3, 9.0)	(2.1, 3.8)	(3.5, 6.5)	(5.7, 7.7)

Notes: CI = confidence interval.
(a) Poisson regression estimate of incidence density.

Source: ADAM.ADSL, ADAM.ADPOP, ADAM.ADTTE, ADAM.ADLBSUM
Run Date: 2025-05-14T14:55:02
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ravuema202501/Files/tables/production/programs/t14_rinf_cum_sen.sas

Table 15.1
Rates of Impaired Renal Function, Cumulative and by Exposure Period
Study Population

	Patients with Untreated Person Time (N=252)	Treated with Eculizumab (Prior to Ravulizumab Switch) (N=301)	Treated with Ravulizumab (N=532)	Treated with Eculizumab Only (N=713)
All patients				
Total patients at risk	252	299	525	712
Number of patients with events	23	17	3	45
Incidence (percent of population at risk, %)	9.1	5.7	0.6	6.3
Number of events	31	20	3	55
Person-years	609.7	2181.6	1155.4	3259.3
Rate per 100 person-years	5.1	0.9	0.3	1.7
Estimated rate per 100 person-years[a]	5.1	0.9	0.3	1.7
95% CI	(3.6, 7.2)	(0.6, 1.4)	(0.1, 0.8)	(1.3, 2.2)

Notes: CI = confidence interval.
(a) Poisson regression estimate of incidence density.

Source: ADAM.ADSL, ADAM.ADPOP, ADAM.ADTTE
Run Date: 2025-05-14T14:55:13
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ravuema202501/Files/tables/production/programs/t15_irf_cum.sas

Table 15.2
Rates of Impaired Renal Function, During the Analysis Period and by Exposure Period[a]
Study Population

	Patients with Untreated Person Time (N=239)	Treated with Eculizumab (Prior to Ravulizumab Switch) (N=278)	Treated with Ravulizumab (N=493)	Treated with Eculizumab Only (N=104)
All patients				
Total patients at risk	23	14	452	78
Number of patients with events	2	0	2	0
Incidence (percent of population at risk, %)	8.7	0.0	0.4	0.0
Number of events	2	0	2	0
Person-years	9.7	5.6	500.0	86.2
Rate per 100 person-years	20.7	0.0	0.4	0.0
Estimated rate per 100 person-years[b]	20.7	n/a	0.4	n/a
95% CI	(5.2, 82.7)	(n/a)	(0.1, 1.6)	(n/a)

Notes: CI = confidence interval.
(a) The analysis period is from 06JAN2023 to 06JAN2025.
(b) Poisson regression estimate of incidence density.

Source: ADAM.ADSL, ADAM.ADPOP, ADAM.ADTTE
Run Date: 2025-05-14T14:55:15
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ravuema202501/Files/tables/production/programs/t15_irf_dur.sas

Table 15.3
Sensitivity Analysis -Rates of Impaired Renal Function, Cumulative and by Exposure Period
Study Population with clone size >= 1%

	Patients with Untreated Person Time (N=200)	Treated with Eculizumab (Prior to Ravulizumab Switch) (N=224)	Treated with Ravulizumab (N=392)	Treated with Eculizumab Only (N=524)
All patients				
Total patients at risk	200	223	387	524
Number of patients with events	17	14	2	33
Incidence (percent of population at risk, %)	8.5	6.3	0.5	6.3
Number of events	25	17	2	38
Person-years	450.2	1478.6	834.9	2359.6
Rate per 100 person-years	5.6	1.1	0.2	1.6
Estimated rate per 100 person-years[a]	5.6	1.1	0.2	1.6
95% CI	(3.8, 8.2)	(0.7, 1.8)	(0.1, 1.0)	(1.2, 2.2)

Notes: CI = confidence interval.
(a) Poisson regression estimate of incidence density.

Source: ADAM.ADSL, ADAM.ADPOP, ADAM.ADTTE, ADAM.ADLBSUM
Run Date: 2025-05-14T14:55:10
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ravuema202501/Files/tables/production/programs/t15_irf_cum_sen.sas

Table 16.1
Rates of Impaired Hepatic Function, Cumulative and by Exposure Period
Study Population

	Patients with Untreated Person Time (N=252)	Treated with Eculizumab (Prior to Ravulizumab Switch) (N=301)	Treated with Ravulizumab (N=532)	Treated with Eculizumab Only (N=713)
All patients				
Total patients at risk	252	299	525	711
Number of patients with events	1	11	6	24
Incidence (percent of population at risk, %)	0.4	3.7	1.1	3.4
Number of events	2	11	8	34
Person-years	609.7	2181.6	1155.4	3258.0
Rate per 100 person-years	0.3	0.5	0.7	1.0
Estimated rate per 100 person-years[a]	0.3	0.5	0.7	1.0
95% CI	(0.1, 1.3)	(0.3, 0.9)	(0.3, 1.4)	(0.7, 1.5)

Notes: CI = confidence interval.
(a) Poisson regression estimate of incidence density.

Source: ADAM.ADSL, ADAM.ADPOP, ADAM.ADTTE
Run Date: 2025-05-14T14:55:19
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ravuema202501/Files/tables/production/programs/t16_ihf_cum.sas

Table 16.2
Rates of Impaired Hepatic Function, During the Analysis Period and by Exposure Period[a]
Study Population

	Patients with Untreated Person Time (N=239)	Treated with Eculizumab (Prior to Ravulizumab Switch) (N=278)	Treated with Ravulizumab (N=493)	Treated with Eculizumab Only (N=104)
All patients				
Total patients at risk	23	14	452	78
Number of patients with events	0	0	2	0
Incidence (percent of population at risk, %)	0.0	0.0	0.4	0.0
Number of events	0	0	3	0
Person-years	9.7	5.6	500.0	86.2
Rate per 100 person-years	0.0	0.0	0.6	0.0
Estimated rate per 100 person-years[b]	n/a	n/a	0.6	n/a
95% CI	(n/a)	(n/a)	(0.2, 1.9)	(n/a)

Notes: CI = confidence interval.
(a) The analysis period is from 06JAN2023 to 06JAN2025.
(b) Poisson regression estimate of incidence density.

Source: ADAM.ADSL, ADAM.ADPOP, ADAM.ADTTE
Run Date: 2025-05-14T14:55:21
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ravuema202501/Files/tables/production/programs/t16_ihf_dur.sas

Table 16.3
Sensitivity Analysis -Rates of Impaired Hepatic Function, Cumulative and by Exposure Period
Study Population with clone size >= 1%

	Patients with Untreated Person Time (N=200)	Treated with Eculizumab (Prior to Ravulizumab Switch) (N=224)	Treated with Ravulizumab (N=392)	Treated with Eculizumab Only (N=524)
All patients				
Total patients at risk	200	223	387	523
Number of patients with events	0	7	3	17
Incidence (percent of population at risk, %)	0.0	3.1	0.8	3.3
Number of events	0	7	3	21
Person-years	450.2	1478.6	834.9	2358.4
Rate per 100 person-years	0.0	0.5	0.4	0.9
Estimated rate per 100 person-years[a]	n/a	0.5	0.4	0.9
95% CI	(n/a)	(0.2, 1.0)	(0.1, 1.1)	(0.6, 1.4)

Notes: CI = confidence interval.
(a) Poisson regression estimate of incidence density.

Source: ADAM.ADSL, ADAM.ADPOP, ADAM.ADTTE, ADAM.ADLBSUM
Run Date: 2025-05-14T14:55:16
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ravuema202501/Files/tables/production/programs/t16_ihf_cum_sen.sas

Table 17.1
Rates of Pulmonary Hypertension, Cumulative and by Exposure Period
Study Population

	Patients with Untreated Person Time (N=252)	Treated with Eculizumab (Prior to Ravulizumab Switch) (N=301)	Treated with Ravulizumab (N=532)	Treated with Eculizumab Only (N=713)
All patients				
Total patients at risk	252	299	525	711
Number of patients with events	8	5	2	17
Incidence (percent of population at risk, %)	3.2	1.7	0.4	2.4
Number of events	9	6	2	20
Person-years	609.7	2181.6	1155.4	3258.0
Rate per 100 person-years	1.5	0.3	0.2	0.6
Estimated rate per 100 person-years[a]	1.5	0.3	0.2	0.6
95% CI	(0.8, 2.8)	(0.1, 0.6)	(0.0, 0.7)	(0.4, 1.0)

Notes: CI = confidence interval.
(a) Poisson regression estimate of incidence density.

Source: ADAM.ADSL, ADAM.ADPOP, ADAM.ADTTE
Run Date: 2025-05-14T14:55:25
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ravuema202501/Files/tables/production/programs/t17_ph_cum.sas

Table 17.2
Rates of Pulmonary Hypertension, During the Analysis Period and by Exposure Period[a]
Study Population

	Patients with Untreated Person Time (N=239)	Treated with Eculizumab (Prior to Ravulizumab Switch) (N=278)	Treated with Ravulizumab (N=493)	Treated with Eculizumab Only (N=104)
All patients				
Total patients at risk	23	14	452	78
Number of patients with events	0	0	0	0
Incidence (percent of population at risk, %)	0.0	0.0	0.0	0.0
Number of events	0	0	0	0
Person-years	9.7	5.6	500.0	86.2
Rate per 100 person-years	0.0	0.0	0.0	0.0
Estimated rate per 100 person-years[b]	n/a	n/a	n/a	n/a
95% CI	(n/a)	(n/a)	(n/a)	(n/a)

Notes: CI = confidence interval.
(a) The analysis period is from 06JAN2023 to 06JAN2025.
(b) Poisson regression estimate of incidence density.

Source: ADAM.ADSL, ADAM.ADPOP, ADAM.ADTTE
Run Date: 2025-05-14T14:55:27
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ravuema202501/Files/tables/production/programs/t17_ph_dur.sas

Table 17.3
Sensitivity Analysis -Rates of Pulmonary Hypertension, Cumulative and by Exposure Period
Study Population with clone size >= 1%

	Patients with Untreated Person Time (N=200)	Treated with Eculizumab (Prior to Ravulizumab Switch) (N=224)	Treated with Ravulizumab (N=392)	Treated with Eculizumab Only (N=524)
All patients				
Total patients at risk	200	223	387	523
Number of patients with events	7	5	1	11
Incidence (percent of population at risk, %)	3.5	2.2	0.3	2.1
Number of events	7	6	1	14
Person-years	450.2	1478.6	834.9	2358.4
Rate per 100 person-years	1.6	0.4	0.1	0.6
Estimated rate per 100 person-years[a]	1.6	0.4	0.1	0.6
95% CI	(0.7, 3.3)	(0.2, 0.9)	(0.0, 0.9)	(0.4, 1.0)

Notes: CI = confidence interval.
(a) Poisson regression estimate of incidence density.

Source: ADAM.ADSL, ADAM.ADPOP, ADAM.ADTTE, ADAM.ADLBSUM
Run Date: 2025-05-14T14:55:22
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ravuema202501/Files/tables/production/programs/t17_ph_cum_sen.sas

Table 18.1
Rates of Ultomiris Infusion Reactions, Cumulative and by Exposure Period
Study Population

	Treated with Ravulizumab (N=532)
All patients	
Total patients at risk	523
Number of patients with events	8
Incidence (percent of population at risk, %)	1.5
Number of events	11
Person-years	1155.1
Rate per 100 person-years	1.0
Estimated rate per 100 person-years[a]	1.0
95% CI	(0.5, 1.7)

Notes: CI = confidence interval.
(a) Poisson regression estimate of incidence density.

Source: ADAM.ADSL, ADAM.ADPOP, ADAM.ADTTE
Run Date: 2025-05-14T14:55:29
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ravuema202501/Files/tables/production/programs/t18_rir_cum.sas

Table 18.2
Rates of Ultomiris Infusion Reactions, During the Analysis Period and by Exposure Period[a]
Study Population

	Treated with Ravulizumab (N=493)
All patients	
Total patients at risk	450
Number of patients with events	2
Incidence (percent of population at risk, %)	0.4
Number of events	5
Person-years	499.7
Rate per 100 person-years	1.0
Estimated rate per 100 person-years[b]	1.0
95% CI	(0.4, 2.4)

Notes: CI = confidence interval.
(a) The analysis period is from 06JAN2023 to 06JAN2025.
(b) Poisson regression estimate of incidence density.

Source: ADAM.ADSL, ADAM.ADPOP, ADAM.ADTTE
Run Date: 2025-05-14T14:55:31
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ravuema202501/Files/tables/production/programs/t18_rir_dur.sas

Table 19.1
Outcome of Pregnancy During Follow-up, Cumulative and by Exposure Period
Female Patients in Study Population

	Patients with Untreated Person Time (N=121)	Treated with Eculizumab (Prior to Ravulizumab Switch) (N=147)	Treated with Ravulizumab (N=257)	Treated with Eculizumab Only (N=391)
Pregnancy outcome type, n (%)				
Number of patients with outcomes reported during follow-up period[a]	3	26	2	55
Total number of outcomes reported	3	45	3	85
Live birth	1 (33.3)	34 (75.6)	2 (66.7)	58 (68.2)
Abortion	1 (33.3)	4 (8.9)	0 (0.0)	9 (10.6)
Miscarriage/Stillbirth	1 (33.3)	7 (15.6)	1 (33.3)	17 (20.0)
Missing outcome	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.2)

Notes:
(a) The follow-up period is from registry enrollment date to last untreated follow-up date for patients with untreated person time, from eculizumab treatment start date to last eculizumab treated follow-up date for patients previously treated with eculizumab and eculizumab only patients, and from ravulizumab treatment start date to last ravulizumab treated follow-up date for patients treated with ravulizumab.

Source: ADAM.ADSL, ADAM.ADPREG
Run Date: 2025-05-14T14:55:35
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ravuema202501/Files/tables/production/programs/t19_preg_cum.sas

Table 19.2
Outcome of Pregnancy During Follow-up, During the Analysis Period and by Exposure Period[a]
Female Patients in Study Population

	Patients with Untreated Person Time (N=116)	Treated with Eculizumab (Prior to Ravulizumab Switch) (N=133)	Treated with Ravulizumab (N=239)	Treated with Eculizumab Only (N=56)
Pregnancy outcome type, n (%)				
Number of patients with outcomes reported during follow-up period[b]	0	0	0	2
Total number of outcomes reported	0	0	0	3
Live birth	0 (0.0)	0 (0.0)	0 (0.0)	1 (33.3)
Abortion	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Miscarriage/Stillbirth	0 (0.0)	0 (0.0)	0 (0.0)	2 (66.7)
Missing outcome	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

Notes:
(a) Includes patients actively enrolled in the registry during the analysis period, which covers the time period from 06JAN2023 to 06JAN2025.
(b) The follow-up period is from the later of 06JAN2023 and enrollment date to last untreated follow-up date for patients with untreated person time, the latest date of eculizumab treatment start date, enrollment date, and 06JAN2023 to last eculizumab treated follow-up date for patients previously treated with eculizumab and eculizumab only patients, and from the latest date of ravulizumab treatment start date, enrollment date, and 06JAN2023 to last ravulizumab treated follow-up date for patients treated with ravulizumab.

Source: ADAM.ADSL, ADAM.ADPREG
Run Date: 2025-05-14T14:55:37
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ravuema202501/Files/tables/production/programs/t19_preg_dur.sas

Table 19.3
Sensitivity Analysis -Outcome of Pregnancy During Follow-up, Cumulative and by Exposure Period
Female Patients in Study Population with clone size >= 1%

	Patients with Untreated Person Time (N=93)	Treated with Eculizumab (Prior to Ravulizumab Switch) (N=109)	Treated with Ravulizumab (N=188)	Treated with Eculizumab Only (N=277)
Pregnancy outcome type, n (%)				
Number of patients with outcomes reported during follow-up period[a]	2	20	2	40
Total number of outcomes reported	2	32	3	68
Live birth	1 (50.0)	26 (81.3)	2 (66.7)	47 (69.1)
Abortion	0 (0.0)	3 (9.4)	0 (0.0)	8 (11.8)
Miscarriage/Stillbirth	1 (50.0)	3 (9.4)	1 (33.3)	13 (19.1)
Missing outcome	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

Notes:
(a) The follow-up period is from registry enrollment date to last untreated follow-up date for patients with untreated person time, from eculizumab treatment start date to last eculizumab treated follow-up date for patients previously treated with eculizumab and eculizumab only patients, and from ravulizumab treatment start date to last ravulizumab treated follow-up date for patients treated with ravulizumab.

Source: ADAM.ADSL, ADAM.ADPREG, ADAM.ADLBSUM
Run Date: 2025-05-14T14:55:32
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ravuema202501/Files/tables/production/programs/t19_preg_cum_sen.sas

Table 20.1
Rates of Bone Marrow Transplant, Cumulative and by Exposure Period
Study Population

	Patients with Untreated Person Time (N=252)	Treated with Eculizumab (Prior to Ravulizumab Switch) (N=301)	Treated with Ravulizumab (N=532)	Treated with Eculizumab Only (N=713)
All patients				
Total patients at risk	252	301	529	713
Number of patients with events	1	0	3	33
Incidence (percent of population at risk, %)	0.4	0.0	0.6	4.6
Number of events	2	0	3	33
Person-years	609.7	2190.5	1162.9	3259.4
Rate per 100 person-years	0.3	0.0	0.3	1.0
Estimated rate per 100 person-years[a]	0.3	n/a	0.3	1.0
95% CI	(0.1, 1.3)	(n/a)	(0.1, 0.8)	(0.7, 1.4)

Notes: CI = confidence interval.
(a) Poisson regression estimate of incidence density.

Source: ADAM.ADSL, ADAM.ADPOP, ADAM.ADTTE
Run Date: 2025-05-14T14:55:41
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ravuema202501/Files/tables/production/programs/t20_bmt_cum.sas

Table 20.2
Rates of Bone Marrow Transplant, During the Analysis Period and by Exposure Period[a]
Study Population

	Patients with Untreated Person Time (N=239)	Treated with Eculizumab (Prior to Ravulizumab Switch) (N=278)	Treated with Ravulizumab (N=493)	Treated with Eculizumab Only (N=104)
All patients				
Total patients at risk	23	14	454	78
Number of patients with events	0	0	1	0
Incidence (percent of population at risk, %)	0.0	0.0	0.2	0.0
Number of events	0	0	1	0
Person-years	9.7	5.6	502.9	86.2
Rate per 100 person-years	0.0	0.0	0.2	0.0
Estimated rate per 100 person-years[b]	n/a	n/a	0.2	n/a
95% CI	(n/a)	(n/a)	(0.0, 1.4)	(n/a)

Notes: CI = confidence interval.
(a) The analysis period is from 06JAN2023 to 06JAN2025.
(b) Poisson regression estimate of incidence density.

Source: ADAM.ADSL, ADAM.ADPOP, ADAM.ADTTE
Run Date: 2025-05-14T14:55:42
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ravuema202501/Files/tables/production/programs/t20_bmt_dur.sas

Table 20.3
Sensitivity Analysis -Rates of Bone Marrow Transplant, Cumulative and by Exposure Period
Study Population with clone size >= 1%

	Patients with Untreated Person Time (N=200)	Treated with Eculizumab (Prior to Ravulizumab Switch) (N=224)	Treated with Ravulizumab (N=392)	Treated with Eculizumab Only (N=524)
All patients				
Total patients at risk	200	224	390	524
Number of patients with events	1	0	1	29
Incidence (percent of population at risk, %)	0.5	0.0	0.3	5.5
Number of events	2	0	1	29
Person-years	450.2	1486.7	840.9	2359.6
Rate per 100 person-years	0.4	0.0	0.1	1.2
Estimated rate per 100 person-years[a]	0.4	n/a	0.1	1.2
95% CI	(0.1, 1.8)	(n/a)	(0.0, 0.8)	(0.9, 1.8)

Notes: CI = confidence interval.
(a) Poisson regression estimate of incidence density.

Source: ADAM.ADSL, ADAM.ADPOP, ADAM.ADTTE, ADAM.ADLBSUM
Run Date: 2025-05-14T14:55:38
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ravuema202501/Files/tables/production/programs/t20_bmt_cum_sen.sas

Table 21.1
Rates of Death, Cumulative and by Exposure Period
Study Population

	Patients with Untreated Person Time (N=252)	Treated with Eculizumab (Prior to Ravulizumab Switch) (N=301)	Treated with Ravulizumab (N=532)	Treated with Eculizumab Only (N=713)
All patients				
Total patients at risk	252	299	525	709
Number of patients with events	0	0	17	78
Incidence (percent of population at risk, %)	0.0	0.0	3.2	11.0
Number of events	0	0	17	78
Person-years	609.7	2181.6	1155.4	3256.6
Rate per 100 person-years	0.0	0.0	1.5	2.4
Estimated rate per 100 person-years[a]	n/a	n/a	1.5	2.4
95% CI	(n/a)	(n/a)	(0.9, 2.4)	(1.9, 3.0)

Notes: CI = confidence interval.
(a) Poisson regression estimate of incidence density.

Source: ADAM.ADSL, ADAM.ADPOP, ADAM.ADTTE
Run Date: 2025-05-14T14:55:47
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ravuema202501/Files/tables/production/programs/t21_death_cum.sas

Table 21.2
Rates of Death, During the Analysis Period and by Exposure Period[a]
Study Population

	Patients with Untreated Person Time (N=239)	Treated with Eculizumab (Prior to Ravulizumab Switch) (N=278)	Treated with Ravulizumab (N=493)	Treated with Eculizumab Only (N=104)
All patients				
Total patients at risk	23	14	452	77
Number of patients with events	0	0	10	3
Incidence (percent of population at risk, %)	0.0	0.0	2.2	3.9
Number of events	0	0	10	3
Person-years	9.7	5.6	500.0	86.0
Rate per 100 person-years	0.0	0.0	2.0	3.5
Estimated rate per 100 person-years[b]	n/a	n/a	2.0	3.5
95% CI	(n/a)	(n/a)	(1.1, 3.7)	(1.1, 10.8)

Notes: CI = confidence interval.
(a) The analysis period is from 06JAN2023 to 06JAN2025.
(b) Poisson regression estimate of incidence density.

Source: ADAM.ADSL, ADAM.ADPOP, ADAM.ADTTE
Run Date: 2025-05-14T14:55:49
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ravuema202501/Files/tables/production/programs/t21_death_dur.sas

Table 21.3
Sensitivity Analysis -Rates of Death, Cumulative and by Exposure Period
Study Population with clone size >= 1%

	Patients with Untreated Person Time (N=200)	Treated with Eculizumab (Prior to Ravulizumab Switch) (N=224)	Treated with Ravulizumab (N=392)	Treated with Eculizumab Only (N=524)
All patients				
Total patients at risk	200	223	387	520
Number of patients with events	0	0	14	60
Incidence (percent of population at risk, %)	0.0	0.0	3.6	11.5
Number of events	0	0	14	60
Person-years	450.2	1478.6	834.9	2356.8
Rate per 100 person-years	0.0	0.0	1.7	2.5
Estimated rate per 100 person-years[a]	n/a	n/a	1.7	2.5
95% CI	(n/a)	(n/a)	(1.0, 2.8)	(2.0, 3.3)

Notes: CI = confidence interval.
(a) Poisson regression estimate of incidence density.

Source: ADAM.ADSL, ADAM.ADPOP, ADAM.ADTTE, ADAM.ADLBSUM
Run Date: 2025-05-14T14:55:44
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ravuema202501/Files/tables/production/programs/t21_death_cum_sen.sas

Listing 1
Registry Discontinuation, Cumulative
Ravulizumab Study Population

Patient Number	Gender	Treatment Status[a]	Enrollment Date	Study Discontinuation Date	Primary Reason for Study Discontinuation	Other, Specify
1003-019	Male	Prior Eculizumab Treatment Unknown	31AUG2011	20FEB2024	Other	Site Closure
1003-036	Male	Prior Eculizumab Treatment Unknown	16NOV2011	20FEB2024	Other	PT discontinued. Site closed
1003-037	Female	Prior Eculizumab Treatment	30NOV2011	20FEB2024	Other	PT discontinued. Site closed
1003-040	Male	Without Prior Eculizumab Treatment	08FEB2012	20FEB2024	Other	Pt discontinued. Site closed
1003-051	Female	Prior Eculizumab Treatment Unknown	25JAN2013	20FEB2024	Other	PT discontinued. Site closed
1003-056	Male	Prior Eculizumab Treatment Unknown	28OCT2013	20FEB2024	Other	Pt discontinued. Site closed
1004-012	Female	Prior Eculizumab Treatment Unknown	29JAN2013	21MAY2024	Enrollment in the IPIG PNH Registry	
1004-013	Male	Prior Eculizumab Treatment	14FEB2013	21MAY2024	Patient enrolled in a clinical trial of PNH treatment	
1004-021	Female	Prior Eculizumab Treatment	24MAY2018	21MAY2024	Enrollment in the IPIG PNH Registry	
1005-001	Male	Prior Eculizumab Treatment	17JUL2009	03NOV2023	Patient enrolled in a clinical trial of PNH treatment	

Note: (a) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.

Source: ADAM.ADSL, ADAM.ADPOP
Run Date: 2025-05-14T14:46:00
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ravuema202501/Files/listings/production/programs/l1_regdis_cum.sas

Listing 1
Registry Discontinuation, Cumulative
Ravulizumab Study Population

Patient Number	Gender	Treatment Status[a]	Enrollment Date	Study Discontinuation Date	Primary Reason for Study Discontinuation	Other, Specify
1005-006	Male	Prior Eculizumab Treatment	24JUL2009	21MAR2024	Other	site closure
1005-007	Female	Prior Eculizumab Treatment	11SEP2009	21MAR2024	Other	site closure
1005-012	Female	Prior Eculizumab Treatment	04MAY2010	21FEB2024	Other	patient lost of follow-up. Last contact at site = 02Dec2022
1005-029	Female	Prior Eculizumab Treatment	12MAR2011	21MAR2024	Other	site closure
1005-053	Female	Without Prior Eculizumab Treatment	27AUG2015	29APR2024	Other	End of PNH Registry
1008-001	Male	Prior Eculizumab Treatment Unknown	27SEP2012	23MAY2024	Enrollment in the IPIG PNH Registry	
1008-019	Female	Prior Eculizumab Treatment Unknown	13JUN2012	23MAY2024	Enrollment in the IPIG PNH Registry	
1008-049	Male	Without Prior Eculizumab Treatment	12MAR2014	22OCT2022	Patient is being treated by another physician	
1008-066	Female	Prior Eculizumab Treatment	28SEP2019	23MAY2024	Enrollment in the IPIG PNH Registry	
1009-004	Male	Prior Eculizumab Treatment	08JUN2005	16MAY2024	Enrollment in the IPIG PNH Registry	

Note: (a) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.

Source: ADAM.ADSL, ADAM.ADPOP
Run Date: 2025-05-14T14:46:00
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ravuema202501/Files/listings/production/programs/l1_regdis_cum.sas

Listing 1
Registry Discontinuation, Cumulative
Ravulizumab Study Population

Patient Number	Gender	Treatment Status[a]	Enrollment Date	Study Discontinuation Date	Primary Reason for Study Discontinuation	Other, Specify
1009-006	Male	Prior Eculizumab Treatment	15JUN2005	21MAY2024	Enrollment in the IPIG PNH Registry	
1009-014	Female	Prior Eculizumab Treatment	17AUG2005	11AUG2024	Enrollment in the IPIG PNH Registry	
1009-023	Female	Prior Eculizumab Treatment	04OCT2005	11SEP2024	Enrollment in the IPIG PNH Registry	
1009-024	Female	Prior Eculizumab Treatment	13OCT2005	29OCT2024	Enrollment in the IPIG PNH Registry	
1009-052	Male	Prior Eculizumab Treatment	30NOV2006	31AUG2024	Enrollment in the IPIG PNH Registry	
1009-057	Female	Without Prior Eculizumab Treatment	02AUG2007	06JUL2024	Enrollment in the IPIG PNH Registry	
1009-062	Female	Prior Eculizumab Treatment Unknown	08JUL2008	29NOV2024	Other	Site closure
1009-070	Female	Prior Eculizumab Treatment Unknown	14OCT2008	31MAY2024	Enrollment in the IPIG PNH Registry	
1009-074	Male	Prior Eculizumab Treatment	31MAR2009	21MAY2024	Enrollment in the IPIG PNH Registry	
1009-076	Male	Prior Eculizumab Treatment	12MAY2009	02AUG2022	Other	Moved abroad

Note: (a) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.

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Listing 1
Registry Discontinuation, Cumulative
Ravulizumab Study Population

Patient Number	Gender	Treatment Status[a]	Enrollment Date	Study Discontinuation Date	Primary Reason for Study Discontinuation	Other, Specify
1009-080	Male	Prior Eculizumab Treatment	08SEP2009	29NOV2024	Other	Site closure
1009-084	Female	Prior Eculizumab Treatment	22SEP2009	20JUN2024	Enrollment in the IPIG PNH Registry	
1009-088	Male	Prior Eculizumab Treatment	22OCT2009	20SEP2024	Other	PHYSICIAN'S DECISION
1009-089	Female	Prior Eculizumab Treatment	27OCT2009	02AUG2024	Enrollment in the IPIG PNH Registry	
1009-093	Female	Prior Eculizumab Treatment Unknown	28JAN2010	31MAY2024	Enrollment in the IPIG PNH Registry	
1009-103	Male	Prior Eculizumab Treatment Unknown	22APR2010	31MAY2024	Enrollment in the IPIG PNH Registry	
1009-115	Male	Prior Eculizumab Treatment	15JUN2010	16SEP2024	Enrollment in the IPIG PNH Registry	
1009-129	Male	Without Prior Eculizumab Treatment	31AUG2010	11JUN2024	Enrollment in the IPIG PNH Registry	
1009-132	Female	Prior Eculizumab Treatment	07SEP2010	29NOV2024	Other	Site closure
1009-133	Male	Without Prior Eculizumab Treatment	27OCT2010	23AUG2023	Patient died	

Note: (a) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.

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Listing 1
Registry Discontinuation, Cumulative
Ravulizumab Study Population

Patient Number	Gender	Treatment Status[a]	Enrollment Date	Study Discontinuation Date	Primary Reason for Study Discontinuation	Other, Specify
1009-145	Male	Prior Eculizumab Treatment	01FEB2011	15OCT2024	Enrollment in the IPIG PNH Registry	
1009-146	Male	Prior Eculizumab Treatment	10FEB2011	05SEP2022	Patient died	
1009-149	Male	Prior Eculizumab Treatment	17FEB2011	07JUL2023	Patient enrolled in a clinical trial of PNH treatment	
1009-151	Female	Prior Eculizumab Treatment	10MAR2011	08OCT2024	Enrollment in the IPIG PNH Registry	
1009-161	Male	Prior Eculizumab Treatment	24MAY2011	28MAY2024	Enrollment in the IPIG PNH Registry	
1009-164	Female	Prior Eculizumab Treatment Unknown	16JUN2011	31MAY2024	Enrollment in the IPIG PNH Registry	
1009-166	Female	Prior Eculizumab Treatment	23JUN2011	28MAY2024	Enrollment in the IPIG PNH Registry	
1009-170	Female	Prior Eculizumab Treatment	11AUG2011	29JUN2024	Enrollment in the IPIG PNH Registry	
1009-176	Female	Prior Eculizumab Treatment	30AUG2011	24SEP2024	Enrollment in the IPIG PNH Registry	
1009-178	Female	Without Prior Eculizumab Treatment	08SEP2011	31MAY2024	Enrollment in the IPIG PNH Registry	

Note: (a) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.

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Listing 1
Registry Discontinuation, Cumulative
Ravulizumab Study Population

Patient Number	Gender	Treatment Status[a]	Enrollment Date	Study Discontinuation Date	Primary Reason for Study Discontinuation	Other, Specify
1009-186	Female	Prior Eculizumab Treatment	06OCT2011	08AUG2024	Enrollment in the IPIG PNH Registry	
1009-195	Female	Prior Eculizumab Treatment Unknown	17NOV2011	31MAY2024	Enrollment in the IPIG PNH Registry	
1009-210	Female	Prior Eculizumab Treatment	23FEB2012	31MAY2024	Enrollment in the IPIG PNH Registry	
1009-221	Female	Prior Eculizumab Treatment	06JUN2012	30MAY2024	Enrollment in the IPIG PNH Registry	
1009-222	Female	Prior Eculizumab Treatment	28JUN2012	26JUL2024	Enrollment in the IPIG PNH Registry	
1009-230	Female	Prior Eculizumab Treatment	04SEP2012	29NOV2024	Other	Site closure
1009-251	Male	Prior Eculizumab Treatment	11JUN2013	31OCT2024	Enrollment in the IPIG PNH Registry	
1009-264	Male	Prior Eculizumab Treatment	24OCT2013	22FEB2024	Patient enrolled in a clinical trial of PNH treatment	
1009-268	Male	Prior Eculizumab Treatment	17DEC2013	05AUG2024	Enrollment in the IPIG PNH Registry	
1009-269	Female	Prior Eculizumab Treatment	07JAN2014	28MAY2024	Enrollment in the IPIG PNH Registry	

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Listing 1
Registry Discontinuation, Cumulative
Ravulizumab Study Population

Patient Number	Gender	Treatment Status[a]	Enrollment Date	Study Discontinuation Date	Primary Reason for Study Discontinuation	Other, Specify
1009-270	Male	Prior Eculizumab Treatment	14JAN2014	29MAY2024	Enrollment in the IPIG PNH Registry	
1009-272	Female	Prior Eculizumab Treatment	21JAN2014	20JUL2024	Enrollment in the IPIG PNH Registry	
1009-275	Male	Prior Eculizumab Treatment	12MAY2014	29NOV2024	Other	Site closure
1009-280	Female	Prior Eculizumab Treatment	15JUL2014	27SEP2024	Enrollment in the IPIG PNH Registry	
1009-287	Female	Prior Eculizumab Treatment	29JUL2014	01OCT2023	Patient died	
1009-292	Female	Prior Eculizumab Treatment	10SEP2014	09AUG2024	Enrollment in the IPIG PNH Registry	
1009-298	Female	Prior Eculizumab Treatment	06NOV2014	19JUN2024	Enrollment in the IPIG PNH Registry	
1009-300	Female	Prior Eculizumab Treatment	18NOV2014	29NOV2024	Other	Site closure
1009-302	Female	Prior Eculizumab Treatment	11DEC2014	31MAY2024	Enrollment in the IPIG PNH Registry	
1009-318	Female	Prior Eculizumab Treatment	13MAY2015	24SEP2024	Enrollment in the IPIG PNH Registry	
1009-320	Male	Prior Eculizumab Treatment	21MAY2015	29JUL2024	Enrollment in the IPIG PNH Registry	

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Listing 1
Registry Discontinuation, Cumulative
Ravulizumab Study Population

Patient Number	Gender	Treatment Status[a]	Enrollment Date	Study Discontinuation Date	Primary Reason for Study Discontinuation	Other, Specify
1009-321	Male	Prior Eculizumab Treatment	21MAY2015	04DEC2023	Patient choice	
1009-323	Male	Prior Eculizumab Treatment	28MAY2015	21JUN2021	Patient enrolled in a clinical trial of PNH treatment	
1009-327	Female	Prior Eculizumab Treatment	24JUN2015	15DEC2022	Patient died	
1009-328	Male	Prior Eculizumab Treatment	07JUL2015	31OCT2023	Patient enrolled in a clinical trial of PNH treatment	
1009-329	Female	Prior Eculizumab Treatment	07JUL2015	26JUL2024	Enrollment in the IPIG PNH Registry	
1009-332	Female	Prior Eculizumab Treatment	21JUL2015	21MAY2024	Enrollment in the IPIG PNH Registry	
1009-346	Female	Prior Eculizumab Treatment Unknown	20OCT2015	29NOV2024	Other	Site closure
1009-353	Female	Prior Eculizumab Treatment	12APR2016	29NOV2024	Other	Site closure
1009-362	Female	Prior Eculizumab Treatment	02JUN2016	01AUG2024	Enrollment in the IPIG PNH Registry	
1009-366	Male	Prior Eculizumab Treatment	05AUG2016	17SEP2024	Enrollment in the IPIG PNH Registry	

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Listing 1
Registry Discontinuation, Cumulative
Ravulizumab Study Population

Patient Number	Gender	Treatment Status[a]	Enrollment Date	Study Discontinuation Date	Primary Reason for Study Discontinuation	Other, Specify
1009-369	Male	Prior Eculizumab Treatment	14JUL2016	03OCT2024	Enrollment in the IPIG PNH Registry	
1009-372	Female	Without Prior Eculizumab Treatment	09AUG2016	26SEP2024	Enrollment in the IPIG PNH Registry	
1009-379	Female	Without Prior Eculizumab Treatment	13SEP2016	05JUN2024	Enrollment in the IPIG PNH Registry	
1009-383	Male	Prior Eculizumab Treatment	29SEP2016	29NOV2024	Other	Site closure
1009-385	Female	Prior Eculizumab Treatment	01NOV2016	15OCT2024	Enrollment in the IPIG PNH Registry	
1009-386	Male	Without Prior Eculizumab Treatment	01NOV2016	26JUL2024	Enrollment in the IPIG PNH Registry	
1009-390	Female	Prior Eculizumab Treatment	29DEC2016	19SEP2024	Enrollment in the IPIG PNH Registry	
1009-405	Female	Prior Eculizumab Treatment	02MAY2017	18JUL2024	Enrollment in the IPIG PNH Registry	
1009-409	Male	Prior Eculizumab Treatment	13JUN2017	17OCT2024	Enrollment in the IPIG PNH Registry	

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Listing 1
Registry Discontinuation, Cumulative
Ravulizumab Study Population

Patient Number	Gender	Treatment Status[a]	Enrollment Date	Study Discontinuation Date	Primary Reason for Study Discontinuation	Other, Specify
1009-410	Male	Without Prior Eculizumab Treatment	20JUN2017	09JUN2023	Patient died	
1009-411	Male	Without Prior Eculizumab Treatment	03AUG2017	01OCT2024	Enrollment in the IPIG PNH Registry	
1009-413	Male	Prior Eculizumab Treatment	22AUG2017	19AUG2024	Enrollment in the IPIG PNH Registry	
1009-418	Female	Prior Eculizumab Treatment	12OCT2017	29NOV2024	Other	Site closure
1009-420	Male	Without Prior Eculizumab Treatment	31OCT2017	05MAR2024	Patient died	
1009-422	Male	Prior Eculizumab Treatment	09NOV2017	02JUL2024	Enrollment in the IPIG PNH Registry	
1009-427	Male	Prior Eculizumab Treatment	09JAN2019	07JUL2022	Patient died	
1009-429	Female	Prior Eculizumab Treatment	21MAR2019	06JUL2023	Patient enrolled in a clinical trial of PNH treatment	
1009-431	Female	Prior Eculizumab Treatment	21JUN2019	27AUG2024	Enrollment in the IPIG PNH Registry	

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Listing 1
Registry Discontinuation, Cumulative
Ravulizumab Study Population

Patient Number	Gender	Treatment Status[a]	Enrollment Date	Study Discontinuation Date	Primary Reason for Study Discontinuation	Other, Specify
1009-432	Female	Prior Eculizumab Treatment	23JUL2019	23JUL2024	Enrollment in the IPIG PNH Registry	
1009-433	Male	Prior Eculizumab Treatment	13AUG2019	29NOV2024	Other	Site closure
1009-434	Female	Prior Eculizumab Treatment	09SEP2019	09JUL2024	Enrollment in the IPIG PNH Registry	
1009-438	Male	Prior Eculizumab Treatment	22JUN2020	26NOV2024	Enrollment in the IPIG PNH Registry	
1009-441	Male	Prior Eculizumab Treatment	16FEB2021	15AUG2024	Enrollment in the IPIG PNH Registry	
1009-442	Male	Prior Eculizumab Treatment	03MAR2021	20JUN2024	Enrollment in the IPIG PNH Registry	
1009-443	Female	Prior Eculizumab Treatment	12MAR2021	20SEP2022	Other	Patient discharged from Service
1009-459	Female	Without Prior Eculizumab Treatment	14NOV2022	23SEP2024	Enrollment in the IPIG PNH Registry	
1009-460	Male	Without Prior Eculizumab Treatment	06JAN2023	13AUG2024	Enrollment in the IPIG PNH Registry	
1013-001	Female	Prior Eculizumab Treatment	19MAY2005	17OCT2023	Patient enrolled in a clinical trial of PNH treatment	

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Listing 1
Registry Discontinuation, Cumulative
Ravulizumab Study Population

Patient Number	Gender	Treatment Status[a]	Enrollment Date	Study Discontinuation Date	Primary Reason for Study Discontinuation	Other, Specify
1013-049	Female	Prior Eculizumab Treatment	26FEB2009	14SEP2021	Patient enrolled in a clinical trial of PNH treatment	
1013-081	Male	Without Prior Eculizumab Treatment	22AUG2010	15MAY2021	Patient received a bone marrow transplant	
1013-100	Female	Prior Eculizumab Treatment	08FEB2012	05APR2024	Other	Site closure
1013-133	Female	Prior Eculizumab Treatment	29JAN2014	29NOV2023	Patient died	
1013-145	Male	Prior Eculizumab Treatment	13AUG2014	16FEB2022	Patient died	
1013-156	Female	Prior Eculizumab Treatment	14JAN2015	14DEC2021	Other	patient is enrolled in a study for PNH therapy
1013-228	Female	Prior Eculizumab Treatment	05NOV2019	14MAY2024	Enrollment in the IPIG PNH Registry	
1013-243	Male	Prior Eculizumab Treatment	08MAR2022	15NOV2023	Patient enrolled in a clinical trial of PNH treatment	
1017-002	Male	Prior Eculizumab Treatment	05SEP2012	29FEB2024	Other	Site close
1017-009	Female	Prior Eculizumab Treatment	13SEP2012	29FEB2024	Other	Site close

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Listing 1
Registry Discontinuation, Cumulative
Ravulizumab Study Population

Patient Number	Gender	Treatment Status[a]	Enrollment Date	Study Discontinuation Date	Primary Reason for Study Discontinuation	Other, Specify
1017-022	Male	Prior Eculizumab Treatment	13JUN2019	29FEB2024	Other	Site close
1017-023	Female	Prior Eculizumab Treatment	27NOV2019	29FEB2024	Other	Site close
1030-007	Male	Without Prior Eculizumab Treatment	05JUN2017	11NOV2023	Patient died	
1030-010	Male	Prior Eculizumab Treatment Unknown	14FEB2023	01JUL2023	Other	lost to follow up
1036-001	Female	Prior Eculizumab Treatment	10JAN2006	10JUL2023	Patient enrolled in a clinical trial of PNH treatment	
1036-002	Female	Prior Eculizumab Treatment	04OCT2011	08APR2022	Patient enrolled in a clinical trial of PNH treatment	
1048-001	Female	Prior Eculizumab Treatment	30MAY2006	13NOV2024	Enrollment in the IPIG PNH Registry	
1048-011	Female	Without Prior Eculizumab Treatment	21DEC2011	29NOV2024	Other	Site closure
1048-020	Female	Prior Eculizumab Treatment	06JAN2014	29NOV2024	Other	Site closure

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Listing 1
Registry Discontinuation, Cumulative
Ravulizumab Study Population

Patient Number	Gender	Treatment Status[a]	Enrollment Date	Study Discontinuation Date	Primary Reason for Study Discontinuation	Other, Specify
1050-001	Female	Prior Eculizumab Treatment	23OCT2006	24MAY2022	Other	Site Closure due to USOR not amending budget/contract to the FMV (Fair Market Value) contract requested by Alexion.
1053-003	Male	Prior Eculizumab Treatment	15MAR2012	24JAN2023	Other	Study Closure
1053-004	Female	Prior Eculizumab Treatment Unknown	22MAY2012	26JAN2023	Other	study closure
1061-004	Male	Prior Eculizumab Treatment	26MAR2007	08APR2024	Enrollment in the IPIG PNH Registry	
1061-008	Male	Prior Eculizumab Treatment	23APR2019	15APR2022	Patient died	
1087-001	Male	Prior Eculizumab Treatment	15MAY2013	09MAY2024	Other	Study termination by sponsor
1087-014	Male	Without Prior Eculizumab Treatment	19MAR2019	09MAY2024	Other	Study termination by sponsor
1093-011	Female	Prior Eculizumab Treatment	09NOV2010	22AUG2022	Other	Lost to FUP
1093-017	Female	Prior Eculizumab Treatment Unknown	08OCT2010	10APR2024	Enrollment in the IPIG PNH Registry	

Note: (a) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.

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Listing 1
Registry Discontinuation, Cumulative
Ravulizumab Study Population

Patient Number	Gender	Treatment Status[a]	Enrollment Date	Study Discontinuation Date	Primary Reason for Study Discontinuation	Other, Specify
1093-024	Female	Prior Eculizumab Treatment	17NOV2010	23MAR2023	Other	Lost to FUP
1093-030	Female	Prior Eculizumab Treatment	03NOV2010	23APR2021	Patient received a bone marrow transplant	
1093-033	Female	Prior Eculizumab Treatment	25JAN2011	08JUN2021	Patient enrolled in a clinical trial of PNH treatment	
1093-042	Male	Prior Eculizumab Treatment Unknown	26APR2011	11JAN2023	Other	Lost to FUP
1093-043	Male	Prior Eculizumab Treatment	10MAY2011	10APR2024	Enrollment in the IPIG PNH Registry	
1093-046	Female	Without Prior Eculizumab Treatment	26JUL2011	05JUN2024	Enrollment in the IPIG PNH Registry	
1093-053	Female	Prior Eculizumab Treatment Unknown	22NOV2011	10APR2024	Other	Lost to FUP
1093-060	Female	Prior Eculizumab Treatment	07AUG2012	10APR2024	Enrollment in the IPIG PNH Registry	
1093-068	Male	Prior Eculizumab Treatment Unknown	13FEB2013	10APR2024	Enrollment in the IPIG PNH Registry	
1093-086	Female	Prior Eculizumab Treatment Unknown	08OCT2013	10APR2024	Enrollment in the IPIG PNH Registry	

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Listing 1
Registry Discontinuation, Cumulative
Ravulizumab Study Population

Patient Number	Gender	Treatment Status[a]	Enrollment Date	Study Discontinuation Date	Primary Reason for Study Discontinuation	Other, Specify
1093-089	Female	Without Prior Eculizumab Treatment	07JAN2014	18APR2024	Other	Site closure
1093-091	Female	Prior Eculizumab Treatment Unknown	28JAN2014	15JUL2017	Patient enrolled in a clinical trial of PNH treatment	
1093-092	Male	Without Prior Eculizumab Treatment	30JAN2014	27SEP2019	Patient choice	
1093-105	Male	Prior Eculizumab Treatment	18AUG2014	10APR2024	Enrollment in the IPIG PNH Registry	
1093-109	Female	Prior Eculizumab Treatment	28OCT2014	23JAN2024	Patient died	
1093-115	Male	Prior Eculizumab Treatment	28NOV2014	10APR2024	Enrollment in the IPIG PNH Registry	
1093-122	Female	Prior Eculizumab Treatment Unknown	17FEB2015	04MAY2021	Other	Lost to FUP
1093-130	Male	Prior Eculizumab Treatment	23APR2015	23MAY2024	Enrollment in the IPIG PNH Registry	
1093-131	Male	Prior Eculizumab Treatment Unknown	04MAY2015	24NOV2020	Patient received a bone marrow transplant	
1093-137	Male	Prior Eculizumab Treatment Unknown	08JUL2015	29APR2024	Other	Changement to IPIC-Registry

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Listing 1
Registry Discontinuation, Cumulative
Ravulizumab Study Population

Patient Number	Gender	Treatment Status[a]	Enrollment Date	Study Discontinuation Date	Primary Reason for Study Discontinuation	Other, Specify
1093-138	Male	Prior Eculizumab Treatment Unknown	10JUL2015	15MAY2024	Enrollment in the IPIG PNH Registry	
1093-140	Male	Without Prior Eculizumab Treatment	19JUL2015	03MAY2024	Enrollment in the IPIG PNH Registry	
1093-153	Female	Without Prior Eculizumab Treatment	19JAN2016	02MAY2024	Enrollment in the IPIG PNH Registry	
1093-171	Male	Prior Eculizumab Treatment Unknown	27NOV2016	15APR2024	Enrollment in the IPIG PNH Registry	
1093-186	Male	Prior Eculizumab Treatment Unknown	04AUG2017	17JUL2024	Enrollment in the IPIG PNH Registry	
1093-191	Female	Prior Eculizumab Treatment	06OCT2017	22MAY2024	Enrollment in the IPIG PNH Registry	
1093-192	Male	Without Prior Eculizumab Treatment	24OCT2017	02MAY2023	Patient died	
1093-204	Male	Without Prior Eculizumab Treatment	13FEB2018	13JAN2020	Other	Lost to FUP
1093-215	Male	Prior Eculizumab Treatment Unknown	08JAN2019	25MAR2022	Patient died	

Note: (a) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.

Source: ADAM.ADSL, ADAM.ADPOP
Run Date: 2025-05-14T14:46:00
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ravuema202501/Files/listings/production/programs/l1_regdis_cum.sas

Listing 1
Registry Discontinuation, Cumulative
Ravulizumab Study Population

Patient Number	Gender	Treatment Status[a]	Enrollment Date	Study Discontinuation Date	Primary Reason for Study Discontinuation	Other, Specify
1093-222	Male	Without Prior Eculizumab Treatment	11DEC2018	23APR2024	Enrollment in the IPIG PNH Registry	
1093-248	Male	Without Prior Eculizumab Treatment	10MAR2020	24APR2024	Enrollment in the IPIG PNH Registry	
1093-249	Male	Prior Eculizumab Treatment Unknown	23MAR2020	01MAR2024	Enrollment in the IPIG PNH Registry	
1093-253	Male	Without Prior Eculizumab Treatment	26JUN2020	11NOV2023	Patient died	
1093-254	Male	Without Prior Eculizumab Treatment	23JUN2020	17APR2024	Enrollment in the IPIG PNH Registry	
1093-260	Female	Prior Eculizumab Treatment Unknown	24JUL2020	07MAR2022	Other	Lost to FUP
1093-284	Female	Prior Eculizumab Treatment Unknown	01MAR2023	06MAY2024	Enrollment in the IPIG PNH Registry	
1094-006	Female	Prior Eculizumab Treatment	29MAY2014	05FEB2022	Patient is being treated by another physician	
1106-034	Male	Prior Eculizumab Treatment Unknown	26MAR2015	05APR2023	Other	study closure

Note: (a) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.

Source: ADAM.ADSL, ADAM.ADPOP
Run Date: 2025-05-14T14:46:00
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ravuema202501/Files/listings/production/programs/l1_regdis_cum.sas

Listing 1
Registry Discontinuation, Cumulative
Ravulizumab Study Population

Patient Number	Gender	Treatment Status[a]	Enrollment Date	Study Discontinuation Date	Primary Reason for Study Discontinuation	Other, Specify
1130-017	Female	Prior Eculizumab Treatment Unknown	29MAY2019	29MAY2024	Other	Study closure by sponsor
1130-018	Male	Prior Eculizumab Treatment Unknown	14NOV2019	29MAY2024	Other	Study closure by study sponsor.
1134-002	Female	Without Prior Eculizumab Treatment	28APR2009	31MAY2024	Other	Site closure
1134-009	Female	Prior Eculizumab Treatment Unknown	06MAY2009	31MAY2024	Other	Site closure
1134-019	Male	Without Prior Eculizumab Treatment	23MAY2009	31MAY2024	Other	Site closure
1134-024	Male	Without Prior Eculizumab Treatment	03JUN2009	31MAY2024	Other	Site closure
1134-025	Male	Without Prior Eculizumab Treatment	05JUN2009	31MAY2024	Other	Site closure
1134-044	Male	Without Prior Eculizumab Treatment	09SEP2009	31MAY2024	Other	site closure

Note: (a) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.

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Listing 1
Registry Discontinuation, Cumulative
Ravulizumab Study Population

Patient Number	Gender	Treatment Status[a]	Enrollment Date	Study Discontinuation Date	Primary Reason for Study Discontinuation	Other, Specify
1134-050	Male	Without Prior Eculizumab Treatment	02NOV2009	30JUN2024	Other	Site closure
1134-052	Female	Prior Eculizumab Treatment Unknown	22FEB2010	31MAY2024	Other	site closure
1134-055	Male	Without Prior Eculizumab Treatment	05MAR2010	31MAY2024	Other	site closure
1134-056	Female	Without Prior Eculizumab Treatment	20MAR2010	31MAY2024	Other	site closure
1134-062	Female	Without Prior Eculizumab Treatment	28JUN2010	31MAY2024	Other	site closure
1134-063	Male	Without Prior Eculizumab Treatment	26JUL2010	31MAY2024	Other	site closure
1134-069	Male	Without Prior Eculizumab Treatment	22OCT2010	31MAY2024	Other	site closure
1134-084	Female	Prior Eculizumab Treatment Unknown	27JUL2011	31MAY2024	Other	site closure

Note: (a) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.

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Listing 1
Registry Discontinuation, Cumulative
Ravulizumab Study Population

Patient Number	Gender	Treatment Status[a]	Enrollment Date	Study Discontinuation Date	Primary Reason for Study Discontinuation	Other, Specify
1134-088	Female	Without Prior Eculizumab Treatment	09JAN2012	31MAY2024	Other	site closure
1134-100	Female	Without Prior Eculizumab Treatment	31MAY2013	31MAY2024	Other	site closure
1134-111	Male	Without Prior Eculizumab Treatment	26SEP2014	31JAN2024	Patient died	
1134-114	Male	Prior Eculizumab Treatment Unknown	22JAN2015	31MAY2024	Other	site closure
1134-116	Female	Without Prior Eculizumab Treatment	05FEB2015	31MAY2024	Other	site closure
1134-120	Female	Without Prior Eculizumab Treatment	04AUG2015	31MAY2024	Other	site closure
1134-124	Male	Without Prior Eculizumab Treatment	11FEB2016	31MAY2024	Other	site closure
1134-135	Male	Without Prior Eculizumab Treatment	03MAY2018	31MAY2024	Other	site closure

Note: (a) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.

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Listing 1
Registry Discontinuation, Cumulative
Ravulizumab Study Population

Patient Number	Gender	Treatment Status[a]	Enrollment Date	Study Discontinuation Date	Primary Reason for Study Discontinuation	Other, Specify
1134-136	Female	Prior Eculizumab Treatment Unknown	05AUG2018	31MAY2024	Other	site closure
1134-140	Male	Without Prior Eculizumab Treatment	13MAR2019	31MAY2024	Other	site closure
1134-143	Female	Without Prior Eculizumab Treatment	12DEC2019	31MAY2024	Other	site closure
1134-146	Female	Without Prior Eculizumab Treatment	08JUN2021	31MAY2024	Other	site closure
1134-148	Male	Without Prior Eculizumab Treatment	09MAY2022	31MAY2024	Other	site closure
1139-002	Female	Prior Eculizumab Treatment	13JUL2009	02OCT2024	Enrollment in the IPIG PNH Registry	
1139-007	Male	Prior Eculizumab Treatment	03AUG2009	14JUN2024	Enrollment in the IPIG PNH Registry	
1139-013	Female	Prior Eculizumab Treatment	27JAN2010	14JUN2024	Enrollment in the IPIG PNH Registry	
1139-029	Female	Prior Eculizumab Treatment Unknown	05OCT2011	14JUN2024	Enrollment in the IPIG PNH Registry	

Note: (a) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.

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Listing 1
Registry Discontinuation, Cumulative
Ravulizumab Study Population

Patient Number	Gender	Treatment Status[a]	Enrollment Date	Study Discontinuation Date	Primary Reason for Study Discontinuation	Other, Specify
1139-031	Male	Prior Eculizumab Treatment	24OCT2014	14JUN2024	Enrollment in the IPIG PNH Registry	
1139-042	Male	Prior Eculizumab Treatment	20AUG2019	14JUN2024	Enrollment in the IPIG PNH Registry	
1140-001	Male	Without Prior Eculizumab Treatment	29JUL2009	08MAY2024	Other	Site closing
1140-002	Male	Prior Eculizumab Treatment	02NOV2010	08MAY2024	Other	Study site closing
1151-002	Female	Without Prior Eculizumab Treatment	06SEP2010	30MAY2024	Other	site closure
1151-006	Female	Without Prior Eculizumab Treatment	11OCT2010	30MAY2024	Other	site closure
1151-011	Female	Without Prior Eculizumab Treatment	18MAY2011	30MAY2024	Other	site closure
1151-014	Male	Prior Eculizumab Treatment	11APR2012	30MAY2024	Other	site closure
1152-001	Female	Prior Eculizumab Treatment	16OCT2010	05JUN2024	Other	site closure

Note: (a) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.

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Listing 1
Registry Discontinuation, Cumulative
Ravulizumab Study Population

Patient Number	Gender	Treatment Status[a]	Enrollment Date	Study Discontinuation Date	Primary Reason for Study Discontinuation	Other, Specify
1152-002	Male	Prior Eculizumab Treatment	26APR2011	05JUN2024	Other	site closure
1163-001	Female	Without Prior Eculizumab Treatment	20JAN2010	19MAR2024	Other	study closure
1163-003	Female	Without Prior Eculizumab Treatment	18MAY2011	19MAR2024	Other	study closure
1163-018	Female	Prior Eculizumab Treatment	16AUG2018	19MAR2024	Other	study closure
1163-024	Female	Without Prior Eculizumab Treatment	19DEC2020	19MAR2024	Other	study closure
1163-027	Male	Prior Eculizumab Treatment	02JUN2022	19MAR2024	Other	study closure
1164-001	Male	Without Prior Eculizumab Treatment	12JAN2010	21MAY2024	Other	FIN d'étude HPN. Patient prévenu par téléphone, message. Mail envoyé
1164-002	Female	Without Prior Eculizumab Treatment	13JAN2010	04APR2024	Other	SPONSOR DECISION

Note: (a) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.

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Listing 1
Registry Discontinuation, Cumulative
Ravulizumab Study Population

Patient Number	Gender	Treatment Status[a]	Enrollment Date	Study Discontinuation Date	Primary Reason for Study Discontinuation	Other, Specify
1164-003	Male	Without Prior Eculizumab Treatment	13JAN2010	30MAY2024	Other	SPONSOR DECISION
1164-007	Male	Without Prior Eculizumab Treatment	19JAN2010	04APR2024	Other	SPONSOR DECISION
1165-010	Female	Without Prior Eculizumab Treatment	19JAN2021	15MAY2024	Other	Site closure.
1169-001	Female	Prior Eculizumab Treatment	17MAR2010	15APR2024	Other	site closure
1169-003	Female	Prior Eculizumab Treatment	07JUL2010	15APR2024	Other	site closure
1169-004	Female	Prior Eculizumab Treatment	16JUL2010	15APR2024	Other	site closure
1169-006	Male	Prior Eculizumab Treatment	27JUL2010	15APR2024	Other	site closure
1169-008	Male	Prior Eculizumab Treatment	12SEP2012	15APR2024	Other	site closure
1170-002	Female	Prior Eculizumab Treatment	18JAN2010	09APR2024	Other	site closure
1170-003	Male	Prior Eculizumab Treatment	01MAR2010	09APR2024	Other	site closure

Note: (a) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.

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Listing 1
Registry Discontinuation, Cumulative
Ravulizumab Study Population

Patient Number	Gender	Treatment Status[a]	Enrollment Date	Study Discontinuation Date	Primary Reason for Study Discontinuation	Other, Specify
1170-006	Male	Without Prior Eculizumab Treatment	14APR2012	09APR2024	Other	site closure
1170-009	Female	Prior Eculizumab Treatment	05JUN2013	09APR2024	Other	site closure
1192-001	Male	Prior Eculizumab Treatment Unknown	29APR2010	15MAY2024	Other	Site closure
1193-002	Male	Without Prior Eculizumab Treatment	23APR2010	15MAR2024	Other	End of PNH Registry
1193-008	Female	Without Prior Eculizumab Treatment	08MAR2012	15MAR2024	Other	End of PNH Registry
1193-015	Female	Without Prior Eculizumab Treatment	18MAY2021	15MAR2024	Other	End of PNH Registry
1193-017	Female	Without Prior Eculizumab Treatment	05OCT2022	15MAR2024	Other	End of PNH Registry
1193-018	Female	Without Prior Eculizumab Treatment	14MAR2023	06FEB2024	Patient died	

Note: (a) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.

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Listing 1
Registry Discontinuation, Cumulative
Ravulizumab Study Population

Patient Number	Gender	Treatment Status[a]	Enrollment Date	Study Discontinuation Date	Primary Reason for Study Discontinuation	Other, Specify
1197-020	Male	Without Prior Eculizumab Treatment	12JAN2012	08JAN2024		Site Closure
1197-027	Male	Prior Eculizumab Treatment	21JUN2018	13APR2023	Patient died	
1197-028	Female	Without Prior Eculizumab Treatment	19NOV2018	30OCT2023	Enrollment in the IPIG PNH Registry	
1197-029	Male	Without Prior Eculizumab Treatment	23NOV2020	30OCT2023	Patient enrolled in a clinical trial of PNH treatment	
1197-030	Male	Prior Eculizumab Treatment	22NOV2021	08APR2024	Enrollment in the IPIG PNH Registry	
1197-031	Male	Prior Eculizumab Treatment	29NOV2021	27OCT2023	Patient enrolled in a clinical trial of PNH treatment	
1200-004	Male	Prior Eculizumab Treatment	19JAN2011	03APR2024	Other	Site Closure
1200-005	Female	Prior Eculizumab Treatment	27JAN2011	03APR2024	Other	Site closure
1209-002	Male	Prior Eculizumab Treatment	17JUN2010	12MAR2024	Enrollment in the IPIG PNH Registry	

Note: (a) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.

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Listing 1
Registry Discontinuation, Cumulative
Ravulizumab Study Population

Patient Number	Gender	Treatment Status[a]	Enrollment Date	Study Discontinuation Date	Primary Reason for Study Discontinuation	Other, Specify
1209-003	Male	Without Prior Eculizumab Treatment	09SEP2010	14MAY2024	Enrollment in the IPIG PNH Registry	
1209-005	Male	Prior Eculizumab Treatment	15SEP2016	12MAR2024	Enrollment in the IPIG PNH Registry	
1210-026	Female	Without Prior Eculizumab Treatment	14OCT2013	09APR2024	Enrollment in the IPIG PNH Registry	
1214-005	Male	Prior Eculizumab Treatment	10OCT2012	29APR2024	Other	Sponsors decision for end of study, maybe enrollment into IPIG-PNH-registry in the future
1214-007	Male	Without Prior Eculizumab Treatment	04SEP2014	29APR2024	Other	Sponsors decision for end of study, maybe enrollment into IPIG-PNH-registry in the future
1214-009	Female	Without Prior Eculizumab Treatment	17NOV2020	30APR2024	Other	Sponsors decision for end of study, maybe enrollment into IPIG-PNH-registry in the future
1219-003	Female	Prior Eculizumab Treatment	12SEP2013	15APR2024	Other	site closure
1226-001	Male	Prior Eculizumab Treatment Unknown	04JUN2010	10SEP2024	Other	Due to Study Closure

Note: (a) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.

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Listing 1
Registry Discontinuation, Cumulative
Ravulizumab Study Population

Patient Number	Gender	Treatment Status[a]	Enrollment Date	Study Discontinuation Date	Primary Reason for Study Discontinuation	Other, Specify
1226-003	Female	Prior Eculizumab Treatment Unknown	06SEP2010	10SEP2024	Other	Due to study closure
1232-001	Female	Prior Eculizumab Treatment Unknown	17JUL2010	12MAR2024	Other	Registry closure, site will not be participating in IPIG PNH Registry
1232-005	Male	Prior Eculizumab Treatment Unknown	16JAN2017	12MAR2024	Other	Registry discontinuation, Site not participating in IPIG PNH Registry
1236-002	Female	Prior Eculizumab Treatment	17FEB2012	05APR2024	Other	Site closure
1236-003	Male	Without Prior Eculizumab Treatment	21JUN2009	05APR2024	Other	Site closure
1250-001	Female	Without Prior Eculizumab Treatment	01FEB2011	01JUL2024	Other	site closure
1250-003	Female	Without Prior Eculizumab Treatment	03MAY2011	24JUN2024	Other	site closure
1251-001	Male	Prior Eculizumab Treatment	21DEC2010	22MAY2024	Enrollment in the IPIG PNH Registry	

Note: (a) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.

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Listing 1
Registry Discontinuation, Cumulative
Ravulizumab Study Population

Patient Number	Gender	Treatment Status[a]	Enrollment Date	Study Discontinuation Date	Primary Reason for Study Discontinuation	Other, Specify
1251-002	Male	Without Prior Eculizumab Treatment	29DEC2010	22MAY2024	Enrollment in the IPIG PNH Registry	
1251-005	Female	Prior Eculizumab Treatment	06APR2016	22MAY2024	Enrollment in the IPIG PNH Registry	
1251-009	Male	Prior Eculizumab Treatment	19FEB2020	22MAY2024	Enrollment in the IPIG PNH Registry	
1252-001	Male	Prior Eculizumab Treatment	21SEP2010	04MAY2023	Other	Investigator decision
1252-002	Male	Prior Eculizumab Treatment	28SEP2010	04MAY2023	Other	Investigator decision
1252-035	Female	Prior Eculizumab Treatment	08OCT2015	04MAY2023	Other	Investigator decision
1252-038	Female	Prior Eculizumab Treatment Unknown	23AUG2016	04MAY2023	Other	Investigator decision
1252-041	Male	Without Prior Eculizumab Treatment	02MAR2021	04MAY2023	Other	Investigator decision
1262-002	Male	Prior Eculizumab Treatment	02FEB2011	05MAR2024	Other	site closure
1262-004	Male	Prior Eculizumab Treatment	14MAR2013	05MAR2024	Other	site closure

Note: (a) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.

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Listing 1
Registry Discontinuation, Cumulative
Ravulizumab Study Population

Patient Number	Gender	Treatment Status[a]	Enrollment Date	Study Discontinuation Date	Primary Reason for Study Discontinuation	Other, Specify
1266-001	Male	Without Prior Eculizumab Treatment	05JAN2011	29APR2024	Other	End of PNH Registry
1266-002	Female	Without Prior Eculizumab Treatment	05JAN2011	30APR2024	Other	End of PNH Registry
1266-005	Male	Without Prior Eculizumab Treatment	02MAR2011	30APR2024	Other	End of PNH Registry
1268-028	Female	Prior Eculizumab Treatment	23MAY2011	04JUL2024	Enrollment in the IPIG PNH Registry	
1268-030	Male	Prior Eculizumab Treatment Unknown	06JUN2011	04JUL2024	Enrollment in the IPIG PNH Registry	
1268-031	Male	Prior Eculizumab Treatment Unknown	10MAY2011	04JUL2024	Enrollment in the IPIG PNH Registry	
1268-049	Female	Prior Eculizumab Treatment Unknown	11OCT2011	04JUL2024	Enrollment in the IPIG PNH Registry	
1268-057	Female	Prior Eculizumab Treatment Unknown	03DEC2012	04JUL2024	Enrollment in the IPIG PNH Registry	
1268-058	Male	Prior Eculizumab Treatment Unknown	21MAY2012	04JUL2024	Enrollment in the IPIG PNH Registry	
1268-071	Female	Prior Eculizumab Treatment	04MAR2013	04JUL2024	Enrollment in the IPIG PNH Registry	

Note: (a) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.

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Listing 1
Registry Discontinuation, Cumulative
Ravulizumab Study Population

Patient Number	Gender	Treatment Status[a]	Enrollment Date	Study Discontinuation Date	Primary Reason for Study Discontinuation	Other, Specify
1268-076	Male	Prior Eculizumab Treatment	23JAN2013	04JUL2024	Enrollment in the IPIG PNH Registry	
1268-083	Female	Prior Eculizumab Treatment	17FEB2014	29NOV2024	Other	Site closure
1268-096	Male	Prior Eculizumab Treatment	13MAY2013	04JUL2024	Enrollment in the IPIG PNH Registry	
1268-103	Female	Without Prior Eculizumab Treatment	04JUN2014	04JUL2024	Enrollment in the IPIG PNH Registry	
1268-104	Female	Prior Eculizumab Treatment	16DEC2015	04JUL2024	Enrollment in the IPIG PNH Registry	
1268-106	Male	Without Prior Eculizumab Treatment	18JUN2014	04JUL2024	Enrollment in the IPIG PNH Registry	
1268-129	Male	Without Prior Eculizumab Treatment	29APR2015	04JUL2024	Enrollment in the IPIG PNH Registry	
1268-167	Female	Prior Eculizumab Treatment	13APR2016	12AUG2024	Enrollment in the IPIG PNH Registry	
1268-197	Female	Without Prior Eculizumab Treatment	20DEC2017	04JUL2024	Enrollment in the IPIG PNH Registry	

Note: (a) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.

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Listing 1
Registry Discontinuation, Cumulative
Ravulizumab Study Population

Patient Number	Gender	Treatment Status[a]	Enrollment Date	Study Discontinuation Date	Primary Reason for Study Discontinuation	Other, Specify
1268-219	Male	Prior Eculizumab Treatment Unknown	05MAR2018	04JUL2024	Enrollment in the IPIG PNH Registry	
1268-235	Male	Prior Eculizumab Treatment	25FEB2019	04JUL2024	Enrollment in the IPIG PNH Registry	
1268-255	Female	Prior Eculizumab Treatment	11SEP2019	04JUL2024	Enrollment in the IPIG PNH Registry	
1268-259	Male	Prior Eculizumab Treatment Unknown	24FEB2020	04JUL2024	Enrollment in the IPIG PNH Registry	
1268-262	Male	Prior Eculizumab Treatment Unknown	17FEB2020	04JUL2024	Enrollment in the IPIG PNH Registry	
1268-263	Female	Prior Eculizumab Treatment Unknown	07JUL2021	04JUL2024	Enrollment in the IPIG PNH Registry	
1268-264	Male	Without Prior Eculizumab Treatment	14JUL2021	04JUL2024	Enrollment in the IPIG PNH Registry	
1268-266	Male	Prior Eculizumab Treatment Unknown	06SEP2021	04JUL2024	Enrollment in the IPIG PNH Registry	
1268-270	Female	Prior Eculizumab Treatment	08SEP2021	04JUL2024	Enrollment in the IPIG PNH Registry	
1268-272	Male	Without Prior Eculizumab Treatment	08SEP2021	24FEB2022	Patient enrolled in a clinical trial of PNH treatment	

Note: (a) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.

Source: ADAM.ADSL, ADAM.ADPOP
Run Date: 2025-05-14T14:46:00
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Listing 1
Registry Discontinuation, Cumulative
Ravulizumab Study Population

Patient Number	Gender	Treatment Status[a]	Enrollment Date	Study Discontinuation Date	Primary Reason for Study Discontinuation	Other, Specify
1268-274	Male	Without Prior Eculizumab Treatment	22SEP2021	04JUL2024	Enrollment in the IPIG PNH Registry	
1268-275	Female	Without Prior Eculizumab Treatment	03AUG2021	04JUL2024	Enrollment in the IPIG PNH Registry	
1268-279	Female	Without Prior Eculizumab Treatment	19FEB2020	04JAN2024	Patient enrolled in a clinical trial of PNH treatment	
1269-001	Male	Prior Eculizumab Treatment	04FEB2011	05DEC2023	Other	Site closure
1269-003	Male	Prior Eculizumab Treatment	24APR2014	05DEC2023	Other	Site closure
1275-002	Female	Prior Eculizumab Treatment	12JAN2011	27MAR2024	Other	site closure
1304-001	Female	Prior Eculizumab Treatment	14MAY2011	11MAR2024	Enrollment in the IPIG PNH Registry	
1304-002	Male	Prior Eculizumab Treatment	10MAY2011	05MAR2024	Enrollment in the IPIG PNH Registry	
1304-003	Male	Without Prior Eculizumab Treatment	27JUL2011	25MAR2024	Enrollment in the IPIG PNH Registry	

Note: (a) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.

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Listing 1
Registry Discontinuation, Cumulative
Ravulizumab Study Population

Patient Number	Gender	Treatment Status[a]	Enrollment Date	Study Discontinuation Date	Primary Reason for Study Discontinuation	Other, Specify
1304-006	Female	Prior Eculizumab Treatment	26FEB2016	28FEB2024	Enrollment in the IPIG PNH Registry	
1319-001	Male	Prior Eculizumab Treatment	08JUN2005	29NOV2024	Other	Site closure
1341-011	Female	Without Prior Eculizumab Treatment	17SEP2015	03JUN2024	Enrollment in the IPIG PNH Registry	
1341-022	Female	Without Prior Eculizumab Treatment	27DEC2019	06JUN2024	Enrollment in the IPIG PNH Registry	
1351-003	Male	Without Prior Eculizumab Treatment	03FEB2017	23JUN2024	Enrollment in the IPIG PNH Registry	
1351-004	Male	Prior Eculizumab Treatment	21MAR2017	23JUN2024	Enrollment in the IPIG PNH Registry	
1351-013	Female	Prior Eculizumab Treatment	11JUN2018	23JUN2024	Enrollment in the IPIG PNH Registry	
1351-023	Female	Without Prior Eculizumab Treatment	29JUL2021	23JUN2024	Enrollment in the IPIG PNH Registry	
1358-001	Male	Prior Eculizumab Treatment Unknown	09JAN2013	21JUN2024	Enrollment in the IPIG PNH Registry	

Note: (a) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.

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Listing 1
Registry Discontinuation, Cumulative
Ravulizumab Study Population

Patient Number	Gender	Treatment Status[a]	Enrollment Date	Study Discontinuation Date	Primary Reason for Study Discontinuation	Other, Specify
1366-001	Male	Prior Eculizumab Treatment	25NOV2011	29FEB2024	Enrollment in the IPIG PNH Registry	
1366-020	Male	Prior Eculizumab Treatment	15MAR2012	29FEB2024	Enrollment in the IPIG PNH Registry	
1366-024	Male	Without Prior Eculizumab Treatment	28MAR2012	18JAN2024	Other	Patient is being treated by another physician. and the subject was newly diagnosed with MDS
1366-033	Female	Prior Eculizumab Treatment	14FEB2013	29FEB2024	Enrollment in the IPIG PNH Registry	
1366-036	Female	Prior Eculizumab Treatment	14MAR2013	29FEB2024	Enrollment in the IPIG PNH Registry	
1366-064	Female	Prior Eculizumab Treatment	18JUN2014	29FEB2024	Enrollment in the IPIG PNH Registry	
1366-075	Female	Prior Eculizumab Treatment	31DEC2014	09DEC2021	Patient enrolled in a clinical trial of PNH treatment	
1366-097	Male	Prior Eculizumab Treatment	21SEP2016	29FEB2024	Enrollment in the IPIG PNH Registry	
1366-108	Female	Prior Eculizumab Treatment	26APR2018	29FEB2024	Enrollment in the IPIG PNH Registry	
1366-111	Male	Prior Eculizumab Treatment	29OCT2018	29FEB2024	Enrollment in the IPIG PNH Registry	

Note: (a) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.

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Listing 1
Registry Discontinuation, Cumulative
Ravulizumab Study Population

Patient Number	Gender	Treatment Status[a]	Enrollment Date	Study Discontinuation Date	Primary Reason for Study Discontinuation	Other, Specify
1366-129	Female	Prior Eculizumab Treatment	22APR2020	29FEB2024	Enrollment in the IPIG PNH Registry	
1366-148	Male	Without Prior Eculizumab Treatment	29MAR2021	29FEB2024	Enrollment in the IPIG PNH Registry	
1366-162	Male	Without Prior Eculizumab Treatment	10AUG2022	29FEB2024	Enrollment in the IPIG PNH Registry	
1366-172	Male	Without Prior Eculizumab Treatment	04MAY2023	29FEB2024	Enrollment in the IPIG PNH Registry	
1366-173	Female	Without Prior Eculizumab Treatment	10MAY2023	29FEB2024	Enrollment in the IPIG PNH Registry	
1381-002	Male	Prior Eculizumab Treatment	15MAR2012	20FEB2024	Other	study closing
1381-003	Female	Prior Eculizumab Treatment	18APR2012	06DEC2023	Other	study closing
1381-008	Male	Prior Eculizumab Treatment	14MAY2015	08FEB2024	Other	study closing
1381-012	Male	Prior Eculizumab Treatment Unknown	29AUG2019	24APR2023	Other	study closing

Note: (a) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.

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Listing 1
Registry Discontinuation, Cumulative
Ravulizumab Study Population

Patient Number	Gender	Treatment Status[a]	Enrollment Date	Study Discontinuation Date	Primary Reason for Study Discontinuation	Other, Specify
1381-014	Male	Without Prior Eculizumab Treatment	20JAN2020	11MAR2024	Other	study closing
1381-016	Male	Prior Eculizumab Treatment Unknown	17JUN2021	23FEB2024	Other	study closing
1381-017	Male	Prior Eculizumab Treatment	10AUG2021	18DEC2023	Other	study closing
1416-001	Male	Prior Eculizumab Treatment	11JUN2013	15APR2024	Enrollment in the IPIG PNH Registry	
1418-009	Female	Prior Eculizumab Treatment	25OCT2012	28MAR2024	Enrollment in the IPIG PNH Registry	
1418-042	Female	Without Prior Eculizumab Treatment	05SEP2017	24MAY2024	Enrollment in the IPIG PNH Registry	
1418-045	Female	Prior Eculizumab Treatment	02OCT2017	24MAY2024	Enrollment in the IPIG PNH Registry	
1418-064	Male	Without Prior Eculizumab Treatment	08NOV2022	24MAY2024	Enrollment in the IPIG PNH Registry	
1419-009	Female	Prior Eculizumab Treatment	28APR2016	12APR2024	Other	Enrollment in the IPIG

Note: (a) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.

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Listing 1
Registry Discontinuation, Cumulative
Ravulizumab Study Population

Patient Number	Gender	Treatment Status[a]	Enrollment Date	Study Discontinuation Date	Primary Reason for Study Discontinuation	Other, Specify
1420-002	Male	Without Prior Eculizumab Treatment	15MAY2012	22APR2024	Enrollment in the IPIG PNH Registry	
1420-004	Male	Prior Eculizumab Treatment	12JUN2012	22APR2024	Enrollment in the IPIG PNH Registry	
1420-006	Female	Prior Eculizumab Treatment	31JUL2012	22APR2024	Enrollment in the IPIG PNH Registry	
1420-009	Male	Prior Eculizumab Treatment	23APR2013	22APR2024	Enrollment in the IPIG PNH Registry	
1421-008	Male	Prior Eculizumab Treatment	04DEC2012	06MAR2024	Enrollment in the IPIG PNH Registry	
1421-009	Male	Without Prior Eculizumab Treatment	04JAN2013	06MAR2024	Enrollment in the IPIG PNH Registry	
1421-024	Male	Without Prior Eculizumab Treatment	26JAN2017	06MAR2024	Enrollment in the IPIG PNH Registry	
1421-029	Female	Without Prior Eculizumab Treatment	02NOV2018	06MAR2024	Enrollment in the IPIG PNH Registry	
1421-031	Male	Without Prior Eculizumab Treatment	07NOV2019	26JUN2022	Patient choice	

Note: (a) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.

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Listing 1
Registry Discontinuation, Cumulative
Ravulizumab Study Population

Patient Number	Gender	Treatment Status[a]	Enrollment Date	Study Discontinuation Date	Primary Reason for Study Discontinuation	Other, Specify
1421-035	Male	Without Prior Eculizumab Treatment	06FEB2024	06MAR2024	Enrollment in the IPIG PNH Registry	
1422-004	Male	Prior Eculizumab Treatment	20NOV2012	04APR2024	Enrollment in the IPIG PNH Registry	
1422-008	Male	Prior Eculizumab Treatment	30JAN2013	04APR2024	Enrollment in the IPIG PNH Registry	
1422-011	Female	Prior Eculizumab Treatment	20MAR2014	04APR2024	Enrollment in the IPIG PNH Registry	
1422-022	Female	Prior Eculizumab Treatment	19MAR2020	04APR2024	Enrollment in the IPIG PNH Registry	
1423-002	Female	Prior Eculizumab Treatment	23AUG2012	28MAR2024	Enrollment in the IPIG PNH Registry	
1423-006	Male	Prior Eculizumab Treatment	23DEC2014	28MAR2024	Enrollment in the IPIG PNH Registry	
1423-008	Male	Prior Eculizumab Treatment	18JUN2015	28MAR2024	Enrollment in the IPIG PNH Registry	
1423-011	Male	Prior Eculizumab Treatment	11NOV2015	28MAR2024	Enrollment in the IPIG PNH Registry	
1423-012	Male	Prior Eculizumab Treatment	07JAN2016	28MAR2024	Enrollment in the IPIG PNH Registry	

Note: (a) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.

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Listing 1
Registry Discontinuation, Cumulative
Ravulizumab Study Population

Patient Number	Gender	Treatment Status[a]	Enrollment Date	Study Discontinuation Date	Primary Reason for Study Discontinuation	Other, Specify
1423-014	Male	Prior Eculizumab Treatment	09JUN2017	28MAR2024	Enrollment in the IPIG PNH Registry	
1423-017	Female	Prior Eculizumab Treatment	12NOV2018	28MAR2024	Enrollment in the IPIG PNH Registry	
1423-018	Male	Prior Eculizumab Treatment	24SEP2019	28MAR2024	Enrollment in the IPIG PNH Registry	
1423-020	Male	Prior Eculizumab Treatment	27MAY2020	28MAR2024	Enrollment in the IPIG PNH Registry	
1423-024	Male	Without Prior Eculizumab Treatment	18NOV2021	28MAR2024	Enrollment in the IPIG PNH Registry	
1424-003	Female	Prior Eculizumab Treatment	31MAR2015	04APR2024	Enrollment in the IPIG PNH Registry	
1424-004	Male	Prior Eculizumab Treatment	24AUG2016	04APR2024	Enrollment in the IPIG PNH Registry	
1425-001	Male	Prior Eculizumab Treatment	11JAN2013	19SEP2023	Other	PNH clone 5.74%
1425-003	Male	Prior Eculizumab Treatment	21JUL2015	24APR2024	Other	site closure
1427-003	Female	Prior Eculizumab Treatment	08NOV2013	21FEB2024	Enrollment in the IPIG PNH Registry	

Note: (a) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.

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Listing 1
Registry Discontinuation, Cumulative
Ravulizumab Study Population

Patient Number	Gender	Treatment Status[a]	Enrollment Date	Study Discontinuation Date	Primary Reason for Study Discontinuation	Other, Specify
1429-001	Female	Prior Eculizumab Treatment Unknown	15NOV2012	04APR2024	Other	site closure
1429-007	Female	Prior Eculizumab Treatment	25SEP2020	04APR2024	Other	site closure
1429-011	Female	Without Prior Eculizumab Treatment	27JUL2021	11MAR2022	Patient died	
1432-001	Male	Prior Eculizumab Treatment	23AUG2012	29FEB2024	Other	site close
1432-003	Female	Prior Eculizumab Treatment	14JAN2016	29FEB2024	Other	site close
1432-004	Female	Without Prior Eculizumab Treatment	21JAN2016	29FEB2024	Other	site close
1432-005	Female	Prior Eculizumab Treatment	21JAN2016	29FEB2024	Other	site close
1432-009	Male	Prior Eculizumab Treatment Unknown	23DEC2019	29FEB2024	Other	site close
1435-002	Male	Without Prior Eculizumab Treatment	15AUG2012	29FEB2024	Other	site close

Note: (a) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.

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Listing 1
Registry Discontinuation, Cumulative
Ravulizumab Study Population

Patient Number	Gender	Treatment Status[a]	Enrollment Date	Study Discontinuation Date	Primary Reason for Study Discontinuation	Other, Specify
1435-005	Female	Without Prior Eculizumab Treatment	11SEP2012	29FEB2024	Other	site close
1435-006	Female	Without Prior Eculizumab Treatment	19SEP2012	29FEB2024	Other	site close
1435-012	Female	Without Prior Eculizumab Treatment	04NOV2021	29FEB2024	Other	site close
1454-001	Female	Prior Eculizumab Treatment	12NOV2012	29FEB2024	Other	site close
1454-002	Male	Prior Eculizumab Treatment	28FEB2013	29FEB2024	Other	Site close
1462-004	Male	Prior Eculizumab Treatment	30NOV2012	08FEB2024	Other	Site close
1462-006	Male	Prior Eculizumab Treatment	07DEC2012	08FEB2024	Other	Site close
1462-008	Male	Prior Eculizumab Treatment	14DEC2012	08FEB2024	Other	Site close
1462-009	Male	Prior Eculizumab Treatment	14DEC2012	08FEB2024	Other	Site close
1462-010	Male	Prior Eculizumab Treatment	21DEC2012	08FEB2024	Other	Site close

Note: (a) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.

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Listing 1
Registry Discontinuation, Cumulative
Ravulizumab Study Population

Patient Number	Gender	Treatment Status[a]	Enrollment Date	Study Discontinuation Date	Primary Reason for Study Discontinuation	Other, Specify
1493-002	Female	Prior Eculizumab Treatment	01MAR2013	29FEB2024	Other	Site close
1493-006	Female	Without Prior Eculizumab Treatment	25MAR2013	29FEB2024	Other	Site close
1493-020	Female	Without Prior Eculizumab Treatment	14MAR2022	29FEB2024	Other	Site close
1493-023	Male	Without Prior Eculizumab Treatment	14MAR2022	29FEB2024	Other	Site close
1493-028	Female	Without Prior Eculizumab Treatment	09NOV2022	29FEB2024	Other	Site close
1493-031	Male	Without Prior Eculizumab Treatment	13FEB2023	29FEB2024	Other	Site close
1493-032	Female	Without Prior Eculizumab Treatment	16FEB2023	29FEB2024	Other	Site close
1494-001	Male	Prior Eculizumab Treatment Unknown	16MAY2013	26MAR2024	Other	Sponsor decision to close this registry trial.

Note: (a) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.

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Listing 1
Registry Discontinuation, Cumulative
Ravulizumab Study Population

Patient Number	Gender	Treatment Status[a]	Enrollment Date	Study Discontinuation Date	Primary Reason for Study Discontinuation	Other, Specify
1494-002	Female	Without Prior Eculizumab Treatment	01AUG2013	26MAR2024	Other	Sponsor decision to close this registry trial.
1494-008	Female	Prior Eculizumab Treatment Unknown	14SEP2023	26MAR2024	Other	Sponsor decision to close this registry trial.
1494-011	Male	Without Prior Eculizumab Treatment	01JUN2023	26APR2024	Other	Sponsor decision to close this registry trial.
1506-010	Female	Without Prior Eculizumab Treatment	17NOV2015	29FEB2024	Other	Site close
1507-002	Male	Prior Eculizumab Treatment	24APR2013	29FEB2024	Other	site close
1507-003	Male	Prior Eculizumab Treatment	08MAY2013	29FEB2024	Other	site close
1507-007	Female	Without Prior Eculizumab Treatment	15MAY2013	29FEB2024	Other	site close
1507-012	Female	Prior Eculizumab Treatment	10JUL2013	29FEB2024	Other	site close
1507-015	Female	Without Prior Eculizumab Treatment	29OCT2018	29FEB2024	Other	site close

Note: (a) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.

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Listing 1
Registry Discontinuation, Cumulative
Ravulizumab Study Population

Patient Number	Gender	Treatment Status[a]	Enrollment Date	Study Discontinuation Date	Primary Reason for Study Discontinuation	Other, Specify
1520-003	Male	Prior Eculizumab Treatment	06JAN2014	29FEB2024	Other	site close
1520-008	Male	Without Prior Eculizumab Treatment	04APR2014	29FEB2024	Other	site close
1520-009	Female	Prior Eculizumab Treatment	18AUG2014	29FEB2024	Other	site close
1520-013	Female	Without Prior Eculizumab Treatment	23AUG2022	29FEB2024	Other	site close
1521-010	Female	Prior Eculizumab Treatment	27JAN2016	31MAY2024	Enrollment in the IPIG PNH Registry	
1521-011	Female	Prior Eculizumab Treatment Unknown	12JAN2017	31MAY2024	Enrollment in the IPIG PNH Registry	
1521-015	Female	Without Prior Eculizumab Treatment	21DEC2017	31MAY2024	Enrollment in the IPIG PNH Registry	
1521-016	Male	Prior Eculizumab Treatment	21DEC2017	31MAY2024	Enrollment in the IPIG PNH Registry	
1521-017	Male	Without Prior Eculizumab Treatment	15MAR2018	31MAY2024	Enrollment in the IPIG PNH Registry	

Note: (a) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.

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Listing 1
Registry Discontinuation, Cumulative
Ravulizumab Study Population

Patient Number	Gender	Treatment Status[a]	Enrollment Date	Study Discontinuation Date	Primary Reason for Study Discontinuation	Other, Specify
1521-019	Female	Without Prior Eculizumab Treatment	03DEC2018	31MAY2024	Enrollment in the IPIG PNH Registry	
1521-020	Male	Prior Eculizumab Treatment	07MAR2019	31MAY2024	Enrollment in the IPIG PNH Registry	
1558-002	Male	Prior Eculizumab Treatment	09JAN2015	02JAN2024	Enrollment in the IPIG PNH Registry	
1558-008	Male	Without Prior Eculizumab Treatment	12DEC2017	02JAN2024	Enrollment in the IPIG PNH Registry	
1600-003	Male	Without Prior Eculizumab Treatment	25MAR2015	26MAR2024	Other	site closure
1600-004	Male	Without Prior Eculizumab Treatment	25MAR2015	26MAR2024	Other	site closure
1600-007	Male	Without Prior Eculizumab Treatment	12DEC2019	16JAN2023	Other	treated by aspaveli
1612-001	Male	Prior Eculizumab Treatment	31JAN2014	24MAY2022	Other	Site Closure due to USOR not amending budget/contract to the FMV (Fair Market Value) contract requested by Alexion.

Note: (a) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.

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Listing 1
Registry Discontinuation, Cumulative
Ravulizumab Study Population

Patient Number	Gender	Treatment Status[a]	Enrollment Date	Study Discontinuation Date	Primary Reason for Study Discontinuation	Other, Specify
1612-002	Male	Prior Eculizumab Treatment Unknown	05MAR2015	24MAY2022	Other	per sponsor study closed
1612-003	Male	Prior Eculizumab Treatment Unknown	11MAR2015	24MAY2022	Other	per sponsor study closed
1612-004	Female	Prior Eculizumab Treatment	30JUN2016	24MAY2022	Other	Site Closure due to USOR not amending budget/contract to the FMV (Fair Market Value) contract requested by Alexion.
1617-003	Female	Prior Eculizumab Treatment	09MAY2014	16DEC2021	Other	Patient withdrew consent
1620-001	Male	Without Prior Eculizumab Treatment	05SEP2014	23DEC2019	Patient choice	
1667-001	Male	Prior Eculizumab Treatment	28MAY2014	18MAR2024	Enrollment in the IPIG PNH Registry	
1667-004	Female	Prior Eculizumab Treatment	07JAN2020	18MAR2024	Enrollment in the IPIG PNH Registry	
1668-001	Female	Prior Eculizumab Treatment	26MAR2014	11MAR2024	Other	site closure
1670-002	Male	Prior Eculizumab Treatment	19MAY2014	07FEB2024	Other	site closure

Note: (a) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.

Source: ADAM.ADSL, ADAM.ADPOP
Run Date: 2025-05-14T14:46:00
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ravuema202501/Files/listings/production/programs/l1_regdis_cum.sas

Listing 1
Registry Discontinuation, Cumulative
Ravulizumab Study Population

Patient Number	Gender	Treatment Status[a]	Enrollment Date	Study Discontinuation Date	Primary Reason for Study Discontinuation	Other, Specify
1677-001	Female	Without Prior Eculizumab Treatment	14NOV2014	05JUN2024	Other	end of study
1677-003	Female	Without Prior Eculizumab Treatment	08DEC2014	05JUN2024	Other	end of study
1677-004	Male	Without Prior Eculizumab Treatment	20APR2015	05JUN2024	Other	end of study
1677-007	Female	Without Prior Eculizumab Treatment	06OCT2015	05JUN2024	Other	end of study
1682-001	Female	Prior Eculizumab Treatment	25OCT2014	30APR2024	Other	Other: sponsor's request - upcoming site closure
1683-016	Male	Without Prior Eculizumab Treatment	22JUN2018	14MAR2024	Enrollment in the IPIG PNH Registry	
1718-001	Female	Prior Eculizumab Treatment Unknown	01OCT2014	29APR2024	Enrollment in the IPIG PNH Registry	
1718-002	Female	Without Prior Eculizumab Treatment	22OCT2014	06MAY2024	Enrollment in the IPIG PNH Registry	

Note: (a) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.

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Run Date: 2025-05-14T14:46:00
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ravuema202501/Files/listings/production/programs/l1_regdis_cum.sas

Listing 1
Registry Discontinuation, Cumulative
Ravulizumab Study Population

Patient Number	Gender	Treatment Status[a]	Enrollment Date	Study Discontinuation Date	Primary Reason for Study Discontinuation	Other, Specify
1718-003	Male	Without Prior Eculizumab Treatment	01DEC2014	08MAY2024	Enrollment in the IPIG PNH Registry	
1718-011	Female	Without Prior Eculizumab Treatment	30APR2019	09MAY2024	Enrollment in the IPIG PNH Registry	
1718-012	Female	Without Prior Eculizumab Treatment	15JUN2020	07MAY2024	Enrollment in the IPIG PNH Registry	
1722-001	Male	Prior Eculizumab Treatment	23APR2015	06AUG2024	Other	SITE CLOSED
1726-001	Male	Without Prior Eculizumab Treatment	23FEB2015	31AUG2021	Patient died	
1726-002	Male	Prior Eculizumab Treatment Unknown	19MAR2015	05APR2024	Other	End of Study
1726-005	Female	Prior Eculizumab Treatment	02MAR2018	27FEB2024	Other	End of Study
1754-030	Female	Without Prior Eculizumab Treatment	19MAR2024	19MAR2024	Enrollment in the IPIG PNH Registry	
1787-003	Male	Prior Eculizumab Treatment	24MAY2016	08APR2024	Other	Enrollment in the IPIG

Note: (a) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.

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Run Date: 2025-05-14T14:46:00
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ravuema202501/Files/listings/production/programs/l1_regdis_cum.sas

Listing 1
Registry Discontinuation, Cumulative
Ravulizumab Study Population

Patient Number	Gender	Treatment Status[a]	Enrollment Date	Study Discontinuation Date	Primary Reason for Study Discontinuation	Other, Specify
1787-005	Male	Prior Eculizumab Treatment	07JUL2016	08APR2024	Other	Enrollment in the IPIG
1787-006	Female	Without Prior Eculizumab Treatment	20NOV2017	08APR2024	Other	Enrollment in the IPIG
1787-008	Male	Prior Eculizumab Treatment	26FEB2021	08APR2024	Other	Enrollment in the IPIG
1796-001	Female	Prior Eculizumab Treatment	12MAY2016	25APR2024	Enrollment in the IPIG PNH Registry	
1796-002	Female	Prior Eculizumab Treatment	12MAY2016	25APR2024	Enrollment in the IPIG PNH Registry	

Note: (a) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.

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Listing 1.1
Registry Discontinuation, During the Analysis Period
Ravulizumab Study Population

Patient Number	Gender	Treatment Status[a]	Enrollment Date	Study Discontinuation Date	Primary Reason for Study Discontinuation	Other, Specify
1003-019	Male	Prior Eculizumab Treatment Unknown	31AUG2011	20FEB2024	Other	Site Closure
1003-036	Male	Prior Eculizumab Treatment Unknown	16NOV2011	20FEB2024	Other	PT discontinued. Site closed
1003-037	Female	Prior Eculizumab Treatment	30NOV2011	20FEB2024	Other	PT discontinued. Site closed
1003-040	Male	Without Prior Eculizumab Treatment	08FEB2012	20FEB2024	Other	Pt discontinued. Site closed
1003-051	Female	Prior Eculizumab Treatment Unknown	25JAN2013	20FEB2024	Other	PT discontinued. Site closed
1003-056	Male	Prior Eculizumab Treatment Unknown	28OCT2013	20FEB2024	Other	Pt discontinued. Site closed
1004-012	Female	Prior Eculizumab Treatment Unknown	29JAN2013	21MAY2024	Enrollment in the IPIG PNH Registry	
1004-013	Male	Prior Eculizumab Treatment	14FEB2013	21MAY2024	Patient enrolled in a clinical trial of PNH treatment	
1004-021	Female	Prior Eculizumab Treatment	24MAY2018	21MAY2024	Enrollment in the IPIG PNH Registry	
1005-001	Male	Prior Eculizumab Treatment	17JUL2009	03NOV2023	Patient enrolled in a clinical trial of PNH treatment	

Note: Includes patients actively enrolled in the registry during the analysis period, which covers the time period from 06JAN2023 to 06JAN2025.
(a) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.

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Listing 1.1
Registry Discontinuation, During the Analysis Period
Ravulizumab Study Population

Patient Number	Gender	Treatment Status[a]	Enrollment Date	Study Discontinuation Date	Primary Reason for Study Discontinuation	Other, Specify
1005-006	Male	Prior Eculizumab Treatment	24JUL2009	21MAR2024	Other	site closure
1005-007	Female	Prior Eculizumab Treatment	11SEP2009	21MAR2024	Other	site closure
1005-012	Female	Prior Eculizumab Treatment	04MAY2010	21FEB2024	Other	patient lost of follow-up. Last contact at site = 02Dec2022
1005-029	Female	Prior Eculizumab Treatment	12MAR2011	21MAR2024	Other	site closure
1005-053	Female	Without Prior Eculizumab Treatment	27AUG2015	29APR2024	Other	End of PNH Registry
1008-001	Male	Prior Eculizumab Treatment Unknown	27SEP2012	23MAY2024	Enrollment in the IPIG PNH Registry	
1008-019	Female	Prior Eculizumab Treatment Unknown	13JUN2012	23MAY2024	Enrollment in the IPIG PNH Registry	
1008-066	Female	Prior Eculizumab Treatment	28SEP2019	23MAY2024	Enrollment in the IPIG PNH Registry	
1009-004	Male	Prior Eculizumab Treatment	08JUN2005	16MAY2024	Enrollment in the IPIG PNH Registry	
1009-006	Male	Prior Eculizumab Treatment	15JUN2005	21MAY2024	Enrollment in the IPIG PNH Registry	

Note: Includes patients actively enrolled in the registry during the analysis period, which covers the time period from 06JAN2023 to 06JAN2025.
(a) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.

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Listing 1.1
Registry Discontinuation, During the Analysis Period
Ravulizumab Study Population

Patient Number	Gender	Treatment Status[a]	Enrollment Date	Study Discontinuation Date	Primary Reason for Study Discontinuation	Other, Specify
1009-014	Female	Prior Eculizumab Treatment	17AUG2005	11AUG2024	Enrollment in the IPIG PNH Registry	
1009-023	Female	Prior Eculizumab Treatment	04OCT2005	11SEP2024	Enrollment in the IPIG PNH Registry	
1009-024	Female	Prior Eculizumab Treatment	13OCT2005	29OCT2024	Enrollment in the IPIG PNH Registry	
1009-052	Male	Prior Eculizumab Treatment	30NOV2006	31AUG2024	Enrollment in the IPIG PNH Registry	
1009-057	Female	Without Prior Eculizumab Treatment	02AUG2007	06JUL2024	Enrollment in the IPIG PNH Registry	
1009-062	Female	Prior Eculizumab Treatment Unknown	08JUL2008	29NOV2024	Other	Site closure
1009-070	Female	Prior Eculizumab Treatment Unknown	14OCT2008	31MAY2024	Enrollment in the IPIG PNH Registry	
1009-074	Male	Prior Eculizumab Treatment	31MAR2009	21MAY2024	Enrollment in the IPIG PNH Registry	
1009-080	Male	Prior Eculizumab Treatment	08SEP2009	29NOV2024	Other	Site closure
1009-084	Female	Prior Eculizumab Treatment	22SEP2009	20JUN2024	Enrollment in the IPIG PNH Registry	

Note: Includes patients actively enrolled in the registry during the analysis period, which covers the time period from 06JAN2023 to 06JAN2025.
(a) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.

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Listing 1.1
Registry Discontinuation, During the Analysis Period
Ravulizumab Study Population

Patient Number	Gender	Treatment Status[a]	Enrollment Date	Study Discontinuation Date	Primary Reason for Study Discontinuation	Other, Specify
1009-088	Male	Prior Eculizumab Treatment	22OCT2009	20SEP2024	Other	PHYSICIAN'S DECISION
1009-089	Female	Prior Eculizumab Treatment	27OCT2009	02AUG2024	Enrollment in the IPIG PNH Registry	
1009-093	Female	Prior Eculizumab Treatment Unknown	28JAN2010	31MAY2024	Enrollment in the IPIG PNH Registry	
1009-103	Male	Prior Eculizumab Treatment Unknown	22APR2010	31MAY2024	Enrollment in the IPIG PNH Registry	
1009-115	Male	Prior Eculizumab Treatment	15JUN2010	16SEP2024	Enrollment in the IPIG PNH Registry	
1009-129	Male	Without Prior Eculizumab Treatment	31AUG2010	11JUN2024	Enrollment in the IPIG PNH Registry	
1009-132	Female	Prior Eculizumab Treatment	07SEP2010	29NOV2024	Other	Site closure
1009-133	Male	Without Prior Eculizumab Treatment	27OCT2010	23AUG2023	Patient died	
1009-145	Male	Prior Eculizumab Treatment	01FEB2011	15OCT2024	Enrollment in the IPIG PNH Registry	
1009-149	Male	Prior Eculizumab Treatment	17FEB2011	07JUL2023	Patient enrolled in a clinical trial of PNH treatment	

Note: Includes patients actively enrolled in the registry during the analysis period, which covers the time period from 06JAN2023 to 06JAN2025.
(a) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.

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Listing 1.1
Registry Discontinuation, During the Analysis Period
Ravulizumab Study Population

Patient Number	Gender	Treatment Status[a]	Enrollment Date	Study Discontinuation Date	Primary Reason for Study Discontinuation	Other, Specify
1009-151	Female	Prior Eculizumab Treatment	10MAR2011	08OCT2024	Enrollment in the IPIG PNH Registry	
1009-161	Male	Prior Eculizumab Treatment	24MAY2011	28MAY2024	Enrollment in the IPIG PNH Registry	
1009-164	Female	Prior Eculizumab Treatment Unknown	16JUN2011	31MAY2024	Enrollment in the IPIG PNH Registry	
1009-166	Female	Prior Eculizumab Treatment	23JUN2011	28MAY2024	Enrollment in the IPIG PNH Registry	
1009-170	Female	Prior Eculizumab Treatment	11AUG2011	29JUN2024	Enrollment in the IPIG PNH Registry	
1009-176	Female	Prior Eculizumab Treatment	30AUG2011	24SEP2024	Enrollment in the IPIG PNH Registry	
1009-178	Female	Without Prior Eculizumab Treatment	08SEP2011	31MAY2024	Enrollment in the IPIG PNH Registry	
1009-186	Female	Prior Eculizumab Treatment	06OCT2011	08AUG2024	Enrollment in the IPIG PNH Registry	
1009-195	Female	Prior Eculizumab Treatment Unknown	17NOV2011	31MAY2024	Enrollment in the IPIG PNH Registry	
1009-210	Female	Prior Eculizumab Treatment	23FEB2012	31MAY2024	Enrollment in the IPIG PNH Registry	

Note: Includes patients actively enrolled in the registry during the analysis period, which covers the time period from 06JAN2023 to 06JAN2025.
(a) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.

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Listing 1.1
Registry Discontinuation, During the Analysis Period
Ravulizumab Study Population

Patient Number	Gender	Treatment Status[a]	Enrollment Date	Study Discontinuation Date	Primary Reason for Study Discontinuation	Other, Specify
1009-221	Female	Prior Eculizumab Treatment	06JUN2012	30MAY2024	Enrollment in the IPIG PNH Registry	
1009-222	Female	Prior Eculizumab Treatment	28JUN2012	26JUL2024	Enrollment in the IPIG PNH Registry	
1009-230	Female	Prior Eculizumab Treatment	04SEP2012	29NOV2024	Other	Site closure
1009-251	Male	Prior Eculizumab Treatment	11JUN2013	31OCT2024	Enrollment in the IPIG PNH Registry	
1009-264	Male	Prior Eculizumab Treatment	24OCT2013	22FEB2024	Patient enrolled in a clinical trial of PNH treatment	
1009-268	Male	Prior Eculizumab Treatment	17DEC2013	05AUG2024	Enrollment in the IPIG PNH Registry	
1009-269	Female	Prior Eculizumab Treatment	07JAN2014	28MAY2024	Enrollment in the IPIG PNH Registry	
1009-270	Male	Prior Eculizumab Treatment	14JAN2014	29MAY2024	Enrollment in the IPIG PNH Registry	
1009-272	Female	Prior Eculizumab Treatment	21JAN2014	20JUL2024	Enrollment in the IPIG PNH Registry	
1009-275	Male	Prior Eculizumab Treatment	12MAY2014	29NOV2024	Other	Site closure

Note: Includes patients actively enrolled in the registry during the analysis period, which covers the time period from 06JAN2023 to 06JAN2025.
(a) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.

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Listing 1.1
Registry Discontinuation, During the Analysis Period
Ravulizumab Study Population

Patient Number	Gender	Treatment Status[a]	Enrollment Date	Study Discontinuation Date	Primary Reason for Study Discontinuation	Other, Specify
1009-280	Female	Prior Eculizumab Treatment	15JUL2014	27SEP2024	Enrollment in the IPIG PNH Registry	
1009-287	Female	Prior Eculizumab Treatment	29JUL2014	01OCT2023	Patient died	
1009-292	Female	Prior Eculizumab Treatment	10SEP2014	09AUG2024	Enrollment in the IPIG PNH Registry	
1009-298	Female	Prior Eculizumab Treatment	06NOV2014	19JUN2024	Enrollment in the IPIG PNH Registry	
1009-300	Female	Prior Eculizumab Treatment	18NOV2014	29NOV2024	Other	Site closure
1009-302	Female	Prior Eculizumab Treatment	11DEC2014	31MAY2024	Enrollment in the IPIG PNH Registry	
1009-318	Female	Prior Eculizumab Treatment	13MAY2015	24SEP2024	Enrollment in the IPIG PNH Registry	
1009-320	Male	Prior Eculizumab Treatment	21MAY2015	29JUL2024	Enrollment in the IPIG PNH Registry	
1009-321	Male	Prior Eculizumab Treatment	21MAY2015	04DEC2023	Patient choice	
1009-328	Male	Prior Eculizumab Treatment	07JUL2015	31OCT2023	Patient enrolled in a clinical trial of PNH treatment	

Note: Includes patients actively enrolled in the registry during the analysis period, which covers the time period from 06JAN2023 to 06JAN2025.
(a) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.

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Listing 1.1
Registry Discontinuation, During the Analysis Period
Ravulizumab Study Population

Patient Number	Gender	Treatment Status[a]	Enrollment Date	Study Discontinuation Date	Primary Reason for Study Discontinuation	Other, Specify
1009-329	Female	Prior Eculizumab Treatment	07JUL2015	26JUL2024	Enrollment in the IPIG PNH Registry	
1009-332	Female	Prior Eculizumab Treatment	21JUL2015	21MAY2024	Enrollment in the IPIG PNH Registry	
1009-346	Female	Prior Eculizumab Treatment Unknown	20OCT2015	29NOV2024	Other	Site closure
1009-353	Female	Prior Eculizumab Treatment	12APR2016	29NOV2024	Other	Site closure
1009-362	Female	Prior Eculizumab Treatment	02JUN2016	01AUG2024	Enrollment in the IPIG PNH Registry	
1009-366	Male	Prior Eculizumab Treatment	05AUG2016	17SEP2024	Enrollment in the IPIG PNH Registry	
1009-369	Male	Prior Eculizumab Treatment	14JUL2016	03OCT2024	Enrollment in the IPIG PNH Registry	
1009-372	Female	Without Prior Eculizumab Treatment	09AUG2016	26SEP2024	Enrollment in the IPIG PNH Registry	
1009-379	Female	Without Prior Eculizumab Treatment	13SEP2016	05JUN2024	Enrollment in the IPIG PNH Registry	
1009-383	Male	Prior Eculizumab Treatment	29SEP2016	29NOV2024	Other	Site closure

Note: Includes patients actively enrolled in the registry during the analysis period, which covers the time period from 06JAN2023 to 06JAN2025.
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Listing 1.1
Registry Discontinuation, During the Analysis Period
Ravulizumab Study Population

Patient Number	Gender	Treatment Status[a]	Enrollment Date	Study Discontinuation Date	Primary Reason for Study Discontinuation	Other, Specify
1009-385	Female	Prior Eculizumab Treatment	01NOV2016	15OCT2024	Enrollment in the IPIG PNH Registry	
1009-386	Male	Without Prior Eculizumab Treatment	01NOV2016	26JUL2024	Enrollment in the IPIG PNH Registry	
1009-390	Female	Prior Eculizumab Treatment	29DEC2016	19SEP2024	Enrollment in the IPIG PNH Registry	
1009-405	Female	Prior Eculizumab Treatment	02MAY2017	18JUL2024	Enrollment in the IPIG PNH Registry	
1009-409	Male	Prior Eculizumab Treatment	13JUN2017	17OCT2024	Enrollment in the IPIG PNH Registry	
1009-410	Male	Without Prior Eculizumab Treatment	20JUN2017	09JUN2023	Patient died	
1009-411	Male	Without Prior Eculizumab Treatment	03AUG2017	01OCT2024	Enrollment in the IPIG PNH Registry	
1009-413	Male	Prior Eculizumab Treatment	22AUG2017	19AUG2024	Enrollment in the IPIG PNH Registry	
1009-418	Female	Prior Eculizumab Treatment	12OCT2017	29NOV2024	Other	Site closure

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Listing 1.1
Registry Discontinuation, During the Analysis Period
Ravulizumab Study Population

Patient Number	Gender	Treatment Status[a]	Enrollment Date	Study Discontinuation Date	Primary Reason for Study Discontinuation	Other, Specify
1009-420	Male	Without Prior Eculizumab Treatment	31OCT2017	05MAR2024	Patient died	
1009-422	Male	Prior Eculizumab Treatment	09NOV2017	02JUL2024	Enrollment in the IPIG PNH Registry	
1009-429	Female	Prior Eculizumab Treatment	21MAR2019	06JUL2023	Patient enrolled in a clinical trial of PNH treatment	
1009-431	Female	Prior Eculizumab Treatment	21JUN2019	27AUG2024	Enrollment in the IPIG PNH Registry	
1009-432	Female	Prior Eculizumab Treatment	23JUL2019	23JUL2024	Enrollment in the IPIG PNH Registry	
1009-433	Male	Prior Eculizumab Treatment	13AUG2019	29NOV2024	Other	Site closure
1009-434	Female	Prior Eculizumab Treatment	09SEP2019	09JUL2024	Enrollment in the IPIG PNH Registry	
1009-438	Male	Prior Eculizumab Treatment	22JUN2020	26NOV2024	Enrollment in the IPIG PNH Registry	
1009-441	Male	Prior Eculizumab Treatment	16FEB2021	15AUG2024	Enrollment in the IPIG PNH Registry	
1009-442	Male	Prior Eculizumab Treatment	03MAR2021	20JUN2024	Enrollment in the IPIG PNH Registry	

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Listing 1.1
Registry Discontinuation, During the Analysis Period
Ravulizumab Study Population

Patient Number	Gender	Treatment Status[a]	Enrollment Date	Study Discontinuation Date	Primary Reason for Study Discontinuation	Other, Specify
1009-459	Female	Without Prior Eculizumab Treatment	14NOV2022	23SEP2024	Enrollment in the IPIG PNH Registry	
1009-460	Male	Without Prior Eculizumab Treatment	06JAN2023	13AUG2024	Enrollment in the IPIG PNH Registry	
1013-001	Female	Prior Eculizumab Treatment	19MAY2005	17OCT2023	Patient enrolled in a clinical trial of PNH treatment	
1013-100	Female	Prior Eculizumab Treatment	08FEB2012	05APR2024	Other	Site closure
1013-133	Female	Prior Eculizumab Treatment	29JAN2014	29NOV2023	Patient died	
1013-228	Female	Prior Eculizumab Treatment	05NOV2019	14MAY2024	Enrollment in the IPIG PNH Registry	
1013-243	Male	Prior Eculizumab Treatment	08MAR2022	15NOV2023	Patient enrolled in a clinical trial of PNH treatment	
1017-002	Male	Prior Eculizumab Treatment	05SEP2012	29FEB2024	Other	Site close
1017-009	Female	Prior Eculizumab Treatment	13SEP2012	29FEB2024	Other	Site close

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Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ravuema202501/Files/listings/production/programs/l1_regdis_dur.sas

Listing 1.1
Registry Discontinuation, During the Analysis Period
Ravulizumab Study Population

Patient Number	Gender	Treatment Status[a]	Enrollment Date	Study Discontinuation Date	Primary Reason for Study Discontinuation	Other, Specify
1017-022	Male	Prior Eculizumab Treatment	13JUN2019	29FEB2024	Other	Site close
1017-023	Female	Prior Eculizumab Treatment	27NOV2019	29FEB2024	Other	Site close
1030-007	Male	Without Prior Eculizumab Treatment	05JUN2017	11NOV2023	Patient died	
1030-010	Male	Prior Eculizumab Treatment Unknown	14FEB2023	01JUL2023	Other	lost to follow up
1036-001	Female	Prior Eculizumab Treatment	10JAN2006	10JUL2023	Patient enrolled in a clinical trial of PNH treatment	
1048-001	Female	Prior Eculizumab Treatment	30MAY2006	13NOV2024	Enrollment in the IPIG PNH Registry	
1048-011	Female	Without Prior Eculizumab Treatment	21DEC2011	29NOV2024	Other	Site closure
1048-020	Female	Prior Eculizumab Treatment	06JAN2014	29NOV2024	Other	Site closure
1053-003	Male	Prior Eculizumab Treatment	15MAR2012	24JAN2023	Other	Study Closure
1053-004	Female	Prior Eculizumab Treatment Unknown	22MAY2012	26JAN2023	Other	study closure

Note: Includes patients actively enrolled in the registry during the analysis period, which covers the time period from 06JAN2023 to 06JAN2025.
(a) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.

Source: ADAM.ADSL, ADAM.ADPOP
Run Date: 2025-05-14T14:46:01
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ravuema202501/Files/listings/production/programs/l1_regdis_dur.sas

Listing 1.1
Registry Discontinuation, During the Analysis Period
Ravulizumab Study Population

Patient Number	Gender	Treatment Status[a]	Enrollment Date	Study Discontinuation Date	Primary Reason for Study Discontinuation	Other, Specify
1061-004	Male	Prior Eculizumab Treatment	26MAR2007	08APR2024	Enrollment in the IPIG PNH Registry	
1087-001	Male	Prior Eculizumab Treatment	15MAY2013	09MAY2024	Other	Study termination by sponsor
1087-014	Male	Without Prior Eculizumab Treatment	19MAR2019	09MAY2024	Other	Study termination by sponsor
1093-017	Female	Prior Eculizumab Treatment Unknown	08OCT2010	10APR2024	Enrollment in the IPIG PNH Registry	
1093-024	Female	Prior Eculizumab Treatment	17NOV2010	23MAR2023	Other	Lost to FUP
1093-042	Male	Prior Eculizumab Treatment Unknown	26APR2011	11JAN2023	Other	Lost to FUP
1093-043	Male	Prior Eculizumab Treatment	10MAY2011	10APR2024	Enrollment in the IPIG PNH Registry	
1093-046	Female	Without Prior Eculizumab Treatment	26JUL2011	05JUN2024	Enrollment in the IPIG PNH Registry	
1093-053	Female	Prior Eculizumab Treatment Unknown	22NOV2011	10APR2024	Other	Lost to FUP
1093-060	Female	Prior Eculizumab Treatment	07AUG2012	10APR2024	Enrollment in the IPIG PNH Registry	

Note: Includes patients actively enrolled in the registry during the analysis period, which covers the time period from 06JAN2023 to 06JAN2025.
(a) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.

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Listing 1.1
Registry Discontinuation, During the Analysis Period
Ravulizumab Study Population

Patient Number	Gender	Treatment Status[a]	Enrollment Date	Study Discontinuation Date	Primary Reason for Study Discontinuation	Other, Specify
1093-068	Male	Prior Eculizumab Treatment Unknown	13FEB2013	10APR2024	Enrollment in the IPIG PNH Registry	
1093-086	Female	Prior Eculizumab Treatment Unknown	08OCT2013	10APR2024	Enrollment in the IPIG PNH Registry	
1093-089	Female	Without Prior Eculizumab Treatment	07JAN2014	18APR2024	Other	Site closure
1093-105	Male	Prior Eculizumab Treatment	18AUG2014	10APR2024	Enrollment in the IPIG PNH Registry	
1093-109	Female	Prior Eculizumab Treatment	28OCT2014	23JAN2024	Patient died	
1093-115	Male	Prior Eculizumab Treatment	28NOV2014	10APR2024	Enrollment in the IPIG PNH Registry	
1093-130	Male	Prior Eculizumab Treatment	23APR2015	23MAY2024	Enrollment in the IPIG PNH Registry	
1093-137	Male	Prior Eculizumab Treatment Unknown	08JUL2015	29APR2024	Other	Changement to IPIC-Registry
1093-138	Male	Prior Eculizumab Treatment Unknown	10JUL2015	15MAY2024	Enrollment in the IPIG PNH Registry	
1093-140	Male	Without Prior Eculizumab Treatment	19JUL2015	03MAY2024	Enrollment in the IPIG PNH Registry	

Note: Includes patients actively enrolled in the registry during the analysis period, which covers the time period from 06JAN2023 to 06JAN2025.
(a) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.

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Listing 1.1
Registry Discontinuation, During the Analysis Period
Ravulizumab Study Population

Patient Number	Gender	Treatment Status[a]	Enrollment Date	Study Discontinuation Date	Primary Reason for Study Discontinuation	Other, Specify
1093-153	Female	Without Prior Eculizumab Treatment	19JAN2016	02MAY2024	Enrollment in the IPIG PNH Registry	
1093-171	Male	Prior Eculizumab Treatment Unknown	27NOV2016	15APR2024	Enrollment in the IPIG PNH Registry	
1093-186	Male	Prior Eculizumab Treatment Unknown	04AUG2017	17JUL2024	Enrollment in the IPIG PNH Registry	
1093-191	Female	Prior Eculizumab Treatment	06OCT2017	22MAY2024	Enrollment in the IPIG PNH Registry	
1093-192	Male	Without Prior Eculizumab Treatment	24OCT2017	02MAY2023	Patient died	
1093-222	Male	Without Prior Eculizumab Treatment	11DEC2018	23APR2024	Enrollment in the IPIG PNH Registry	
1093-248	Male	Without Prior Eculizumab Treatment	10MAR2020	24APR2024	Enrollment in the IPIG PNH Registry	
1093-249	Male	Prior Eculizumab Treatment Unknown	23MAR2020	01MAR2024	Enrollment in the IPIG PNH Registry	
1093-253	Male	Without Prior Eculizumab Treatment	26JUN2020	11NOV2023	Patient died	

Note: Includes patients actively enrolled in the registry during the analysis period, which covers the time period from 06JAN2023 to 06JAN2025.
(a) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.

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Listing 1.1
Registry Discontinuation, During the Analysis Period
Ravulizumab Study Population

Patient Number	Gender	Treatment Status[a]	Enrollment Date	Study Discontinuation Date	Primary Reason for Study Discontinuation	Other, Specify
1093-254	Male	Without Prior Eculizumab Treatment	23JUN2020	17APR2024	Enrollment in the IPIG PNH Registry	
1093-284	Female	Prior Eculizumab Treatment Unknown	01MAR2023	06MAY2024	Enrollment in the IPIG PNH Registry	
1106-034	Male	Prior Eculizumab Treatment Unknown	26MAR2015	05APR2023	Other	study closure
1130-017	Female	Prior Eculizumab Treatment Unknown	29MAY2019	29MAY2024	Other	Study closure by sponsor
1130-018	Male	Prior Eculizumab Treatment Unknown	14NOV2019	29MAY2024	Other	Study closure by study sponsor.
1134-002	Female	Without Prior Eculizumab Treatment	28APR2009	31MAY2024	Other	Site closure
1134-009	Female	Prior Eculizumab Treatment Unknown	06MAY2009	31MAY2024	Other	Site closure
1134-019	Male	Without Prior Eculizumab Treatment	23MAY2009	31MAY2024	Other	Site closure
1134-024	Male	Without Prior Eculizumab Treatment	03JUN2009	31MAY2024	Other	Site closure

Note: Includes patients actively enrolled in the registry during the analysis period, which covers the time period from 06JAN2023 to 06JAN2025.
(a) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.

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Listing 1.1
Registry Discontinuation, During the Analysis Period
Ravulizumab Study Population

Patient Number	Gender	Treatment Status[a]	Enrollment Date	Study Discontinuation Date	Primary Reason for Study Discontinuation	Other, Specify
1134-025	Male	Without Prior Eculizumab Treatment	05JUN2009	31MAY2024	Other	Site closure
1134-044	Male	Without Prior Eculizumab Treatment	09SEP2009	31MAY2024	Other	site closure
1134-050	Male	Without Prior Eculizumab Treatment	02NOV2009	30JUN2024	Other	Site closure
1134-052	Female	Prior Eculizumab Treatment Unknown	22FEB2010	31MAY2024	Other	site closure
1134-055	Male	Without Prior Eculizumab Treatment	05MAR2010	31MAY2024	Other	site closure
1134-056	Female	Without Prior Eculizumab Treatment	20MAR2010	31MAY2024	Other	site closure
1134-062	Female	Without Prior Eculizumab Treatment	28JUN2010	31MAY2024	Other	site closure
1134-063	Male	Without Prior Eculizumab Treatment	26JUL2010	31MAY2024	Other	site closure

Note: Includes patients actively enrolled in the registry during the analysis period, which covers the time period from 06JAN2023 to 06JAN2025.
(a) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.

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Listing 1.1
Registry Discontinuation, During the Analysis Period
Ravulizumab Study Population

Patient Number	Gender	Treatment Status[a]	Enrollment Date	Study Discontinuation Date	Primary Reason for Study Discontinuation	Other, Specify
1134-069	Male	Without Prior Eculizumab Treatment	22OCT2010	31MAY2024	Other	site closure
1134-084	Female	Prior Eculizumab Treatment Unknown	27JUL2011	31MAY2024	Other	site closure
1134-088	Female	Without Prior Eculizumab Treatment	09JAN2012	31MAY2024	Other	site closure
1134-100	Female	Without Prior Eculizumab Treatment	31MAY2013	31MAY2024	Other	site closure
1134-111	Male	Without Prior Eculizumab Treatment	26SEP2014	31JAN2024	Patient died	
1134-114	Male	Prior Eculizumab Treatment Unknown	22JAN2015	31MAY2024	Other	site closure
1134-116	Female	Without Prior Eculizumab Treatment	05FEB2015	31MAY2024	Other	site closure
1134-120	Female	Without Prior Eculizumab Treatment	04AUG2015	31MAY2024	Other	site closure

Note: Includes patients actively enrolled in the registry during the analysis period, which covers the time period from 06JAN2023 to 06JAN2025.
(a) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.

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Listing 1.1
Registry Discontinuation, During the Analysis Period
Ravulizumab Study Population

Patient Number	Gender	Treatment Status[a]	Enrollment Date	Study Discontinuation Date	Primary Reason for Study Discontinuation	Other, Specify
1134-124	Male	Without Prior Eculizumab Treatment	11FEB2016	31MAY2024	Other	site closure
1134-135	Male	Without Prior Eculizumab Treatment	03MAY2018	31MAY2024	Other	site closure
1134-136	Female	Prior Eculizumab Treatment Unknown	05AUG2018	31MAY2024	Other	site closure
1134-140	Male	Without Prior Eculizumab Treatment	13MAR2019	31MAY2024	Other	site closure
1134-143	Female	Without Prior Eculizumab Treatment	12DEC2019	31MAY2024	Other	site closure
1134-146	Female	Without Prior Eculizumab Treatment	08JUN2021	31MAY2024	Other	site closure
1134-148	Male	Without Prior Eculizumab Treatment	09MAY2022	31MAY2024	Other	site closure
1139-002	Female	Prior Eculizumab Treatment	13JUL2009	02OCT2024	Enrollment in the IPIG PNH Registry	

Note: Includes patients actively enrolled in the registry during the analysis period, which covers the time period from 06JAN2023 to 06JAN2025.
(a) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.

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Listing 1.1
Registry Discontinuation, During the Analysis Period
Ravulizumab Study Population

Patient Number	Gender	Treatment Status[a]	Enrollment Date	Study Discontinuation Date	Primary Reason for Study Discontinuation	Other, Specify
1139-007	Male	Prior Eculizumab Treatment	03AUG2009	14JUN2024	Enrollment in the IPIG PNH Registry	
1139-013	Female	Prior Eculizumab Treatment	27JAN2010	14JUN2024	Enrollment in the IPIG PNH Registry	
1139-029	Female	Prior Eculizumab Treatment Unknown	05OCT2011	14JUN2024	Enrollment in the IPIG PNH Registry	
1139-031	Male	Prior Eculizumab Treatment	24OCT2014	14JUN2024	Enrollment in the IPIG PNH Registry	
1139-042	Male	Prior Eculizumab Treatment	20AUG2019	14JUN2024	Enrollment in the IPIG PNH Registry	
1140-001	Male	Without Prior Eculizumab Treatment	29JUL2009	08MAY2024	Other	Site closing
1140-002	Male	Prior Eculizumab Treatment	02NOV2010	08MAY2024	Other	Study site closing
1151-002	Female	Without Prior Eculizumab Treatment	06SEP2010	30MAY2024	Other	site closure
1151-006	Female	Without Prior Eculizumab Treatment	11OCT2010	30MAY2024	Other	site closure

Note: Includes patients actively enrolled in the registry during the analysis period, which covers the time period from 06JAN2023 to 06JAN2025.
(a) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.

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Listing 1.1
Registry Discontinuation, During the Analysis Period
Ravulizumab Study Population

Patient Number	Gender	Treatment Status[a]	Enrollment Date	Study Discontinuation Date	Primary Reason for Study Discontinuation	Other, Specify
1151-011	Female	Without Prior Eculizumab Treatment	18MAY2011	30MAY2024	Other	site closure
1151-014	Male	Prior Eculizumab Treatment	11APR2012	30MAY2024	Other	site closure
1152-001	Female	Prior Eculizumab Treatment	16OCT2010	05JUN2024	Other	site closure
1152-002	Male	Prior Eculizumab Treatment	26APR2011	05JUN2024	Other	site closure
1163-001	Female	Without Prior Eculizumab Treatment	20JAN2010	19MAR2024	Other	study closure
1163-003	Female	Without Prior Eculizumab Treatment	18MAY2011	19MAR2024	Other	study closure
1163-018	Female	Prior Eculizumab Treatment	16AUG2018	19MAR2024	Other	study closure
1163-024	Female	Without Prior Eculizumab Treatment	19DEC2020	19MAR2024	Other	study closure
1163-027	Male	Prior Eculizumab Treatment	02JUN2022	19MAR2024	Other	study closure

Note: Includes patients actively enrolled in the registry during the analysis period, which covers the time period from 06JAN2023 to 06JAN2025.
(a) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.

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Listing 1.1
Registry Discontinuation, During the Analysis Period
Ravulizumab Study Population

Patient Number	Gender	Treatment Status[a]	Enrollment Date	Study Discontinuation Date	Primary Reason for Study Discontinuation	Other, Specify
1164-001	Male	Without Prior Eculizumab Treatment	12JAN2010	21MAY2024	Other	FIN d'étude HPN. Patient prévenu par téléphone, message. Mail envoyé
1164-002	Female	Without Prior Eculizumab Treatment	13JAN2010	04APR2024	Other	SPONSOR DECISION
1164-003	Male	Without Prior Eculizumab Treatment	13JAN2010	30MAY2024	Other	SPONSOR DECISION
1164-007	Male	Without Prior Eculizumab Treatment	19JAN2010	04APR2024	Other	SPONSOR DECISION
1165-010	Female	Without Prior Eculizumab Treatment	19JAN2021	15MAY2024	Other	Site closure.
1169-001	Female	Prior Eculizumab Treatment	17MAR2010	15APR2024	Other	site closure
1169-003	Female	Prior Eculizumab Treatment	07JUL2010	15APR2024	Other	site closure
1169-004	Female	Prior Eculizumab Treatment	16JUL2010	15APR2024	Other	site closure
1169-006	Male	Prior Eculizumab Treatment	27JUL2010	15APR2024	Other	site closure

Note: Includes patients actively enrolled in the registry during the analysis period, which covers the time period from 06JAN2023 to 06JAN2025.
(a) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.

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Listing 1.1
Registry Discontinuation, During the Analysis Period
Ravulizumab Study Population

Patient Number	Gender	Treatment Status[a]	Enrollment Date	Study Discontinuation Date	Primary Reason for Study Discontinuation	Other, Specify
1169-008	Male	Prior Eculizumab Treatment	12SEP2012	15APR2024	Other	site closure
1170-002	Female	Prior Eculizumab Treatment	18JAN2010	09APR2024	Other	site closure
1170-003	Male	Prior Eculizumab Treatment	01MAR2010	09APR2024	Other	site closure
1170-006	Male	Without Prior Eculizumab Treatment	14APR2012	09APR2024	Other	site closure
1170-009	Female	Prior Eculizumab Treatment	05JUN2013	09APR2024	Other	site closure
1192-001	Male	Prior Eculizumab Treatment Unknown	29APR2010	15MAY2024	Other	Site closure
1193-002	Male	Without Prior Eculizumab Treatment	23APR2010	15MAR2024	Other	End of PNH Registry
1193-008	Female	Without Prior Eculizumab Treatment	08MAR2012	15MAR2024	Other	End of PNH Registry
1193-015	Female	Without Prior Eculizumab Treatment	18MAY2021	15MAR2024	Other	End of PNH Registry

Note: Includes patients actively enrolled in the registry during the analysis period, which covers the time period from 06JAN2023 to 06JAN2025.
(a) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.

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Listing 1.1
Registry Discontinuation, During the Analysis Period
Ravulizumab Study Population

Patient Number	Gender	Treatment Status[a]	Enrollment Date	Study Discontinuation Date	Primary Reason for Study Discontinuation	Other, Specify
1193-017	Female	Without Prior Eculizumab Treatment	05OCT2022	15MAR2024	Other	End of PNH Registry
1193-018	Female	Without Prior Eculizumab Treatment	14MAR2023	06FEB2024	Patient died	
1197-020	Male	Without Prior Eculizumab Treatment	12JAN2012	08JAN2024		Site Closure
1197-027	Male	Prior Eculizumab Treatment	21JUN2018	13APR2023	Patient died	
1197-028	Female	Without Prior Eculizumab Treatment	19NOV2018	30OCT2023	Enrollment in the IPIG PNH Registry	
1197-029	Male	Without Prior Eculizumab Treatment	23NOV2020	30OCT2023	Patient enrolled in a clinical trial of PNH treatment	
1197-030	Male	Prior Eculizumab Treatment	22NOV2021	08APR2024	Enrollment in the IPIG PNH Registry	
1197-031	Male	Prior Eculizumab Treatment	29NOV2021	27OCT2023	Patient enrolled in a clinical trial of PNH treatment	

Note: Includes patients actively enrolled in the registry during the analysis period, which covers the time period from 06JAN2023 to 06JAN2025.
(a) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.

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Listing 1.1
Registry Discontinuation, During the Analysis Period
Ravulizumab Study Population

Patient Number	Gender	Treatment Status[a]	Enrollment Date	Study Discontinuation Date	Primary Reason for Study Discontinuation	Other, Specify
1200-004	Male	Prior Eculizumab Treatment	19JAN2011	03APR2024	Other	Site Closure
1200-005	Female	Prior Eculizumab Treatment	27JAN2011	03APR2024	Other	Site closure
1209-002	Male	Prior Eculizumab Treatment	17JUN2010	12MAR2024	Enrollment in the IPIG PNH Registry	
1209-003	Male	Without Prior Eculizumab Treatment	09SEP2010	14MAY2024	Enrollment in the IPIG PNH Registry	
1209-005	Male	Prior Eculizumab Treatment	15SEP2016	12MAR2024	Enrollment in the IPIG PNH Registry	
1210-026	Female	Without Prior Eculizumab Treatment	14OCT2013	09APR2024	Enrollment in the IPIG PNH Registry	
1214-005	Male	Prior Eculizumab Treatment	10OCT2012	29APR2024	Other	Sponsors decision for end of study, maybe enrollment into IPIG-PNH-registry in the future
1214-007	Male	Without Prior Eculizumab Treatment	04SEP2014	29APR2024	Other	Sponsors decision for end of study, maybe enrollment into IPIG-PNH-registry in the future

Note: Includes patients actively enrolled in the registry during the analysis period, which covers the time period from 06JAN2023 to 06JAN2025.
(a) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.

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Listing 1.1
Registry Discontinuation, During the Analysis Period
Ravulizumab Study Population

Patient Number	Gender	Treatment Status[a]	Enrollment Date	Study Discontinuation Date	Primary Reason for Study Discontinuation	Other, Specify
1214-009	Female	Without Prior Eculizumab Treatment	17NOV2020	30APR2024	Other	Sponsors decision for end of study, maybe enrollment into IPIG-PNH-registry in the future
1219-003	Female	Prior Eculizumab Treatment	12SEP2013	15APR2024	Other	site closure
1226-001	Male	Prior Eculizumab Treatment Unknown	04JUN2010	10SEP2024	Other	Due to Study Closure
1226-003	Female	Prior Eculizumab Treatment Unknown	06SEP2010	10SEP2024	Other	Due to study closure
1232-001	Female	Prior Eculizumab Treatment Unknown	17JUL2010	12MAR2024	Other	Registry closure, site will not be participating in IPIG PNH Registry
1232-005	Male	Prior Eculizumab Treatment Unknown	16JAN2017	12MAR2024	Other	Registry discontinuation, Site not participating in IPIG PNH Registry
1236-002	Female	Prior Eculizumab Treatment	17FEB2012	05APR2024	Other	Site closure
1236-003	Male	Without Prior Eculizumab Treatment	21JUN2009	05APR2024	Other	Site closure

Note: Includes patients actively enrolled in the registry during the analysis period, which covers the time period from 06JAN2023 to 06JAN2025.
(a) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.

Source: ADAM.ADSL, ADAM.ADPOP
Run Date: 2025-05-14T14:46:01
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ravuema202501/Files/listings/production/programs/l1_regdis_dur.sas

Listing 1.1
Registry Discontinuation, During the Analysis Period
Ravulizumab Study Population

Patient Number	Gender	Treatment Status[a]	Enrollment Date	Study Discontinuation Date	Primary Reason for Study Discontinuation	Other, Specify
1250-001	Female	Without Prior Eculizumab Treatment	01FEB2011	01JUL2024	Other	site closure
1250-003	Female	Without Prior Eculizumab Treatment	03MAY2011	24JUN2024	Other	site closure
1251-001	Male	Prior Eculizumab Treatment	21DEC2010	22MAY2024	Enrollment in the IPIG PNH Registry	
1251-002	Male	Without Prior Eculizumab Treatment	29DEC2010	22MAY2024	Enrollment in the IPIG PNH Registry	
1251-005	Female	Prior Eculizumab Treatment	06APR2016	22MAY2024	Enrollment in the IPIG PNH Registry	
1251-009	Male	Prior Eculizumab Treatment	19FEB2020	22MAY2024	Enrollment in the IPIG PNH Registry	
1252-001	Male	Prior Eculizumab Treatment	21SEP2010	04MAY2023	Other	Investigator decision
1252-002	Male	Prior Eculizumab Treatment	28SEP2010	04MAY2023	Other	Investigator decision
1252-035	Female	Prior Eculizumab Treatment	08OCT2015	04MAY2023	Other	Investigator decision
1252-038	Female	Prior Eculizumab Treatment Unknown	23AUG2016	04MAY2023	Other	Investigator decision

Note: Includes patients actively enrolled in the registry during the analysis period, which covers the time period from 06JAN2023 to 06JAN2025.
(a) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.

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Run Date: 2025-05-14T14:46:01
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ravuema202501/Files/listings/production/programs/l1_regdis_dur.sas

Listing 1.1
Registry Discontinuation, During the Analysis Period
Ravulizumab Study Population

Patient Number	Gender	Treatment Status[a]	Enrollment Date	Study Discontinuation Date	Primary Reason for Study Discontinuation	Other, Specify
1252-041	Male	Without Prior Eculizumab Treatment	02MAR2021	04MAY2023	Other	Investigator decision
1262-002	Male	Prior Eculizumab Treatment	02FEB2011	05MAR2024	Other	site closure
1262-004	Male	Prior Eculizumab Treatment	14MAR2013	05MAR2024	Other	site closure
1266-001	Male	Without Prior Eculizumab Treatment	05JAN2011	29APR2024	Other	End of PNH Registry
1266-002	Female	Without Prior Eculizumab Treatment	05JAN2011	30APR2024	Other	End of PNH Registry
1266-005	Male	Without Prior Eculizumab Treatment	02MAR2011	30APR2024	Other	End of PNH Registry
1268-028	Female	Prior Eculizumab Treatment	23MAY2011	04JUL2024	Enrollment in the IPIG PNH Registry	
1268-030	Male	Prior Eculizumab Treatment Unknown	06JUN2011	04JUL2024	Enrollment in the IPIG PNH Registry	
1268-031	Male	Prior Eculizumab Treatment Unknown	10MAY2011	04JUL2024	Enrollment in the IPIG PNH Registry	

Note: Includes patients actively enrolled in the registry during the analysis period, which covers the time period from 06JAN2023 to 06JAN2025.
(a) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.

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Listing 1.1
Registry Discontinuation, During the Analysis Period
Ravulizumab Study Population

Patient Number	Gender	Treatment Status[a]	Enrollment Date	Study Discontinuation Date	Primary Reason for Study Discontinuation	Other, Specify
1268-049	Female	Prior Eculizumab Treatment Unknown	11OCT2011	04JUL2024	Enrollment in the IPIG PNH Registry	
1268-057	Female	Prior Eculizumab Treatment Unknown	03DEC2012	04JUL2024	Enrollment in the IPIG PNH Registry	
1268-058	Male	Prior Eculizumab Treatment Unknown	21MAY2012	04JUL2024	Enrollment in the IPIG PNH Registry	
1268-071	Female	Prior Eculizumab Treatment	04MAR2013	04JUL2024	Enrollment in the IPIG PNH Registry	
1268-076	Male	Prior Eculizumab Treatment	23JAN2013	04JUL2024	Enrollment in the IPIG PNH Registry	
1268-083	Female	Prior Eculizumab Treatment	17FEB2014	29NOV2024	Other	Site closure
1268-096	Male	Prior Eculizumab Treatment	13MAY2013	04JUL2024	Enrollment in the IPIG PNH Registry	
1268-103	Female	Without Prior Eculizumab Treatment	04JUN2014	04JUL2024	Enrollment in the IPIG PNH Registry	
1268-104	Female	Prior Eculizumab Treatment	16DEC2015	04JUL2024	Enrollment in the IPIG PNH Registry	
1268-106	Male	Without Prior Eculizumab Treatment	18JUN2014	04JUL2024	Enrollment in the IPIG PNH Registry	

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(a) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.

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Listing 1.1
Registry Discontinuation, During the Analysis Period
Ravulizumab Study Population

Patient Number	Gender	Treatment Status[a]	Enrollment Date	Study Discontinuation Date	Primary Reason for Study Discontinuation	Other, Specify
1268-129	Male	Without Prior Eculizumab Treatment	29APR2015	04JUL2024	Enrollment in the IPIG PNH Registry	
1268-167	Female	Prior Eculizumab Treatment	13APR2016	12AUG2024	Enrollment in the IPIG PNH Registry	
1268-197	Female	Without Prior Eculizumab Treatment	20DEC2017	04JUL2024	Enrollment in the IPIG PNH Registry	
1268-219	Male	Prior Eculizumab Treatment Unknown	05MAR2018	04JUL2024	Enrollment in the IPIG PNH Registry	
1268-235	Male	Prior Eculizumab Treatment	25FEB2019	04JUL2024	Enrollment in the IPIG PNH Registry	
1268-255	Female	Prior Eculizumab Treatment	11SEP2019	04JUL2024	Enrollment in the IPIG PNH Registry	
1268-259	Male	Prior Eculizumab Treatment Unknown	24FEB2020	04JUL2024	Enrollment in the IPIG PNH Registry	
1268-262	Male	Prior Eculizumab Treatment Unknown	17FEB2020	04JUL2024	Enrollment in the IPIG PNH Registry	
1268-263	Female	Prior Eculizumab Treatment Unknown	07JUL2021	04JUL2024	Enrollment in the IPIG PNH Registry	
1268-264	Male	Without Prior Eculizumab Treatment	14JUL2021	04JUL2024	Enrollment in the IPIG PNH Registry	

Note: Includes patients actively enrolled in the registry during the analysis period, which covers the time period from 06JAN2023 to 06JAN2025.
(a) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.

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Listing 1.1
Registry Discontinuation, During the Analysis Period
Ravulizumab Study Population

Patient Number	Gender	Treatment Status[a]	Enrollment Date	Study Discontinuation Date	Primary Reason for Study Discontinuation	Other, Specify
1268-266	Male	Prior Eculizumab Treatment Unknown	06SEP2021	04JUL2024	Enrollment in the IPIG PNH Registry	
1268-270	Female	Prior Eculizumab Treatment	08SEP2021	04JUL2024	Enrollment in the IPIG PNH Registry	
1268-274	Male	Without Prior Eculizumab Treatment	22SEP2021	04JUL2024	Enrollment in the IPIG PNH Registry	
1268-275	Female	Without Prior Eculizumab Treatment	03AUG2021	04JUL2024	Enrollment in the IPIG PNH Registry	
1268-279	Female	Without Prior Eculizumab Treatment	19FEB2020	04JAN2024	Patient enrolled in a clinical trial of PNH treatment	
1269-001	Male	Prior Eculizumab Treatment	04FEB2011	05DEC2023	Other	Site closure
1269-003	Male	Prior Eculizumab Treatment	24APR2014	05DEC2023	Other	Site closure
1275-002	Female	Prior Eculizumab Treatment	12JAN2011	27MAR2024	Other	site closure
1304-001	Female	Prior Eculizumab Treatment	14MAY2011	11MAR2024	Enrollment in the IPIG PNH Registry	
1304-002	Male	Prior Eculizumab Treatment	10MAY2011	05MAR2024	Enrollment in the IPIG PNH Registry	

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(a) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.

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Listing 1.1
Registry Discontinuation, During the Analysis Period
Ravulizumab Study Population

Patient Number	Gender	Treatment Status[a]	Enrollment Date	Study Discontinuation Date	Primary Reason for Study Discontinuation	Other, Specify
1304-003	Male	Without Prior Eculizumab Treatment	27JUL2011	25MAR2024	Enrollment in the IPIG PNH Registry	
1304-006	Female	Prior Eculizumab Treatment	26FEB2016	28FEB2024	Enrollment in the IPIG PNH Registry	
1319-001	Male	Prior Eculizumab Treatment	08JUN2005	29NOV2024	Other	Site closure
1341-011	Female	Without Prior Eculizumab Treatment	17SEP2015	03JUN2024	Enrollment in the IPIG PNH Registry	
1341-022	Female	Without Prior Eculizumab Treatment	27DEC2019	06JUN2024	Enrollment in the IPIG PNH Registry	
1351-003	Male	Without Prior Eculizumab Treatment	03FEB2017	23JUN2024	Enrollment in the IPIG PNH Registry	
1351-004	Male	Prior Eculizumab Treatment	21MAR2017	23JUN2024	Enrollment in the IPIG PNH Registry	
1351-013	Female	Prior Eculizumab Treatment	11JUN2018	23JUN2024	Enrollment in the IPIG PNH Registry	
1351-023	Female	Without Prior Eculizumab Treatment	29JUL2021	23JUN2024	Enrollment in the IPIG PNH Registry	

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Listing 1.1
Registry Discontinuation, During the Analysis Period
Ravulizumab Study Population

Patient Number	Gender	Treatment Status[a]	Enrollment Date	Study Discontinuation Date	Primary Reason for Study Discontinuation	Other, Specify
1358-001	Male	Prior Eculizumab Treatment Unknown	09JAN2013	21JUN2024	Enrollment in the IPIG PNH Registry	
1366-001	Male	Prior Eculizumab Treatment	25NOV2011	29FEB2024	Enrollment in the IPIG PNH Registry	
1366-020	Male	Prior Eculizumab Treatment	15MAR2012	29FEB2024	Enrollment in the IPIG PNH Registry	
1366-024	Male	Without Prior Eculizumab Treatment	28MAR2012	18JAN2024	Other	Patient is being treated by another physician. and the subject was newly diagnosed with MDS
1366-033	Female	Prior Eculizumab Treatment	14FEB2013	29FEB2024	Enrollment in the IPIG PNH Registry	
1366-036	Female	Prior Eculizumab Treatment	14MAR2013	29FEB2024	Enrollment in the IPIG PNH Registry	
1366-064	Female	Prior Eculizumab Treatment	18JUN2014	29FEB2024	Enrollment in the IPIG PNH Registry	
1366-097	Male	Prior Eculizumab Treatment	21SEP2016	29FEB2024	Enrollment in the IPIG PNH Registry	
1366-108	Female	Prior Eculizumab Treatment	26APR2018	29FEB2024	Enrollment in the IPIG PNH Registry	
1366-111	Male	Prior Eculizumab Treatment	29OCT2018	29FEB2024	Enrollment in the IPIG PNH Registry	

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(a) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.

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Listing 1.1
Registry Discontinuation, During the Analysis Period
Ravulizumab Study Population

Patient Number	Gender	Treatment Status[a]	Enrollment Date	Study Discontinuation Date	Primary Reason for Study Discontinuation	Other, Specify
1366-129	Female	Prior Eculizumab Treatment	22APR2020	29FEB2024	Enrollment in the IPIG PNH Registry	
1366-148	Male	Without Prior Eculizumab Treatment	29MAR2021	29FEB2024	Enrollment in the IPIG PNH Registry	
1366-162	Male	Without Prior Eculizumab Treatment	10AUG2022	29FEB2024	Enrollment in the IPIG PNH Registry	
1366-172	Male	Without Prior Eculizumab Treatment	04MAY2023	29FEB2024	Enrollment in the IPIG PNH Registry	
1366-173	Female	Without Prior Eculizumab Treatment	10MAY2023	29FEB2024	Enrollment in the IPIG PNH Registry	
1381-002	Male	Prior Eculizumab Treatment	15MAR2012	20FEB2024	Other	study closing
1381-003	Female	Prior Eculizumab Treatment	18APR2012	06DEC2023	Other	study closing
1381-008	Male	Prior Eculizumab Treatment	14MAY2015	08FEB2024	Other	study closing
1381-012	Male	Prior Eculizumab Treatment Unknown	29AUG2019	24APR2023	Other	study closing

Note: Includes patients actively enrolled in the registry during the analysis period, which covers the time period from 06JAN2023 to 06JAN2025.
(a) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.

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Listing 1.1
Registry Discontinuation, During the Analysis Period
Ravulizumab Study Population

Patient Number	Gender	Treatment Status[a]	Enrollment Date	Study Discontinuation Date	Primary Reason for Study Discontinuation	Other, Specify
1381-014	Male	Without Prior Eculizumab Treatment	20JAN2020	11MAR2024	Other	study closing
1381-016	Male	Prior Eculizumab Treatment Unknown	17JUN2021	23FEB2024	Other	study closing
1381-017	Male	Prior Eculizumab Treatment	10AUG2021	18DEC2023	Other	study closing
1416-001	Male	Prior Eculizumab Treatment	11JUN2013	15APR2024	Enrollment in the IPIG PNH Registry	
1418-009	Female	Prior Eculizumab Treatment	25OCT2012	28MAR2024	Enrollment in the IPIG PNH Registry	
1418-042	Female	Without Prior Eculizumab Treatment	05SEP2017	24MAY2024	Enrollment in the IPIG PNH Registry	
1418-045	Female	Prior Eculizumab Treatment	02OCT2017	24MAY2024	Enrollment in the IPIG PNH Registry	
1418-064	Male	Without Prior Eculizumab Treatment	08NOV2022	24MAY2024	Enrollment in the IPIG PNH Registry	
1419-009	Female	Prior Eculizumab Treatment	28APR2016	12APR2024	Other	Enrollment in the IPIG

Note: Includes patients actively enrolled in the registry during the analysis period, which covers the time period from 06JAN2023 to 06JAN2025.
(a) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.

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Listing 1.1
Registry Discontinuation, During the Analysis Period
Ravulizumab Study Population

Patient Number	Gender	Treatment Status[a]	Enrollment Date	Study Discontinuation Date	Primary Reason for Study Discontinuation	Other, Specify
1420-002	Male	Without Prior Eculizumab Treatment	15MAY2012	22APR2024	Enrollment in the IPIG PNH Registry	
1420-004	Male	Prior Eculizumab Treatment	12JUN2012	22APR2024	Enrollment in the IPIG PNH Registry	
1420-006	Female	Prior Eculizumab Treatment	31JUL2012	22APR2024	Enrollment in the IPIG PNH Registry	
1420-009	Male	Prior Eculizumab Treatment	23APR2013	22APR2024	Enrollment in the IPIG PNH Registry	
1421-008	Male	Prior Eculizumab Treatment	04DEC2012	06MAR2024	Enrollment in the IPIG PNH Registry	
1421-009	Male	Without Prior Eculizumab Treatment	04JAN2013	06MAR2024	Enrollment in the IPIG PNH Registry	
1421-024	Male	Without Prior Eculizumab Treatment	26JAN2017	06MAR2024	Enrollment in the IPIG PNH Registry	
1421-029	Female	Without Prior Eculizumab Treatment	02NOV2018	06MAR2024	Enrollment in the IPIG PNH Registry	
1421-035	Male	Without Prior Eculizumab Treatment	06FEB2024	06MAR2024	Enrollment in the IPIG PNH Registry	

Note: Includes patients actively enrolled in the registry during the analysis period, which covers the time period from 06JAN2023 to 06JAN2025.
(a) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.

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Listing 1.1
Registry Discontinuation, During the Analysis Period
Ravulizumab Study Population

Patient Number	Gender	Treatment Status[a]	Enrollment Date	Study Discontinuation Date	Primary Reason for Study Discontinuation	Other, Specify
1422-004	Male	Prior Eculizumab Treatment	20NOV2012	04APR2024	Enrollment in the IPIG PNH Registry	
1422-008	Male	Prior Eculizumab Treatment	30JAN2013	04APR2024	Enrollment in the IPIG PNH Registry	
1422-011	Female	Prior Eculizumab Treatment	20MAR2014	04APR2024	Enrollment in the IPIG PNH Registry	
1422-022	Female	Prior Eculizumab Treatment	19MAR2020	04APR2024	Enrollment in the IPIG PNH Registry	
1423-002	Female	Prior Eculizumab Treatment	23AUG2012	28MAR2024	Enrollment in the IPIG PNH Registry	
1423-006	Male	Prior Eculizumab Treatment	23DEC2014	28MAR2024	Enrollment in the IPIG PNH Registry	
1423-008	Male	Prior Eculizumab Treatment	18JUN2015	28MAR2024	Enrollment in the IPIG PNH Registry	
1423-011	Male	Prior Eculizumab Treatment	11NOV2015	28MAR2024	Enrollment in the IPIG PNH Registry	
1423-012	Male	Prior Eculizumab Treatment	07JAN2016	28MAR2024	Enrollment in the IPIG PNH Registry	
1423-014	Male	Prior Eculizumab Treatment	09JUN2017	28MAR2024	Enrollment in the IPIG PNH Registry	
1423-017	Female	Prior Eculizumab Treatment	12NOV2018	28MAR2024	Enrollment in the IPIG PNH Registry	

Note: Includes patients actively enrolled in the registry during the analysis period, which covers the time period from 06JAN2023 to 06JAN2025.
(a) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.

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Listing 1.1
Registry Discontinuation, During the Analysis Period
Ravulizumab Study Population

Patient Number	Gender	Treatment Status[a]	Enrollment Date	Study Discontinuation Date	Primary Reason for Study Discontinuation	Other, Specify
1423-018	Male	Prior Eculizumab Treatment	24SEP2019	28MAR2024	Enrollment in the IPIG PNH Registry	
1423-020	Male	Prior Eculizumab Treatment	27MAY2020	28MAR2024	Enrollment in the IPIG PNH Registry	
1423-024	Male	Without Prior Eculizumab Treatment	18NOV2021	28MAR2024	Enrollment in the IPIG PNH Registry	
1424-003	Female	Prior Eculizumab Treatment	31MAR2015	04APR2024	Enrollment in the IPIG PNH Registry	
1424-004	Male	Prior Eculizumab Treatment	24AUG2016	04APR2024	Enrollment in the IPIG PNH Registry	
1425-001	Male	Prior Eculizumab Treatment	11JAN2013	19SEP2023	Other	PNH clone 5.74%
1425-003	Male	Prior Eculizumab Treatment	21JUL2015	24APR2024	Other	site closure
1427-003	Female	Prior Eculizumab Treatment	08NOV2013	21FEB2024	Enrollment in the IPIG PNH Registry	
1429-001	Female	Prior Eculizumab Treatment Unknown	15NOV2012	04APR2024	Other	site closure
1429-007	Female	Prior Eculizumab Treatment	25SEP2020	04APR2024	Other	site closure

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Listing 1.1
Registry Discontinuation, During the Analysis Period
Ravulizumab Study Population

Patient Number	Gender	Treatment Status[a]	Enrollment Date	Study Discontinuation Date	Primary Reason for Study Discontinuation	Other, Specify
1432-001	Male	Prior Eculizumab Treatment	23AUG2012	29FEB2024	Other	site close
1432-003	Female	Prior Eculizumab Treatment	14JAN2016	29FEB2024	Other	site close
1432-004	Female	Without Prior Eculizumab Treatment	21JAN2016	29FEB2024	Other	site close
1432-005	Female	Prior Eculizumab Treatment	21JAN2016	29FEB2024	Other	site close
1432-009	Male	Prior Eculizumab Treatment Unknown	23DEC2019	29FEB2024	Other	site close
1435-002	Male	Without Prior Eculizumab Treatment	15AUG2012	29FEB2024	Other	site close
1435-005	Female	Without Prior Eculizumab Treatment	11SEP2012	29FEB2024	Other	site close
1435-006	Female	Without Prior Eculizumab Treatment	19SEP2012	29FEB2024	Other	site close
1435-012	Female	Without Prior Eculizumab Treatment	04NOV2021	29FEB2024	Other	site close

Note: Includes patients actively enrolled in the registry during the analysis period, which covers the time period from 06JAN2023 to 06JAN2025.
(a) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.

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Listing 1.1
Registry Discontinuation, During the Analysis Period
Ravulizumab Study Population

Patient Number	Gender	Treatment Status[a]	Enrollment Date	Study Discontinuation Date	Primary Reason for Study Discontinuation	Other, Specify
1454-001	Female	Prior Eculizumab Treatment	12NOV2012	29FEB2024	Other	site close
1454-002	Male	Prior Eculizumab Treatment	28FEB2013	29FEB2024	Other	Site close
1462-004	Male	Prior Eculizumab Treatment	30NOV2012	08FEB2024	Other	Site close
1462-006	Male	Prior Eculizumab Treatment	07DEC2012	08FEB2024	Other	Site close
1462-008	Male	Prior Eculizumab Treatment	14DEC2012	08FEB2024	Other	Site close
1462-009	Male	Prior Eculizumab Treatment	14DEC2012	08FEB2024	Other	Site close
1462-010	Male	Prior Eculizumab Treatment	21DEC2012	08FEB2024	Other	Site close
1493-002	Female	Prior Eculizumab Treatment	01MAR2013	29FEB2024	Other	Site close
1493-006	Female	Without Prior Eculizumab Treatment	25MAR2013	29FEB2024	Other	Site close
1493-020	Female	Without Prior Eculizumab Treatment	14MAR2022	29FEB2024	Other	Site close

Note: Includes patients actively enrolled in the registry during the analysis period, which covers the time period from 06JAN2023 to 06JAN2025.
(a) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.

Source: ADAM.ADSL, ADAM.ADPOP
Run Date: 2025-05-14T14:46:01
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ravuema202501/Files/listings/production/programs/l1_regdis_dur.sas

Listing 1.1
Registry Discontinuation, During the Analysis Period
Ravulizumab Study Population

Patient Number	Gender	Treatment Status[a]	Enrollment Date	Study Discontinuation Date	Primary Reason for Study Discontinuation	Other, Specify
1493-023	Male	Without Prior Eculizumab Treatment	14MAR2022	29FEB2024	Other	Site close
1493-028	Female	Without Prior Eculizumab Treatment	09NOV2022	29FEB2024	Other	Site close
1493-031	Male	Without Prior Eculizumab Treatment	13FEB2023	29FEB2024	Other	Site close
1493-032	Female	Without Prior Eculizumab Treatment	16FEB2023	29FEB2024	Other	Site close
1494-001	Male	Prior Eculizumab Treatment Unknown	16MAY2013	26MAR2024	Other	Sponsor decision to close this registry trial.
1494-002	Female	Without Prior Eculizumab Treatment	01AUG2013	26MAR2024	Other	Sponsor decision to close this registry trial.
1494-008	Female	Prior Eculizumab Treatment Unknown	14SEP2023	26MAR2024	Other	Sponsor decision to close this registry trial.
1494-011	Male	Without Prior Eculizumab Treatment	01JUN2023	26APR2024	Other	Sponsor decision to close this registry trial.

Note: Includes patients actively enrolled in the registry during the analysis period, which covers the time period from 06JAN2023 to 06JAN2025.
(a) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.

Source: ADAM.ADSL, ADAM.ADPOP
Run Date: 2025-05-14T14:46:01
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ravuema202501/Files/listings/production/programs/l1_regdis_dur.sas

Listing 1.1
Registry Discontinuation, During the Analysis Period
Ravulizumab Study Population

Patient Number	Gender	Treatment Status[a]	Enrollment Date	Study Discontinuation Date	Primary Reason for Study Discontinuation	Other, Specify
1506-010	Female	Without Prior Eculizumab Treatment	17NOV2015	29FEB2024	Other	Site close
1507-002	Male	Prior Eculizumab Treatment	24APR2013	29FEB2024	Other	site close
1507-003	Male	Prior Eculizumab Treatment	08MAY2013	29FEB2024	Other	site close
1507-007	Female	Without Prior Eculizumab Treatment	15MAY2013	29FEB2024	Other	site close
1507-012	Female	Prior Eculizumab Treatment	10JUL2013	29FEB2024	Other	site close
1507-015	Female	Without Prior Eculizumab Treatment	29OCT2018	29FEB2024	Other	site close
1520-003	Male	Prior Eculizumab Treatment	06JAN2014	29FEB2024	Other	site close
1520-008	Male	Without Prior Eculizumab Treatment	04APR2014	29FEB2024	Other	site close
1520-009	Female	Prior Eculizumab Treatment	18AUG2014	29FEB2024	Other	site close

Note: Includes patients actively enrolled in the registry during the analysis period, which covers the time period from 06JAN2023 to 06JAN2025.
(a) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.

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Run Date: 2025-05-14T14:46:01
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ravuema202501/Files/listings/production/programs/l1_regdis_dur.sas

Listing 1.1
Registry Discontinuation, During the Analysis Period
Ravulizumab Study Population

Patient Number	Gender	Treatment Status[a]	Enrollment Date	Study Discontinuation Date	Primary Reason for Study Discontinuation	Other, Specify
1520-013	Female	Without Prior Eculizumab Treatment	23AUG2022	29FEB2024	Other	site close
1521-010	Female	Prior Eculizumab Treatment	27JAN2016	31MAY2024	Enrollment in the IPIG PNH Registry	
1521-011	Female	Prior Eculizumab Treatment Unknown	12JAN2017	31MAY2024	Enrollment in the IPIG PNH Registry	
1521-015	Female	Without Prior Eculizumab Treatment	21DEC2017	31MAY2024	Enrollment in the IPIG PNH Registry	
1521-016	Male	Prior Eculizumab Treatment	21DEC2017	31MAY2024	Enrollment in the IPIG PNH Registry	
1521-017	Male	Without Prior Eculizumab Treatment	15MAR2018	31MAY2024	Enrollment in the IPIG PNH Registry	
1521-019	Female	Without Prior Eculizumab Treatment	03DEC2018	31MAY2024	Enrollment in the IPIG PNH Registry	
1521-020	Male	Prior Eculizumab Treatment	07MAR2019	31MAY2024	Enrollment in the IPIG PNH Registry	
1558-002	Male	Prior Eculizumab Treatment	09JAN2015	02JAN2024	Enrollment in the IPIG PNH Registry	

Note: Includes patients actively enrolled in the registry during the analysis period, which covers the time period from 06JAN2023 to 06JAN2025.
(a) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.

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Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ravuema202501/Files/listings/production/programs/l1_regdis_dur.sas

Listing 1.1
Registry Discontinuation, During the Analysis Period
Ravulizumab Study Population

Patient Number	Gender	Treatment Status[a]	Enrollment Date	Study Discontinuation Date	Primary Reason for Study Discontinuation	Other, Specify
1558-008	Male	Without Prior Eculizumab Treatment	12DEC2017	02JAN2024	Enrollment in the IPIG PNH Registry	
1600-003	Male	Without Prior Eculizumab Treatment	25MAR2015	26MAR2024	Other	site closure
1600-004	Male	Without Prior Eculizumab Treatment	25MAR2015	26MAR2024	Other	site closure
1600-007	Male	Without Prior Eculizumab Treatment	12DEC2019	16JAN2023	Other	treated by aspaveli
1667-001	Male	Prior Eculizumab Treatment	28MAY2014	18MAR2024	Enrollment in the IPIG PNH Registry	
1667-004	Female	Prior Eculizumab Treatment	07JAN2020	18MAR2024	Enrollment in the IPIG PNH Registry	
1668-001	Female	Prior Eculizumab Treatment	26MAR2014	11MAR2024	Other	site closure
1670-002	Male	Prior Eculizumab Treatment	19MAY2014	07FEB2024	Other	site closure
1677-001	Female	Without Prior Eculizumab Treatment	14NOV2014	05JUN2024	Other	end of study

Note: Includes patients actively enrolled in the registry during the analysis period, which covers the time period from 06JAN2023 to 06JAN2025.
(a) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.

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Listing 1.1
Registry Discontinuation, During the Analysis Period
Ravulizumab Study Population

Patient Number	Gender	Treatment Status[a]	Enrollment Date	Study Discontinuation Date	Primary Reason for Study Discontinuation	Other, Specify
1677-003	Female	Without Prior Eculizumab Treatment	08DEC2014	05JUN2024	Other	end of study
1677-004	Male	Without Prior Eculizumab Treatment	20APR2015	05JUN2024	Other	end of study
1677-007	Female	Without Prior Eculizumab Treatment	06OCT2015	05JUN2024	Other	end of study
1682-001	Female	Prior Eculizumab Treatment	25OCT2014	30APR2024	Other	Other: sponsor's request - upcoming site closure
1683-016	Male	Without Prior Eculizumab Treatment	22JUN2018	14MAR2024	Enrollment in the IPIG PNH Registry	
1718-001	Female	Prior Eculizumab Treatment Unknown	01OCT2014	29APR2024	Enrollment in the IPIG PNH Registry	
1718-002	Female	Without Prior Eculizumab Treatment	22OCT2014	06MAY2024	Enrollment in the IPIG PNH Registry	
1718-003	Male	Without Prior Eculizumab Treatment	01DEC2014	08MAY2024	Enrollment in the IPIG PNH Registry	

Note: Includes patients actively enrolled in the registry during the analysis period, which covers the time period from 06JAN2023 to 06JAN2025.
(a) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.

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Listing 1.1
Registry Discontinuation, During the Analysis Period
Ravulizumab Study Population

Patient Number	Gender	Treatment Status[a]	Enrollment Date	Study Discontinuation Date	Primary Reason for Study Discontinuation	Other, Specify
1718-011	Female	Without Prior Eculizumab Treatment	30APR2019	09MAY2024	Enrollment in the IPIG PNH Registry	
1718-012	Female	Without Prior Eculizumab Treatment	15JUN2020	07MAY2024	Enrollment in the IPIG PNH Registry	
1722-001	Male	Prior Eculizumab Treatment	23APR2015	06AUG2024	Other	SITE CLOSED
1726-002	Male	Prior Eculizumab Treatment Unknown	19MAR2015	05APR2024	Other	End of Study
1726-005	Female	Prior Eculizumab Treatment	02MAR2018	27FEB2024	Other	End of Study
1754-030	Female	Without Prior Eculizumab Treatment	19MAR2024	19MAR2024	Enrollment in the IPIG PNH Registry	
1787-003	Male	Prior Eculizumab Treatment	24MAY2016	08APR2024	Other	Enrollment in the IPIG
1787-005	Male	Prior Eculizumab Treatment	07JUL2016	08APR2024	Other	Enrollment in the IPIG
1787-006	Female	Without Prior Eculizumab Treatment	20NOV2017	08APR2024	Other	Enrollment in the IPIG

Note: Includes patients actively enrolled in the registry during the analysis period, which covers the time period from 06JAN2023 to 06JAN2025.
(a) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.

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Listing 1.1
Registry Discontinuation, During the Analysis Period
Ravulizumab Study Population

Patient Number	Gender	Treatment Status[a]	Enrollment Date	Study Discontinuation Date	Primary Reason for Study Discontinuation	Other, Specify
1787-008	Male	Prior Eculizumab Treatment	26FEB2021	08APR2024	Other	Enrollment in the IPIG
1796-001	Female	Prior Eculizumab Treatment	12MAY2016	25APR2024	Enrollment in the IPIG PNH Registry	
1796-002	Female	Prior Eculizumab Treatment	12MAY2016	25APR2024	Enrollment in the IPIG PNH Registry	

Note: Includes patients actively enrolled in the registry during the analysis period, which covers the time period from 06JAN2023 to 06JAN2025.
(a) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.

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Listing 2
Discontinuation from Ultomiris, Cumulative
Ravulizumab Study Population

Patient Number	Enrollment Date	Treatment Status[a]	Ravulizumab Initiation Date	Last Recorded Date of Ravulizumab Infusion	Primary Reason for Ravulizumab Discontinuation	Specify
1004-012	29JAN2013	Prior Eculizumab Treatment Unknown	21JUN2019	22JUL2019	Patient choice	patient choice
1004-021	24MAY2018	Prior Eculizumab Treatment	13FEB2020	13FEB2020		
1005-001	17JUL2009	Prior Eculizumab Treatment	24NOV2022	22SEP2023	Physician decision	patient is enrolled in a clinical trial
1009-052	30NOV2006	Prior Eculizumab Treatment	18OCT2021	23JAN2023	Switch to other anti-complement treatment	
1009-057	02AUG2007	Without Prior Eculizumab Treatment	21OCT2022	28APR2023	Lack of Efficacy	Patient has not seen major benefit in her fatigue with Ravulizumab.
1009-074	31MAR2009	Prior Eculizumab Treatment	12JAN2022	23JAN2024	Switch to other anti-complement treatment	
1009-084	22SEP2009	Prior Eculizumab Treatment	23FEB2022	31MAY2023	Switch to other anti-complement treatment	

Note: (a) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.

Source: ADAM.ADSL, ADAM.ADPOP, ADAM.ADEX
Run Date: 2025-05-14T14:46:16
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ravuema202501/Files/listings/production/programs/l2_ravudis_cum.sas

Listing 2
Discontinuation from Ultomiris, Cumulative
Ravulizumab Study Population

Patient Number	Enrollment Date	Treatment Status[a]	Ravulizumab Initiation Date	Last Recorded Date of Ravulizumab Infusion	Primary Reason for Ravulizumab Discontinuation	Specify
1009-088	22OCT2009	Prior Eculizumab Treatment	09FEB2022	11JUL2023	Switch to other anti-complement treatment	
1009-103	22APR2010	Prior Eculizumab Treatment Unknown	15AUG2022	12MAR2024	Physician decision	clone size decreased
1009-133	27OCT2010	Without Prior Eculizumab Treatment	04MAR2022	03AUG2023	Death	
1009-146	10FEB2011	Prior Eculizumab Treatment	15NOV2021	05SEP2022	Death	
1009-178	08SEP2011	Without Prior Eculizumab Treatment	13JUN2022	01SEP2023	Lack of Efficacy	
1009-287	29JUL2014	Prior Eculizumab Treatment	10JAN2022	08AUG2023	Death	
1009-327	24JUN2015	Prior Eculizumab Treatment	12AUG2021	17NOV2022	Death	
1009-328	07JUL2015	Prior Eculizumab Treatment	27SEP2021	10SEP2023	Switch to other anti-complement treatment	

Note: (a) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.

Source: ADAM.ADSL, ADAM.ADPOP, ADAM.ADEX
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Listing 2
Discontinuation from Ultomiris, Cumulative
Ravulizumab Study Population

Patient Number	Enrollment Date	Treatment Status[a]	Ravulizumab Initiation Date	Last Recorded Date of Ravulizumab Infusion	Primary Reason for Ravulizumab Discontinuation	Specify
1009-346	20OCT2015	Prior Eculizumab Treatment Unknown	18AUG2021	21DEC2021	Patient choice	Patient experienced decreased quality of life on Ravulizumab.
1009-410	20JUN2017	Without Prior Eculizumab Treatment	07MAR2023	09JUN2023	Death	
1009-420	31OCT2017	Without Prior Eculizumab Treatment	16MAR2022	30MAR2022		
1009-427	09JAN2019	Prior Eculizumab Treatment	24NOV2021	24MAY2022	Death	
1009-429	21MAR2019	Prior Eculizumab Treatment	19AUG2021	11MAY2023	Switch to other anti-complement treatment	
1009-443	12MAR2021	Prior Eculizumab Treatment	08OCT2021	10FEB2022	Physician decision	PNH clone <10%
1009-459	14NOV2022	Without Prior Eculizumab Treatment	07DEC2022	15JUN2023	Switch to other anti-complement treatment	
1013-001	19MAY2005	Prior Eculizumab Treatment	03NOV2020	17NOV2020	Lack of Efficacy	

Note: (a) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.

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Listing 2
Discontinuation from Ultomiris, Cumulative
Ravulizumab Study Population

Patient Number	Enrollment Date	Treatment Status[a]	Ravulizumab Initiation Date	Last Recorded Date of Ravulizumab Infusion	Primary Reason for Ravulizumab Discontinuation	Specify
1013-011	19MAY2006	Prior Eculizumab Treatment Unknown	15NOV2022	30MAY2023	Switch to other anti-complement treatment	
1013-049	26FEB2009	Prior Eculizumab Treatment	23SEP2019	06JUL2021	Switch to eculizumab IV	
1013-061	15JUL2009	Prior Eculizumab Treatment	01OCT2019	26DEC2020	Adverse Event	
1013-081	22AUG2010	Without Prior Eculizumab Treatment	15NOV2019	01MAY2021	Switch to eculizumab IV	
1013-133	29JAN2014	Prior Eculizumab Treatment	10SEP2019	24SEP2019	Death	
1013-145	13AUG2014	Prior Eculizumab Treatment	21AUG2019	01FEB2022	Physician decision	
1013-156	14JAN2015	Prior Eculizumab Treatment	04SEP2019	14DEC2021	Switch to eculizumab IV	
1013-166	12MAY2015	Prior Eculizumab Treatment	15AUG2019	15AUG2022	Switch to other anti-complement treatment	
1013-228	05NOV2019	Prior Eculizumab Treatment	15APR2020	29APR2020	Switch to other anti-complement treatment	

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Listing 2
Discontinuation from Ultomiris, Cumulative
Ravulizumab Study Population

Patient Number	Enrollment Date	Treatment Status[a]	Ravulizumab Initiation Date	Last Recorded Date of Ravulizumab Infusion	Primary Reason for Ravulizumab Discontinuation	Specify
1013-243	08MAR2022	Prior Eculizumab Treatment	01SEP2022	01OCT2022	Lack of Efficacy	
1030-007	05JUN2017	Without Prior Eculizumab Treatment	27MAY2022	10NOV2023	Death	
1061-008	23APR2019	Prior Eculizumab Treatment	27AUG2019	09FEB2022	Physician decision	PI delayed treatment due to ongoing Adverse Event.
1093-030	03NOV2010	Prior Eculizumab Treatment	14APR2020	28APR2020	Lack of Efficacy	Bone marrow transplant 23. apr. 2021
1093-033	25JAN2011	Prior Eculizumab Treatment	30JUL2019	13AUG2019	Switch to other anti-complement treatment	
1093-043	10MAY2011	Prior Eculizumab Treatment	24JUL2019	07AUG2019	Switch to other anti-complement treatment	
1093-109	28OCT2014	Prior Eculizumab Treatment	15AUG2019	15AUG2019		

Note: (a) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.

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Listing 2
Discontinuation from Ultomiris, Cumulative
Ravulizumab Study Population

Patient Number	Enrollment Date	Treatment Status[a]	Ravulizumab Initiation Date	Last Recorded Date of Ravulizumab Infusion	Primary Reason for Ravulizumab Discontinuation	Specify
1093-131	04MAY2015	Prior Eculizumab Treatment Unknown	31JUL2019	14AUG2019	Lack of Efficacy	BMT at 24.11.2020/Bone Marrow Transplantant
1093-192	24OCT2017	Without Prior Eculizumab Treatment	07AUG2019	21AUG2019		
1093-215	08JAN2019	Prior Eculizumab Treatment Unknown	18MAR2021	01APR2021		
1093-222	11DEC2018	Without Prior Eculizumab Treatment	24JAN2024	07FEB2024	Switch to other anti-complement treatment	
1093-253	26JUN2020	Without Prior Eculizumab Treatment	29SEP2020	13OCT2020	Switch to other anti-complement treatment	
1134-111	26SEP2014	Without Prior Eculizumab Treatment	02OCT2023	16OCT2023		
1151-014	11APR2012	Prior Eculizumab Treatment	09DEC2020	11JAN2023	Physician decision	suspected extravascular hemolysis

Note: (a) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.

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Listing 2
Discontinuation from Ultomiris, Cumulative
Ravulizumab Study Population

Patient Number	Enrollment Date	Treatment Status[a]	Ravulizumab Initiation Date	Last Recorded Date of Ravulizumab Infusion	Primary Reason for Ravulizumab Discontinuation	Specify
1165-010	19JAN2021	Without Prior Eculizumab Treatment	24MAR2022	08FEB2024	Switch to eculizumab IV	
1193-018	14MAR2023	Without Prior Eculizumab Treatment	31JUL2023	18AUG2023		
1197-027	21JUN2018	Prior Eculizumab Treatment	02JAN2023	13MAR2023	Death	
1197-031	29NOV2021	Prior Eculizumab Treatment	30DEC2022	13JAN2023	Switch to other anti-complement treatment	
1341-022	27DEC2019	Without Prior Eculizumab Treatment	25MAY2022	08JUN2022	Lack of Efficacy	
1381-002	15MAR2012	Prior Eculizumab Treatment	21DEC2019	04JAN2020		
1381-016	17JUN2021	Prior Eculizumab Treatment Unknown	17JUN2021	26JAN2024	Physician decision site study closing	
1381-017	10AUG2021	Prior Eculizumab Treatment	10AUG2021	23APR2024	Physician decision site study closing	

Note: (a) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.

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Listing 2
Discontinuation from Ultomiris, Cumulative
Ravulizumab Study Population

Patient Number	Enrollment Date	Treatment Status[a]	Ravulizumab Initiation Date	Last Recorded Date of Ravulizumab Infusion	Primary Reason for Ravulizumab Discontinuation	Specify
1420-002	15MAY2012	Without Prior Eculizumab Treatment	22JUN2022	26DEC2022	Lack of Efficacy	medical insurance was suspended due to no LDH reduction and drug administration was stopped
1423-012	07JAN2016	Prior Eculizumab Treatment	10NOV2021	06DEC2023	Physician decision	PNH Flowcytometry negative
1429-011	27JUL2021	Without Prior Eculizumab Treatment	28DEC2021	11JAN2022	Death	
1432-009	23DEC2019	Prior Eculizumab Treatment Unknown	10JAN2020	19MAR2020	Switch to eculizumab IV	
1558-002	09JAN2015	Prior Eculizumab Treatment	19JUL2022	03JUL2023	Lack of Efficacy	
1617-003	09MAY2014	Prior Eculizumab Treatment	25JUN2019	09JUL2019	Patient choice	patient withdrew from study
1677-003	08DEC2014	Without Prior Eculizumab Treatment	12JUL2022	26JUL2022	Physician decision	allogenic transplantation
1726-001	23FEB2015	Without Prior Eculizumab Treatment	15NOV2019	15NOV2019	Cost or access considerations	

Note: (a) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.

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Listing 2.1
Discontinuation from Ultomiris, During the Analysis Period
Ravulizumab Study Population

Patient Number	Enrollment Date	Treatment Status[a]	Ravulizumab Initiation Date	Last Recorded Date of Ravulizumab Infusion	Primary Reason for Ravulizumab Discontinuation	Specify
1004-012	29JAN2013	Prior Eculizumab Treatment Unknown	21JUN2019	22JUL2019	Patient choice	patient choice
1004-021	24MAY2018	Prior Eculizumab Treatment	13FEB2020	13FEB2020		
1005-001	17JUL2009	Prior Eculizumab Treatment	24NOV2022	22SEP2023	Physician decision	patient is enrolled in a clinical trial
1009-052	30NOV2006	Prior Eculizumab Treatment	18OCT2021	23JAN2023	Switch to other anti-complement treatment	
1009-057	02AUG2007	Without Prior Eculizumab Treatment	21OCT2022	28APR2023	Lack of Efficacy	Patient has not seen major benefit in her fatigue with Ravulizumab.
1009-074	31MAR2009	Prior Eculizumab Treatment	12JAN2022	23JAN2024	Switch to other anti-complement treatment	
1009-084	22SEP2009	Prior Eculizumab Treatment	23FEB2022	31MAY2023	Switch to other anti-complement treatment	

Note: Includes patients actively enrolled in the registry during the analysis period, which covers the time period from 06JAN2023 to 06JAN2025.
(a) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.

Source: ADAM.ADSL, ADAM.ADPOP, ADAM.ADEX
Run Date: 2025-05-14T14:46:17
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ravuema202501/Files/listings/production/programs/l2_ravudis_dur.sas

Listing 2.1
Discontinuation from Ultomiris, During the Analysis Period
Ravulizumab Study Population

Patient Number	Enrollment Date	Treatment Status[a]	Ravulizumab Initiation Date	Last Recorded Date of Ravulizumab Infusion	Primary Reason for Ravulizumab Discontinuation	Specify
1009-088	22OCT2009	Prior Eculizumab Treatment	09FEB2022	11JUL2023	Switch to other anti-complement treatment	
1009-103	22APR2010	Prior Eculizumab Treatment Unknown	15AUG2022	12MAR2024	Physician decision	clone size decreased
1009-133	27OCT2010	Without Prior Eculizumab Treatment	04MAR2022	03AUG2023	Death	
1009-178	08SEP2011	Without Prior Eculizumab Treatment	13JUN2022	01SEP2023	Lack of Efficacy	
1009-287	29JUL2014	Prior Eculizumab Treatment	10JAN2022	08AUG2023	Death	
1009-328	07JUL2015	Prior Eculizumab Treatment	27SEP2021	10SEP2023	Switch to other anti-complement treatment	
1009-346	20OCT2015	Prior Eculizumab Treatment Unknown	18AUG2021	21DEC2021	Patient choice	Patient experienced decreased quality of life on Ravulizumab.

Note: Includes patients actively enrolled in the registry during the analysis period, which covers the time period from 06JAN2023 to 06JAN2025.
(a) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.

Source: ADAM.ADSL, ADAM.ADPOP, ADAM.ADEX
Run Date: 2025-05-14T14:46:17
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ravuema202501/Files/listings/production/programs/l2_ravudis_dur.sas

Listing 2.1
Discontinuation from Ultomiris, During the Analysis Period
Ravulizumab Study Population

Patient Number	Enrollment Date	Treatment Status[a]	Ravulizumab Initiation Date	Last Recorded Date of Ravulizumab Infusion	Primary Reason for Ravulizumab Discontinuation	Specify
1009-410	20JUN2017	Without Prior Eculizumab Treatment	07MAR2023	09JUN2023	Death	
1009-420	31OCT2017	Without Prior Eculizumab Treatment	16MAR2022	30MAR2022		
1009-429	21MAR2019	Prior Eculizumab Treatment	19AUG2021	11MAY2023	Switch to other anti-complement treatment	
1009-459	14NOV2022	Without Prior Eculizumab Treatment	07DEC2022	15JUN2023	Switch to other anti-complement treatment	
1013-001	19MAY2005	Prior Eculizumab Treatment	03NOV2020	17NOV2020	Lack of Efficacy	
1013-011	19MAY2006	Prior Eculizumab Treatment Unknown	15NOV2022	30MAY2023	Switch to other anti-complement treatment	
1013-061	15JUL2009	Prior Eculizumab Treatment	01OCT2019	26DEC2020	Adverse Event	
1013-133	29JAN2014	Prior Eculizumab Treatment	10SEP2019	24SEP2019	Death	

Note: Includes patients actively enrolled in the registry during the analysis period, which covers the time period from 06JAN2023 to 06JAN2025.
(a) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.

Source: ADAM.ADSL, ADAM.ADPOP, ADAM.ADEX
Run Date: 2025-05-14T14:46:17
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ravuema202501/Files/listings/production/programs/l2_ravudis_dur.sas

Listing 2.1
Discontinuation from Ultomiris, During the Analysis Period
Ravulizumab Study Population

Patient Number	Enrollment Date	Treatment Status[a]	Ravulizumab Initiation Date	Last Recorded Date of Ravulizumab Infusion	Primary Reason for Ravulizumab Discontinuation	Specify
1013-166	12MAY2015	Prior Eculizumab Treatment	15AUG2019	15AUG2022	Switch to other anti-complement treatment	
1013-228	05NOV2019	Prior Eculizumab Treatment	15APR2020	29APR2020	Switch to other anti-complement treatment	
1013-243	08MAR2022	Prior Eculizumab Treatment	01SEP2022	01OCT2022	Lack of Efficacy	
1030-007	05JUN2017	Without Prior Eculizumab Treatment	27MAY2022	10NOV2023	Death	
1093-043	10MAY2011	Prior Eculizumab Treatment	24JUL2019	07AUG2019	Switch to other anti-complement treatment	
1093-109	28OCT2014	Prior Eculizumab Treatment	15AUG2019	15AUG2019		
1093-192	24OCT2017	Without Prior Eculizumab Treatment	07AUG2019	21AUG2019		
1093-222	11DEC2018	Without Prior Eculizumab Treatment	24JAN2024	07FEB2024	Switch to other anti-complement treatment	

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(a) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.

Source: ADAM.ADSL, ADAM.ADPOP, ADAM.ADEX
Run Date: 2025-05-14T14:46:17
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ravuema202501/Files/listings/production/programs/l2_ravudis_dur.sas

Listing 2.1
Discontinuation from Ultomiris, During the Analysis Period
Ravulizumab Study Population

Patient Number	Enrollment Date	Treatment Status[a]	Ravulizumab Initiation Date	Last Recorded Date of Ravulizumab Infusion	Primary Reason for Ravulizumab Discontinuation	Specify
1093-253	26JUN2020	Without Prior Eculizumab Treatment	29SEP2020	13OCT2020	Switch to other anti-complement treatment	
1134-111	26SEP2014	Without Prior Eculizumab Treatment	02OCT2023	16OCT2023		
1151-014	11APR2012	Prior Eculizumab Treatment	09DEC2020	11JAN2023	Physician decision	suspected extravascular hemolysis
1165-010	19JAN2021	Without Prior Eculizumab Treatment	24MAR2022	08FEB2024	Switch to eculizumab IV	
1193-018	14MAR2023	Without Prior Eculizumab Treatment	31JUL2023	18AUG2023		
1197-027	21JUN2018	Prior Eculizumab Treatment	02JAN2023	13MAR2023	Death	
1197-031	29NOV2021	Prior Eculizumab Treatment	30DEC2022	13JAN2023	Switch to other anti-complement treatment	
1341-022	27DEC2019	Without Prior Eculizumab Treatment	25MAY2022	08JUN2022	Lack of Efficacy	

Note: Includes patients actively enrolled in the registry during the analysis period, which covers the time period from 06JAN2023 to 06JAN2025.
(a) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.

Source: ADAM.ADSL, ADAM.ADPOP, ADAM.ADEX
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Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ravuema202501/Files/listings/production/programs/l2_ravudis_dur.sas

Listing 2.1
Discontinuation from Ultomiris, During the Analysis Period
Ravulizumab Study Population

Patient Number	Enrollment Date	Treatment Status[a]	Ravulizumab Initiation Date	Last Recorded Date of Ravulizumab Infusion	Primary Reason for Ravulizumab Discontinuation	Specify
1381-002	15MAR2012	Prior Eculizumab Treatment	21DEC2019	04JAN2020		
1381-016	17JUN2021	Prior Eculizumab Treatment Unknown	17JUN2021	26JAN2024	Physician decision	site study closing
1381-017	10AUG2021	Prior Eculizumab Treatment	10AUG2021	23APR2024	Physician decision	site study closing
1420-002	15MAY2012	Without Prior Eculizumab Treatment	22JUN2022	26DEC2022	Lack of Efficacy	medical insurance was suspended due to no LDH reduction and drug administration was stopped
1423-012	07JAN2016	Prior Eculizumab Treatment	10NOV2021	06DEC2023	Physician decision	PNH Flowcytometry negative
1432-009	23DEC2019	Prior Eculizumab Treatment Unknown	10JAN2020	19MAR2020	Switch to eculizumab IV	
1558-002	09JAN2015	Prior Eculizumab Treatment	19JUL2022	03JUL2023	Lack of Efficacy	
1677-003	08DEC2014	Without Prior Eculizumab Treatment	12JUL2022	26JUL2022	Physician decision	allogenic transplantation

Note: Includes patients actively enrolled in the registry during the analysis period, which covers the time period from 06JAN2023 to 06JAN2025.
(a) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.

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Run Date: 2025-05-14T14:46:17
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ravuema202501/Files/listings/production/programs/l2_ravudis_dur.sas

Listing 3
Deaths, Cumulative
Ravulizumab Study Population

Patient Number	Enrollment Date	Treatment Exposure at Time of Death	Ravulizumab Initiation Date	Ravulizumab Discontinuation Date	Date of Death	Age at Death	Category for Cause of Death	Preferred Term for Cause of Death	Reported Cause of Death
1009-133	27OCT2010	Ravulizumab	04MAR2022	03AUG2023	23AUG2023	48.1	Neoplasms benign, malignant and unspecified (incl cysts and polyps)	Colorectal Cancer	Metastatic bowel cancer
1009-146	10FEB2011	Ravulizumab	15NOV2021	05SEP2022	05SEP2022	56.2	Unknown	Unknown	Metastatic clear cell papillary renal cell carcinoma
1009-287	29JUL2014	Ravulizumab	10JAN2022	08AUG2023	01OCT2023	88.3	Nervous system disorders	Stroke	Stroke
1009-327	24JUN2015	Ravulizumab	12AUG2021	17NOV2022	15DEC2022	79.5	Neoplasms benign, malignant and unspecified (incl cysts and polyps)	Squamous cell carcinoma of the vulva	Metastatic squamous cell carcinoma of vulva
1009-410	20JUN2017	Ravulizumab	07MAR2023	09JUN2023	09JUN2023	76.9	Neoplasms benign, malignant and unspecified (incl cysts and polyps)	Gastric cancer	Advanced Gastric Cancer
1009-420	31OCT2017	Ravulizumab	16MAR2022	05MAR2024	05MAR2024	75.7	Infections and infestations	Sepsis	Gram negative sepsis
1009-427	09JAN2019	Ravulizumab	24NOV2021	24MAY2022	07JUL2022	74.0	Unknown	Unknown	Patient transformed from AA to acute leukaemia
1013-145	13AUG2014	Ravulizumab	21AUG2019	01FEB2022	16FEB2022	79.6	Lung infection	Pneumonia	pulmonary infection

Listing 3
Deaths, Cumulative
Ravulizumab Study Population

Patient Number	Enrollment Date	Treatment Exposure at Time of Death	Ravulizumab Initiation Date	Ravulizumab Discontinuation Date	Date of Death	Age at Death	Category for Cause of Death	Preferred Term for Cause of Death	Reported Cause of Death
1030-007	05JUN2017	Ravulizumab	27MAY2022	10NOV2023	11NOV2023	49.4	Injury, poisoning and procedural complications	Accident	mountain bike accident
1061-008	23APR2019	Ravulizumab	27AUG2019	09FEB2022	15APR2022	77.8	General disorders and administration site conditions	Disease progression	Disease progression
1093-109	28OCT2014	Ravulizumab	15AUG2019	23JAN2024	23JAN2024	74.6	Unknown	Unknown	Unfortunatly no further details. Information by telephon only from Patients Son at 06. March 2024
1093-192	24OCT2017	Ravulizumab	07AUG2019	02MAY2023	02MAY2023	84.8	General disorders and administration site conditions	Death NOS	

Listing 3
Deaths, Cumulative
Ravulizumab Study Population

Patient Number	Enrollment Date	Treatment Exposure at Time of Death	Ravulizumab Initiation Date	Ravulizumab Discontinuation Date	Date of Death	Age at Death	Category for Cause of Death	Preferred Term for Cause of Death	Reported Cause of Death
1093-215	08JAN2019	Ravulizumab	18MAR2021	25MAR2022	25MAR2022	67.7	Neoplasms benign, malignant and unspecified (incl cysts and polyps)	Acute myeloid leukaemia	AML (acute myeloid leukemia)/MDS (Myelodysplastic syndrome) passed away in other hospital. Refused further drug treatment and chemotherapy.
1134-111	26SEP2014	Ravulizumab	02OCT2023	31JAN2024	31JAN2024	84.6	General disorders and administration site conditions	Death	General decline due to aging.
1193-018	14MAR2023	Ravulizumab	31JUL2023	06FEB2024	06FEB2024	71.6	General disorders and administration site conditions	Death NOS	Unknown
1197-027	21JUN2018	Ravulizumab	02JAN2023	13MAR2023	13APR2023	78.8	Neoplasms benign, malignant and unspecified (incl cysts and polyps)	Myelodysplastic syndrome	Severe renal failure associated with infectious complications
1429-011	27JUL2021	Ravulizumab	28DEC2021	11JAN2022	11MAR2022	37.7	Nervous system disorders	Haemorrhage intracranial	intracerebral hemorrhage

Listing 3.1
Deaths, During the Analysis Period
Ravulizumab Study Population

Patient Number	Enrollment Date	Treatment Exposure at Time of Death	Ravulizumab Initiation Date	Ravulizumab Discontinuation Date	Date of Death	Age at Death	Category for Cause of Death	Preferred Term for Cause of Death	Reported Cause of Death
1009-133	27OCT2010	Ravulizumab	04MAR2022	03AUG2023	23AUG2023	48.1	Neoplasms benign, malignant and unspecified (incl cysts and polyps)	Colorectal Cancer	Metastatic bowel cancer
1009-287	29JUL2014	Ravulizumab	10JAN2022	08AUG2023	01OCT2023	88.3	Nervous system disorders	Stroke	Stroke
1009-410	20JUN2017	Ravulizumab	07MAR2023	09JUN2023	09JUN2023	76.9	Neoplasms benign, malignant and unspecified (incl cysts and polyps)	Gastric cancer	Advanced Gastric Cancer
1009-420	31OCT2017	Ravulizumab	16MAR2022	05MAR2024	05MAR2024	75.7	Infections and infestations	Sepsis	Gram negative sepsis
1030-007	05JUN2017	Ravulizumab	27MAY2022	10NOV2023	11NOV2023	49.4	Injury, poisoning and procedural complications	Accident	mountain bike accident
1093-109	28OCT2014	Ravulizumab	15AUG2019	23JAN2024	23JAN2024	74.6	Unknown	Unknown	Unfortunatly no further details. Information by telephon only from Patients Son at 06. March 2024

Note: Includes patients actively enrolled in the registry during the analysis period, which covers the time period from 06JAN2023 to 06JAN2025.

Source: ADAM.ADSL, ADAM.ADPOP
Run Date: 2025-05-14T14:46:19
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ravuema202501/Files/listings/production/programs/l3_death_dur.sas

Listing 3.1
Deaths, During the Analysis Period
Ravulizumab Study Population

Patient Number	Enrollment Date	Treatment Exposure at Time of Death	Ravulizumab Initiation Date	Ravulizumab Discontinuation Date	Date of Death	Age at Death	Category for Cause of Death	Preferred Term for Cause of Death	Reported Cause of Death
1093-192	24OCT2017	Ravulizumab	07AUG2019	02MAY2023	02MAY2023	84.8	General disorders and administration site conditions	Death NOS	
1134-111	26SEP2014	Ravulizumab	02OCT2023	31JAN2024	31JAN2024	84.6	General disorders and administration site conditions	Death	General decline due to aging.
1193-018	14MAR2023	Ravulizumab	31JUL2023	06FEB2024	06FEB2024	71.6	General disorders and administration site conditions	Death NOS	Unknown
1197-027	21JUN2018	Ravulizumab	02JAN2023	13MAR2023	13APR2023	78.8	Neoplasms benign, malignant and unspecified (incl cysts and polyps)	Myelodysplastic syndrome	Severe renal failure associated with infectious complications

Note: Includes patients actively enrolled in the registry during the analysis period, which covers the time period from 06JAN2023 to 06JAN2025.

Source: ADAM.ADSL, ADAM.ADPOP
Run Date: 2025-05-14T14:46:19
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ravuema202501/Files/listings/production/programs/l3_death_dur.sas

Listing 4
Major Adverse Vascular Events
Ravulizumab Study Population

Patient Number	Enrollment Date	Enrollment Status	Treatment Exposure at time of event	Ravulizumab Initiation Date	Date of Event	Event Detail	Type	Outcome	Resolution Date
1005-006	24JUL2009		Ravulizumab	13OCT2022	15DEC2023	stenosis of the left anterior descending artery	Other		29JAN2024
1005-007	11SEP2009		Eculizumab	06DEC2022	11JAN2012	Thrombophlebitis/ Deep Vein Thrombosis	Venous		07FEB2012
1009-074	31MAR2009		Eculizumab	12JAN2022	01JUL2014	Angina	Other	Ongoing	
1009-076	12MAY2009		Untreated	13AUG2021	12MAY2009	Hepatic/Portal Vein Thrombosis	Venous	Resolved	12MAY2009
1009-080	08SEP2009		Eculizumab	07SEP2021	15JUL2009	Other Major Adverse Vascular Event	Other	Resolved	07SEP2009
1009-084	22SEP2009		Eculizumab	23FEB2022	17MAY2012	Cerebral Arterial Occlusion/CVA	Arterial	Ongoing	
1009-149	17FEB2011		Untreated	12AUG2021	15APR2011	Gastric varices	Other		09SEP2011
1009-164	16JUN2011		Untreated	25NOV2021	02DEC2011	Renal Arterial Thrombosis	Arterial	Ongoing	
1009-292	10SEP2014		Eculizumab	14SEP2021	10SEP2014	Pulmonary Embolus	Other	Resolved	15OCT2014
1009-320	21MAY2015		Eculizumab	04OCT2021	21MAY2015	Thrombophlebitis/ Deep Vein Thrombosis	Venous	Resolved	01JUL2015
1009-323	28MAY2015		Eculizumab	15AUG2021	15FEB2017	Transient Ischemic Attack	Other		

Listing 4
Major Adverse Vascular Events
Ravulizumab Study Population

Patient Number	Enrollment Date	Enrollment Status	Treatment Exposure at time of event	Ravulizumab Initiation Date	Date of Event	Event Detail	Type	Outcome	Resolution Date
1009-409	13JUN2017		Eculizumab	02AUG2021	18OCT2020	Hepatic/Portal Vein Thrombosis	Venous	Ongoing	
1009-427	09JAN2019		Eculizumab	24NOV2021	11MAR2019	Thrombophlebitis/ Deep Vein Thrombosis	Venous	Ongoing	
1013-061	15JUL2009	Active	Eculizumab	01OCT2019	06FEB2012	Thrombophlebitis/ Deep Vein Thrombosis	Venous		06FEB2012
1013-155	14JAN2015	Active	Eculizumab	04SEP2019	15OCT2014	Pulmonary Embolus	Other	Resolved	15OCT2014
1061-004	26MAR2007		Eculizumab	04APR2022	08DEC2014	Hepatic/Portal Vein Thrombosis	Venous	Ongoing	
1093-030	03NOV2010		Untreated	14APR2020	15MAY2014	Thrombophlebitis/ Deep Vein Thrombosis	Venous		15MAY2014
1093-130	23APR2015		Untreated	28AUG2019	27OCT2017	Cerebral Arterial Occlusion/CVA	Arterial		03NOV2017
	23APR2015		Untreated	28AUG2019	15NOV2018	Cerebral Arterial Occlusion/CVA	Arterial		15NOV2018
1093-254	23JUN2020		Ravulizumab	01JUL2020	28SEP2020	Thrombophlebitis/ Deep Vein Thrombosis	Venous		28SEP2020
1134-062	28JUN2010		Untreated	15FEB2024	01JAN2011	Cerebral Venous Occlusion	Venous	Ongoing	

Listing 4
Major Adverse Vascular Events
Ravulizumab Study Population

Patient Number	Enrollment Date	Enrollment Status	Treatment Exposure at time of event	Ravulizumab Initiation Date	Date of Event	Event Detail	Type	Outcome	Resolution Date
1134-088	09JAN2012		Untreated	04SEP2023	20MAY2012	Thrombophlebitis/ Deep Vein Thrombosis	Venous		20JUN2012
	09JAN2012		Untreated	04SEP2023	12JUL2012	Myocardial Infarction	Other		12JUL2012
	09JAN2012		Untreated	04SEP2023	02DEC2020	Thrombophlebitis/ Deep Vein Thrombosis	Venous		02DEC2020
1134-140	13MAR2019		Untreated	26FEB2024	07JUN2019	Thrombophlebitis/ Deep Vein Thrombosis	Venous		12JUN2019
1139-013	27JAN2010		Eculizumab	12MAY2022	15APR2015	Thrombosis of superficial varicose vein right lower thigh	Other		
1140-002	02NOV2010		Eculizumab	20FEB2019	12NOV2014	Thrombophlebitis/ Deep Vein Thrombosis	Venous		01FEB2015
1170-002	18JAN2010		Eculizumab	04JUL2022	10APR2012	Thrombophlebitis/ Deep Vein Thrombosis	Venous		20JUN2012
1200-005	27JAN2011		Eculizumab	15JUL2020	15MAR2017	Thrombophlebitis/ Deep Vein Thrombosis	Venous		16MAR2017

Listing 4
Major Adverse Vascular Events
Ravulizumab Study Population

Patient Number	Enrollment Date	Enrollment Status	Treatment Exposure at time of event	Ravulizumab Initiation Date	Date of Event	Event Detail	Type	Outcome	Resolution Date
1209-003	09SEP2010		Untreated	12APR2022	01FEB2018	Hepatic/Portal Vein Thrombosis	Venous	Ongoing	
1219-003	12SEP2013		Untreated	15JUL2022	07SEP2017	possible superficial thrombus	Other		18SEP2017
1226-001	04JUN2010		Ravulizumab	18MAY2022	30JUN2022	Myocardial Infarction	Other		03JUL2022
1304-002	10MAY2011		Untreated	15SEP2022	20JUN2011	Hepatic/Portal Vein Thrombosis	Venous		15SEP2011
1304-003	27JUL2011		Untreated	11AUG2022	26JAN2019	Ischemic Stroke	Other		06MAR2019
	27JUL2011		Untreated	11AUG2022	05JUL2019	ISCHEMIC STROKE	Other		18JUL2019
1351-013	11JUN2018		Eculizumab	06OCT2021	15FEB2021	Pulmonary Embolus	Other		01JUL2021
1366-020	15MAR2012		Untreated	21JUL2021	08FEB2019	splenic varix with multifocal thrombus	Other		16APR2020
1366-024	28MAR2012		Untreated	21JUL2022	18MAY2022	Hepatic/Portal Vein Thrombosis	Venous	Ongoing	
1366-075	31DEC2014		Untreated	22JUL2021	03AUG2018	Thrombophlebitis/ Deep Vein Thrombosis	Venous		09AUG2018
1366-108	26APR2018		Untreated	18AUG2021	13MAR2019	Thrombophlebitis/ Deep Vein Thrombosis	Venous	Ongoing	

Listing 4
Major Adverse Vascular Events
Ravulizumab Study Population

Patient Number	Enrollment Date	Enrollment Status	Treatment Exposure at time of event	Ravulizumab Initiation Date	Date of Event	Event Detail	Type	Outcome	Resolution Date
1366-129	22APR2020		Untreated	18AUG2021	25MAY2020	Pulmonary Embolus	Other		01FEB2021
1366-148	29MAR2021		Untreated	15SEP2021	16APR2021	Thrombophlebitis/ Deep Vein Thrombosis	Venous		18MAR2022
1366-162	10AUG2022		Untreated	31AUG2022	23AUG2022	Thrombophlebitis/ Deep Vein Thrombosis	Venous		02MAR2023
1381-017	10AUG2021		Ravulizumab	10AUG2021	12DEC2021	Thrombophlebitis/ Deep Vein Thrombosis	Venous		12DEC2021
1420-002	15MAY2012		Untreated	22JUN2022	15MAY2012	Other Major Adverse Vascular Event	Other	Ongoing	
1422-011	20MAR2014		Untreated	10AUG2021	25JAN2017	Dural sinus thrombosis	Other	Ongoing	
1462-004	30NOV2012		Eculizumab	01NOV2019	04NOV2015	Renal Vein Thrombosis	Venous	Ongoing	
1462-008	14DEC2012		Ravulizumab	01NOV2019	10JAN2024	Thrombophlebitis/ Deep Vein Thrombosis	Venous	Ongoing	
	14DEC2012		Ravulizumab	01NOV2019	10JAN2024	Pulmonary Embolus	Other	Ongoing	

Listing 4
Major Adverse Vascular Events
Ravulizumab Study Population

Patient Number	Enrollment Date	Enrollment Status	Treatment Exposure at time of event	Ravulizumab Initiation Date	Date of Event	Event Detail	Type	Outcome	Resolution Date
1493-020	14MAR2022		Untreated	03AUG2023	18JUN2023	Cerebral Venous Occlusion	Venous		22AUG2023
1612-004	30JUN2016		Eculizumab	28MAR2019	13SEP2017	Thrombophlebitis/ Deep Vein Thrombosis	Venous	Ongoing	

Listing 5
Malignancy
Ravulizumab Study Population

Patient Number	Enrollment Date	Ravulizumab Initiation Date	Status	Treatment Exposure at time of event	Date of Event	Category	Subcategory	Event Detail	Outcome	Resolution Date
1005-006	24JUL2009	13OCT2022		Eculizumab	14JUN2011	Solid Tumor	Liver and biliary	Discovery of a carcinoma on gallbladder during cholecystectomy	Resolved	14JUN2011
1008-019	13JUN2012	03JAN2020		Ravulizumab	12OCT2023	Solid Tumor	Pancreatic carcinoma	pancreatic cancer	Ongoing	
1009-074	31MAR2009	12JAN2022		Eculizumab	15FEB2012	Hematologic	MDS	Myelodysplastic Syndrome	Ongoing	
1009-088	22OCT2009	09FEB2022		Eculizumab	15JAN2012	Solid Tumor	NMSC (Non-melanoma skin cancer)	Basal cell carcinoma	Resolved	09JUL2012
				Ravulizumab	29JUN2022	Solid Tumor	Skin neoplasm excision	Lesion from right shin (fully excised basal cell carcinoma).	Resolved	10FEB2023
1009-089	27OCT2009	15SEP2021		Eculizumab	05APR2018	Solid Tumor	Breast	Ductal carcinoma in situ of the breast	Resolved	07AUG2018
1009-129	31AUG2010	17JAN2023		Ravulizumab	05JUN2023	Solid Tumor	Colorectal	Adenocarcinoma of the Sigmoid Colon	Ongoing	
					15JUN2023	Solid Tumor	Colorectal	Distal sigmoid cancer	Ongoing	

Listing 5
Malignancy
Ravulizumab Study Population

Patient Number	Enrollment Date	Ravulizumab Initiation Date	Status	Treatment Exposure at time of event	Date of Event	Category	Subcategory	Event Detail	Outcome	Resolution Date
1009-133	27OCT2010	04MAR2022		Ravulizumab	15MAR2022	Solid Tumor	Gastric	Metastatic bowel cancer	Ongoing	
1009-146	10FEB2011	15NOV2021		Eculizumab	15JAN2021	Solid Tumor	Renal	Relapse of clear cell renal cell carcinoma	Ongoing	
				Untreated	10FEB2011	Unknown		Malignancy	Ongoing	
1009-318	13MAY2015	26JAN2022		Eculizumab	15NOV2018	Solid Tumor	Breast	breast cancer	Ongoing	
1009-327	24JUN2015	12AUG2021		Ravulizumab	01JUL2022	Solid Tumor	Other	Metastatic squamous cell carcinoma of the vulva.	Ongoing	
1009-410	20JUN2017	07MAR2023		Untreated	12FEB2023	Solid Tumor	Gastric	Gastric adenocarcinoma.	Ongoing	
1009-420	31OCT2017	16MAR2022		Ravulizumab	15SEP2022	Solid Tumor	NMSC (Non-melanoma skin cancer)	Basal cell carcinoma	Ongoing	
1009-434	09SEP2019	03AUG2021		Ravulizumab	08FEB2024	Solid Tumor	Breast	Breast cancer	Ongoing	
1013-001	19MAY2005	03NOV2020	Discontinued	Eculizumab	15JUN2010	Solid Tumor	Breast	Mamma-Ca left	Resolved with sequelae	01JUL2010
1013-058	19MAY2009	07AUG2019	Active	Ravulizumab	11NOV2019	Solid Tumor	Melanoma	malign melanoma right lower leg	Resolved	13NOV2019

Listing 5
Malignancy
Ravulizumab Study Population

Patient Number	Enrollment Date	Ravulizumab Initiation Date	Status	Treatment Exposure at time of event	Date of Event	Category	Subcategory	Event Detail	Outcome	Resolution Date
1013-076	24MAR2010	15OCT2019	Active	Eculizumab	15AUG2011	Solid Tumor	Liver and biliary	papillary carcinoma in gall bladder	Resolved	20SEP2011
1013-081	22AUG2010	15NOV2019	Discontinued	Ravulizumab	15JAN2021	Hematologic	MDS	Myelodysplastic Syndrome	Ongoing	
					15JAN2021	Hematologic	MDS	MDS-MLD	Ongoing	
1013-145	13AUG2014	21AUG2019	Discontinued	Ravulizumab	22JAN2020	Hematologic	Lymphoma	lymph node carcinoma	Ongoing	
1013-151	07OCT2014	05DEC2019	Active	Eculizumab	26MAY2016	Solid Tumor	Prostate	Prostata-Ca	Resolved	26MAY2016
					05SEP2016	Hematologic	Lymphoma	B-cell-Lymphoma	Ongoing	
				Ravulizumab	27JUL2023	Hematologic	MDS	Myelodysplastic Syndrome	Ongoing	
1093-140	19JUL2015	01JUL2020		Untreated	15FEB2019	Solid Tumor	Prostate	prostate carcinoma	Ongoing	
1130-018	14NOV2019	28MAY2020		Ravulizumab	28NOV2022	Hematologic	Leukemia	Chronic myelomonocytic leukemia	Ongoing	
1134-088	09JAN2012	04SEP2023		Ravulizumab	13DEC2023	Hematologic	MDS	Myelodysplastic Syndrome	Ongoing	
1151-014	11APR2012	09DEC2020		Ravulizumab	15MAR2022	Solid Tumor	Other	Adenocarcinoma	Ongoing	

Listing 5
Malignancy
Ravulizumab Study Population

Patient Number	Enrollment Date	Ravulizumab Initiation Date	Status	Treatment Exposure at time of event	Date of Event	Category	Subcategory	Event Detail	Outcome	Resolution Date
1164-003	13JAN2010	15NOV2022		Ravulizumab	15NOV2022	Solid Tumor	NMSC (Non-melanoma skin cancer)	Trabecular basal cell carcinoma of the left side of the nose	Resolved	09NOV2022
1197-027	21JUN2018	02JAN2023		Eculizumab	27JAN2021	Solid Tumor	Colorectal	Mucinous colorectal adenocarcinoma	Resolved	05FEB2021
					11NOV2022	Hematologic	Lymphoma	T-cell chronic lymphoproliferative disorder	Ongoing	
1200-005	27JAN2011	15JUL2020		Eculizumab	15FEB2010	Unknown		Malignancy	Resolved	15FEB2010
1251-005	06APR2016	26APR2023		Eculizumab	01JUN2022	Solid Tumor	Breast	BREAST CARCINOMA	Ongoing	
1366-024	28MAR2012	21JUL2022		Untreated	31MAY2016	Solid Tumor	Gastric	Stomach ca T1aN0M0	Ongoing	
1418-009	25OCT2012	24AUG2021		Eculizumab	15JUN2016	Solid Tumor	Breast	breast cancer	Ongoing	
1423-006	23DEC2014	24AUG2021		Ravulizumab	24FEB2022	Hematologic	MDS	Myelodysplastic Syndrome	Ongoing	
1462-004	30NOV2012	01NOV2019		Eculizumab	25DEC2015	Solid Tumor	Gastric	Gastric cancer	Resolved	08FEB2016
				Ravulizumab	20JUL2020	Solid Tumor	Liver and biliary	Hepatocellular Carcinoma	Ongoing	

Listing 5
Malignancy
Ravulizumab Study Population

Patient Number	Enrollment Date	Ravulizumab Initiation Date	Status	Treatment Exposure at time of event	Date of Event	Category	Subcategory	Event Detail	Outcome	Resolution Date
1558-002	09JAN2015	19JUL2022		Eculizumab	15JAN2019	Solid Tumor	Head and neck	Primary salivary gland carcinoma	Ongoing	
				Ravulizumab	12SEP2022	Solid Tumor	Lung	Lung lesion as metastasis of previous parotid carcinoma.	Ongoing	
1617-003	09MAY2014	25JUN2019		Eculizumab	16SEP2016	Solid Tumor	Breast	Right breast invasive ductal carcinoma	Resolved	03NOV2016
1682-001	25OCT2014	29MAR2023		Eculizumab	26SEP2016	Solid Tumor	NMSC (Non-melanoma skin cancer)	Basal cell carcinoma	Resolved	20FEB2017
1787-003	24MAY2016	14JUL2021		Ravulizumab	05APR2023	Solid Tumor	Prostate	Malignant neoplasm of prostate	Ongoing	

Listing 6
Infection
Ravulizumab Study Population

Patient Number	Enrollment Date	Ravulizumab Initiation Date	Status	Treatment Exposure at time of event	Date of Event	Category	Subcategory	Event Detail	Outcome	Resolution Date
1005-006	24JUL2009	13OCT2022		Eculizumab	16MAY2021	Other Infection	Other Organism	Escherichia Coli (positive hemoculture)	Resolved	22MAY2021
1005-007	11SEP2009	06DEC2022		Eculizumab	19OCT2019	Other Infection	Other Organism	STAPHYLOCOCCUS EPIDERMITIS	Resolved	07JAN2020
1009-014	17AUG2005	19JAN2022		Ravulizumab	23NOV2023	Other Infection	Other Organism	COVID-19 positive	Resolved	31JAN2024
1009-088	22OCT2009	09FEB2022		Eculizumab	11MAR2010	Other Infection	Unknown Organism	Urine infection - 5 days of antibiotics	Resolved	16MAR2010
					01FEB2015	Other Infection	Other Organism	Viral Infection	Resolved	01FEB2015
					09FEB2016	Other Infection	Unknown Organism	Chest infection	Resolved	01MAR2016
1009-089	27OCT2009	15SEP2021		Eculizumab	15NOV2014	Other Infection	Unknown Organism	Sinusitis	Resolved	27APR2015
				Ravulizumab	15DEC2022	Other Infection	Other Organism	Covid-19	Resolved	05JUN2023
1009-149	17FEB2011	12AUG2021		Eculizumab	15MAR2015	Other Infection	Other Organism	Ecoli	Resolved	23MAR2015
1009-151	10MAR2011	04JAN2022		Ravulizumab	03AUG2022	Other Infection	Other Organism	COVID-19	Resolved	30AUG2022
1009-195	17NOV2011	01JUL2022		Ravulizumab	15OCT2022	Other Infection	Unknown Organism	unknown	Resolved	19DEC2022

Listing 6
Infection
Ravulizumab Study Population

Patient Number	Enrollment Date	Ravulizumab Initiation Date	Status	Treatment Exposure at time of event	Date of Event	Category	Subcategory	Event Detail	Outcome	Resolution Date
1009-210	23FEB2012	22OCT2021		Ravulizumab	15JUL2023	Other Infection	Other Organism	Covid-19 infection	Resolved	06SEP2023
				Untreated	14NOV2014	Other Infection	Other Organism	Scarlet Fever	Resolved	11DEC2014
					10DEC2014	Other Infection	Other Organism	Scarlet Fever	Resolved	10DEC2014
1009-221	06JUN2012	21JUN2022		Eculizumab	15MAY2013	Other Infection	Other Organism	viral infection	Resolved	01JUL2013
					15DEC2013	Other Infection	Unknown Organism	Lower Respiratory tract infection	Resolved	16DEC2013
1009-222	28JUN2012	26OCT2021		Eculizumab	15NOV2013	Other Infection	Unknown Organism	cold and cough	Resolved	05FEB2014
1009-251	11JUN2013	03AUG2021		Eculizumab	22NOV2013	Other Infection	Other Organism	chryseobacterium gleum and Acinetobacter Ursingli	Resolved	28NOV2013
1009-264	24OCT2013	06AUG2021		Eculizumab	13JAN2017	Neisseria	Meningococcal	Meningococcus (Y strain)	Resolved	23JAN2017
					01OCT2019	Other Infection	Unknown Organism	oral strep bacteraemia	Resolved	15OCT2019
1009-280	15JUL2014	10SEP2021		Eculizumab	15NOV2014	Other Infection	Other Organism	Viral infection	Resolved	22DEC2014

Listing 6
Infection
Ravulizumab Study Population

Patient Number	Enrollment Date	Ravulizumab Initiation Date	Status	Treatment Exposure at time of event	Date of Event	Category	Subcategory	Event Detail	Outcome	Resolution Date
1009-318	13MAY2015	26JAN2022		Ravulizumab	05OCT2023	Other Infection	Other Organism	Bacterial infection of ureteric stent site.	Ongoing	
1009-328	07JUL2015	27SEP2021		Ravulizumab	24AUG2023	Other Infection	Other Organism	COVID-19 Positive	Resolved	30OCT2023
				Untreated	17NOV2015	Other Infection	Other Organism	Viral infection	Resolved	12JAN2016
					31DEC2015	Other Infection	Other Organism	Viral infection which triggered hemoysis.	Resolved	12JAN2016
1009-366	05AUG2016	07OCT2021		Eculizumab	03FEB2020	Other Infection	Unknown Organism	chest infection	Resolved	05FEB2020
				Ravulizumab	08MAR2022	Other Infection	Other Organism	COVID-19	Resolved	30MAR2022
1009-386	01NOV2016	30AUG2022		Ravulizumab	15APR2024	Other Infection	Unknown Organism	Respiratory infection	Resolved	22APR2024
1009-405	02MAY2017	09SEP2021		Eculizumab	23JAN2020	Other Infection	Other Organism	Influenza A positive	Resolved	06FEB2020
1009-422	09NOV2017	11JAN2022		Eculizumab	15JUL2019	Other Infection	Unknown Organism	cellulitis	Resolved	12AUG2019
1009-442	03MAR2021	01APR2022		Ravulizumab	10MAY2023	Other Infection	Other Organism	COVID-19 Positive	Resolved	17MAY2023

Listing 6
Infection
Ravulizumab Study Population

Patient Number	Enrollment Date	Ravulizumab Initiation Date	Status	Treatment Exposure at time of event	Date of Event	Category	Subcategory	Event Detail	Outcome	Resolution Date
1013-008	06APR2006	23AUG2019	Active	Ravulizumab	15FEB2023	Other Infection	Unknown Organism	unknown	Resolved	12OCT2023
1013-062	05AUG2009	28AUG2019	Active	Eculizumab	29JAN2019	Other Infection	Unknown Organism	fever, infection	Resolved	13FEB2019
1013-071	23OCT2009	05SEP2019	Active	Ravulizumab	24FEB2023	Other Infection	Unknown Organism	unknown	Resolved	08OCT2023
1013-076	24MAR2010	15OCT2019	Active	Eculizumab	09MAR2011	Other Infection	Unknown Organism	GI-Infect ->Hepatopathie	Resolved	20MAR2011
1013-079	14JUL2010	15SEP2019	Active	Ravulizumab	01JUL2023	Other Infection	Unknown Organism	unknown	Resolved	25FEB2024
1013-100	08FEB2012	31MAY2021		Ravulizumab	07MAR2022	Other Infection	Unknown Organism	ENT infection	Resolved	15MAR2022
1013-140	15MAY2014	26AUG2019	Active	Ravulizumab	15FEB2024	Other Infection	Unknown Organism	unknown	Resolved	25APR2024
1013-161	01FEB2012	09AUG2019	Active	Ravulizumab	09DEC2020	Other Infection	Other Organism	Sars-Cov-2	Resolved	29DEC2020
1013-166	12MAY2015	15AUG2019	Active	Ravulizumab	20MAR2020	Other Infection	Unknown Organism	organism not known, otitis media	Resolved	30MAR2020
1013-169	17JUN2015	11NOV2020	Active	Ravulizumab	15OCT2022	Other Infection	Other Organism	Covid 19 infection	Resolved	01DEC2022
1013-175	05AUG2015	12SEP2019	Active	Ravulizumab	29APR2024	Other Infection	Unknown Organism	unknown	Resolved	03MAY2024

Listing 6
Infection
Ravulizumab Study Population

Patient Number	Enrollment Date	Ravulizumab Initiation Date	Status	Treatment Exposure at time of event	Date of Event	Category	Subcategory	Event Detail	Outcome	Resolution Date
1013-191	09DEC2015	01AUG2019	Active	Ravulizumab	03APR2021	Other Infection	Other Organism	Covid-19 infection	Resolved	15APR2021
					04OCT2021	Other Infection	Other Organism	Herpes simplex Typ 1	Resolved	13OCT2021
					01JUL2023	Other Infection	Other Organism	Herpes Genitales	Resolved	26NOV2023
1013-216	26MAR2019	23JUL2019	Active	Ravulizumab	15AUG2023	Other Infection	Unknown Organism	unknown	Resolved	11OCT2023
1013-241	27JUL2021	27JUL2021	Active	Ravulizumab	15DEC2023	Other Infection	Other Organism	Covid 19 infection	Resolved	07FEB2024
					15JAN2024	Other Infection	Other Organism	Norovirus infection	Resolved	07FEB2024
1017-023	27NOV2019	02DEC2019		Ravulizumab	01FEB2022			ＳＡＲＳ－ＣｏＶ－２	Resolved	07FEB2022
1030-007	05JUN2017	27MAY2022		Untreated	26JUN2018	Other Infection	Other Organism	E.Coli	Resolved	04JUL2018
1036-001	10JAN2006	03APR2019		Eculizumab	21AUG2010	Other Infection	Unknown Organism	Staph (otherwise unknown)	Resolved	23AUG2010

Listing 6
Infection
Ravulizumab Study Population

Patient Number	Enrollment Date	Ravulizumab Initiation Date	Status	Treatment Exposure at time of event	Date of Event	Category	Subcategory	Event Detail	Outcome	Resolution Date
1036-002	04OCT2011	15OCT2019		Eculizumab	18JAN2013	Other Infection	Other Organism	Chlamydia Trachomatis	Ongoing	
					27OCT2015	Other Infection	Other Organism	methicillin-sensitive staphylococcus epidermis	Resolved	02NOV2015
					01FEB2017	Other Infection	Other Organism	streptococcus	Resolved	03MAR2017
1048-020	06JAN2014	15MAR2022		Eculizumab	14JAN2014	Neisseria	Meningococcal	Neisseria Meningitidis	Resolved	23JAN2014
					11FEB2015	Other Infection	Other Organism	E Coli	Ongoing	
1050-001	23OCT2006	10DEC2019		Ravulizumab	04SEP2020	Other Infection	Other Organism	SARS-COV-2	Resolved	08SEP2020

Listing 6
Infection
Ravulizumab Study Population

Patient Number	Enrollment Date	Ravulizumab Initiation Date	Status	Treatment Exposure at time of event	Date of Event	Category	Subcategory	Event Detail	Outcome	Resolution Date
1093-043	10MAY2011	24JUL2019		Eculizumab	15JUN2016	Other Infection	Other Organism	Herpes labialis	Resolved	20SEP2016
					02NOV2016	Other Infection	Unknown Organism	Folliculitis left axillary	Resolved	07FEB2017
					15JAN2017	Other Infection	Other Organism	Herpeslabialis	Resolved	25JAN2017
					15MAY2017	Other Infection	Unknown Organism	fever unkown cause with headache	Resolved	26DEC2017
					07AUG2017	Other Infection	Unknown Organism	bacterial Infect unkown origin with fever	Resolved	09AUG2017
1093-105	18AUG2014	15OCT2019		Eculizumab	15OCT2017	Other Infection	Unknown Organism	gastro-enteritis with fever unkown cause	Resolved	15JAN2018
					21MAR2018	Other Infection	Other Organism	2) fever unkown cause	Resolved	21MAR2018
1093-122	17FEB2015	01OCT2020		Untreated	15JUL2017	Other Infection	Unknown Organism	respiratory infect	Ongoing	
1093-130	23APR2015	28AUG2019		Untreated	15MAR2017	Other Infection	Unknown Organism	respiratoryn Infect	Resolved	15JUN2017

Source: ADAM.ADSL, ADAM.ADPOP, CONV.ALL_SITES, ADAM.ADMEIN
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Listing 6
Infection
Ravulizumab Study Population

Patient Number	Enrollment Date	Ravulizumab Initiation Date	Status	Treatment Exposure at time of event	Date of Event	Category	Subcategory	Event Detail	Outcome	Resolution Date
1093-138	10JUL2015	26JUL2019		Ravulizumab	24FEB2023	Other Infection	Other Organism	Respiratory infection with cough and sputum	Resolved	14APR2023
1093-186	04AUG2017	15OCT2019		Ravulizumab	15AUG2022	Other Infection	Other Organism	Covid 19 infection	Resolved	28AUG2022
1134-025	05JUN2009	16NOV2023		Ravulizumab	23DEC2023	Other Infection	Other Organism	COVID-19	Resolved	22JAN2024
1134-044	09SEP2009	25MAR2024		Untreated	17DEC2021	Other Infection	Other Organism	Candida albicans	Resolved	24JAN2022
					15FEB2023	Other Infection	Other Organism	Influenza B respiratory infection	Resolved	15FEB2023

Listing 6
Infection
Ravulizumab Study Population

Patient Number	Enrollment Date	Ravulizumab Initiation Date	Status	Treatment Exposure at time of event	Date of Event	Category	Subcategory	Event Detail	Outcome	Resolution Date
1134-052	22FEB2010	08FEB2024		Untreated	05AUG2010	Other Infection	Other Organism	Borrelia	Resolved	31AUG2010
					14DEC2010	Other Infection	Unknown Organism	unknown	Resolved	16MAR2011
					12MAR2011	Other Infection	Other Organism	Herpes Symplex	Resolved	16MAR2011
					30MAR2011	Other Infection	Unknown Organism	unknown	Resolved	07APR2011
					25APR2011	Other Infection	Other Organism	Herpes Symplex	Resolved	16MAY2011
					01OCT2011	Other Infection	Unknown Organism	Unknown (urinary tract infection)	Resolved	04OCT2011
1134-088	09JAN2012	04SEP2023		Untreated	02JAN2018	Other Infection	Unknown Organism	unknown	Resolved	17JAN2019
					15APR2018	Other Infection	Unknown Organism	unknown	Resolved	29JUL2018
					08JAN2020	Other Infection	Unknown Organism	unknown	Resolved	11JAN2020

Listing 6
Infection
Ravulizumab Study Population

Patient Number	Enrollment Date	Ravulizumab Initiation Date	Status	Treatment Exposure at time of event	Date of Event	Category	Subcategory	Event Detail	Outcome	Resolution Date
1134-136	05AUG2018	13NOV2023		Untreated	01JUL2022	Other Infection	Other Organism	SARS-COV-2 infection	Resolved	02JUL2022
					15OCT2022	Other Infection	Unknown Organism	infection respiratory (unknown organism)	Resolved	08JAN2023
					15DEC2022	Other Infection	Unknown Organism	urinary tract infection (unknown organism)	Resolved	08JAN2023
1134-146	08JUN2021	16NOV2023		Untreated	15JUN2022	Other Infection	Other Organism	recurrent UTI by e. coli	Ongoing	
					20FEB2023	Other Infection	Other Organism	COVID-19 INFECTION	Resolved	02MAR2023
1151-011	18MAY2011	22JUN2023		Ravulizumab	10FEB2024	Other Infection	Other Organism	Norovirus Infection	Resolved	14FEB2024
1151-014	11APR2012	09DEC2020		Eculizumab	30MAR2019	Other Infection	Other Organism	Metapneumovirus	Resolved	09APR2019
					12JUL2020	Other Infection	Other Organism	campylobacter jejuni	Resolved	20JUL2020
1170-002	18JAN2010	04JUL2022		Eculizumab	14JAN2014	Neisseria	Meningococcal	Neisseria meningitidis	Ongoing	
1170-006	14APR2012	11SEP2023		Untreated	15SEP2013	Other Infection	Unknown Organism	BRONCHITIS INFECTION	Ongoing	

Source: ADAM.ADSL, ADAM.ADPOP, CONV.ALL_SITES, ADAM.ADMEIN
Run Date: 2025-05-14T14:46:27
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Listing 6
Infection
Ravulizumab Study Population

Patient Number	Enrollment Date	Ravulizumab Initiation Date	Status	Treatment Exposure at time of event	Date of Event	Category	Subcategory	Event Detail	Outcome	Resolution Date
1192-001	29APR2010	12APR2021		Ravulizumab	31JAN2022	Other Infection	Other Organism	Covid-19	Resolved	04FEB2022
1197-027	21JUN2018	02JAN2023		Eculizumab	21JAN2020	Other Infection	Other Organism	Bacteroides salyersiae	Resolved	28JAN2020
					12DEC2022	Other Infection	Other Organism	COVID-19	Resolved	30DEC2022
				Ravulizumab	08MAR2023	Other Infection	Other Organism	Enterococcus faecium	Death	13APR2023
1200-005	27JAN2011	15JUL2020		Eculizumab	09JAN2013	Other Infection	Unknown Organism	cellulitis	Resolved	22JAN2013
				Ravulizumab	17DEC2021	Other Infection	Unknown Organism	Unspecified infection of the spine	Resolved	09MAR2022
					04MAY2022	Other Infection	Other Organism	Septic Arthritis	Resolved	20SEP2022
1214-005	10OCT2012	16OCT2019		Eculizumab	03MAR2019	Other Infection	Unknown Organism	leg	Resolved	17MAR2019
1226-003	06SEP2010	22APR2022		Ravulizumab	10JUN2022	Other Infection	Other Organism	COVID-19 Infection	Resolved	17JUN2022

Listing 6
Infection
Ravulizumab Study Population

Patient Number	Enrollment Date	Ravulizumab Initiation Date	Status	Treatment Exposure at time of event	Date of Event	Category	Subcategory	Event Detail	Outcome	Resolution Date
1236-002	17FEB2012	21OCT2021		Eculizumab	11JUL2016	Other Infection	Unknown Organism	influenza	Resolved	14JUL2016
					06JAN2018	Other Infection	Unknown Organism	Tonsillitis	Resolved	11JAN2018
				Ravulizumab	20MAY2022	Other Infection	Other Organism	Covid 19	Resolved	30MAY2022
					20AUG2022	Other Infection	Unknown Organism	conjunctivitis	Resolved	30AUG2022
					23NOV2022	Other Infection	Unknown Organism	cystitis	Resolved	25NOV2022
					22FEB2023	Other Infection	Unknown Organism	gastrointestinal tract infection	Resolved	06MAR2023
					18DEC2023	Other Infection	Unknown Organism	upper respiratory tract	Resolved	05JAN2024
1236-003	21JUN2009	01AUG2019		Ravulizumab	02AUG2019	Other Infection	Unknown Organism	Sinusitis	Resolved	01SEP2019
					16OCT2021	Other Infection	Other Organism	Covid-19-infection	Resolved	25OCT2021
1251-005	06APR2016	26APR2023		Untreated	18JUL2017	Other Infection	Unknown Organism	not found Pneumonia	Resolved	19JUL2017
1251-009	19FEB2020	27APR2023		Untreated	08JUN2020	Other Infection	Other Organism	HERPES	Resolved	01JUL2020

Source: ADAM.ADSL, ADAM.ADPOP, CONV.ALL_SITES, ADAM.ADMEIN
Run Date: 2025-05-14T14:46:27
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ravuema202501/Files/listings/production/programs/l6_infect.sas

Listing 6
Infection
Ravulizumab Study Population

Patient Number	Enrollment Date	Ravulizumab Initiation Date	Status	Treatment Exposure at time of event	Date of Event	Category	Subcategory	Event Detail	Outcome	Resolution Date
1252-035	08OCT2015	11OCT2022		Eculizumab	04AUG2021	Other Infection	Other Organism	Klebsiella pneumoniae	Resolved	10AUG2022
					06APR2022	Other Infection	Other Organism	Staphylococcus epidermidis	Resolved	29APR2022
1262-002	02FEB2011	17FEB2023		Eculizumab	16JUL2015	Other Infection	Other Organism	SALMONELLA TYPHIMURIUM	Resolved	21JUL2015
1319-001	08JUN2005	06JAN2022		Untreated	15APR2011	Encapsulated Bacteria	Haemophilus Influenza	haemophilus influenzae	Resolved	15APR2011
					02OCT2012	Other Infection	Unknown Organism	unknown, upper respiratory tract infection	Resolved	14OCT2012
1366-036	14MAR2013	19AUG2021		Ravulizumab	14AUG2022	Other Infection	Other Organism	SARS-CoV-2	Resolved	03SEP2022
1366-108	26APR2018	18AUG2021		Eculizumab	16MAY2021	Other Infection	Unknown Organism	infectious colitis	Resolved	27MAY2021
1381-003	18APR2012	08JAN2020		Eculizumab	23AUG2017	Other Infection	Unknown Organism	upper respiratory infection	Resolved	10SEP2017
				Ravulizumab	10APR2022	Other Infection	Other Organism	Vancomycin-resistant enterococci	Resolved	20APR2022
1381-008	14MAY2015	22MAR2019		Ravulizumab	15JUL2021	Other Infection	Other Organism	Odontogenic Abscess infection	Resolved	19JUL2021

Source: ADAM.ADSL, ADAM.ADPOP, CONV.ALL_SITES, ADAM.ADMEIN
Run Date: 2025-05-14T14:46:27
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ravuema202501/Files/listings/production/programs/l6_infect.sas

Listing 6
Infection
Ravulizumab Study Population

Patient Number	Enrollment Date	Ravulizumab Initiation Date	Status	Treatment Exposure at time of event	Date of Event	Category	Subcategory	Event Detail	Outcome	Resolution Date
1422-008	30JAN2013	11AUG2021		Eculizumab	24MAR2015	Other Infection	Unknown Organism	Bronchus	Resolved	26MAR2016
1422-011	20MAR2014	10AUG2021		Untreated	23FEB2017	Other Infection	Unknown Organism	Kidney	Resolved	11MAR2017
1423-008	18JUN2015	10NOV2021		Untreated	06MAR2020	Other Infection	Other Organism	Cryptococcus neoformans	Resolved	23MAR2020
1423-011	11NOV2015	24AUG2021		Ravulizumab	23AUG2023	Other Infection	Other Organism	Staphylococcus epidermidis	Resolved	15SEP2023
					28AUG2023	Other Infection	Other Organism	Klebsiella pneumoniae	Resolved	15SEP2023
1423-012	07JAN2016	10NOV2021		Ravulizumab	29MAR2023	Other Infection	Other Organism	Staphylococcus aureus bacteremia	Resolved	11APR2023
					03MAY2023	Other Infection	Other Organism	Escherichia coli bacteremia	Resolved	19MAY2023
1432-003	14JAN2016	30NOV2019		Eculizumab	07APR2016	Other Infection	Other Organism	influenza B virus	Resolved	14APR2016
					19JUL2018	Other Infection	Unknown Organism	Unknown	Resolved	01AUG2018
1432-004	21JAN2016	28AUG2020		Untreated	12JAN2019	Other Infection	Other Organism	Influenza virus	Resolved	14JAN2019
1432-005	21JAN2016	10JAN2020		Untreated	21JAN2016	Other Infection	Other Organism	E,Coli	Resolved	05MAR2016

Listing 6
Infection
Ravulizumab Study Population

Patient Number	Enrollment Date	Ravulizumab Initiation Date	Status	Treatment Exposure at time of event	Date of Event	Category	Subcategory	Event Detail	Outcome	Resolution Date
1462-004	30NOV2012	01NOV2019		Eculizumab	08JUN2016	Other Infection	Unknown Organism	Negative	Resolved	08JUL2016
					04NOV2017	Other Infection	Other Organism	Streptococcus bovis bacteremia	Resolved	17NOV2017
				Ravulizumab	04SEP2021				Resolved	10SEP2021
1462-006	07DEC2012	08NOV2019		Ravulizumab	07FEB2020	Neisseria	Gonorrhea	Disseminated gonococcal infection	Resolved	28FEB2020
					21DEC2022	Other Infection	Other Organism	SARS-CoV-2 infection	Resolved	28DEC2022
1462-009	14DEC2012	13DEC2019		Eculizumab	25JAN2019	Other Infection	Other Organism	Influenza A virus infection	Resolved	01FEB2019
1507-002	24APR2013	06JAN2020		Eculizumab	12JUN2019	Other Infection	Other Organism	Moraxella lacunata	Resolved	25JUN2019
				Untreated	25APR2013	Other Infection	Other Organism	NOROVIRUS suspected	Resolved	01MAY2013
1507-003	08MAY2013	28OCT2019		Eculizumab	15SEP2009	Neisseria	Unknown	Neisseria Infection	Resolved	15SEP2009
				Ravulizumab	20JUL2023	Other Infection	Unknown Organism	unknown infection	Resolved	29JUL2023

Listing 6
Infection
Ravulizumab Study Population

Patient Number	Enrollment Date	Ravulizumab Initiation Date	Status	Treatment Exposure at time of event	Date of Event	Category	Subcategory	Event Detail	Outcome	Resolution Date
1521-010	27JAN2016	04JUN2021		Eculizumab	10SEP2017	Other Infection	Unknown Organism	Meningitis - unknown strain	Resolved	19SEP2017
					04MAY2020				Resolved	15MAY2020
				Ravulizumab	29NOV2021	Other Infection	Other Organism	Covid-19	Resolved	23FEB2022
1521-017	15MAR2018	18JUN2021		Ravulizumab	29JUL2023	Other Infection	Other Organism	grampositive cocci enterococcus faecalis infection	Resolved	28AUG2023
				Untreated	04MAR2020	Other Infection	Other Organism	Staphylococcus epidermidis	Resolved	06MAR2020
1521-020	07MAR2019	13MAR2024		Eculizumab	25DEC2019	Other Infection	Other Organism	Influenza A virus test positive	Resolved	27DEC2019
					28FEB2021	Other Infection	Unknown Organism	unknown source of infection	Resolved	02MAR2021
1558-002	09JAN2015	19JUL2022		Eculizumab	13JAN2019	Other Infection	Unknown Organism	Upper espiratory tract infection	Resolved	18JAN2019
1600-003	25MAR2015	13APR2022		Ravulizumab	15DEC2023	Other Infection	Other Organism	COVID19 test positive	Resolved	03JAN2024

Listing 6
Infection
Ravulizumab Study Population

Patient Number	Enrollment Date	Ravulizumab Initiation Date	Status	Treatment Exposure at time of event	Date of Event	Category	Subcategory	Event Detail	Outcome	Resolution Date
1668-001	26MAR2014	17AUG2021		Eculizumab	17AUG2015	Other Infection	Unknown Organism	upper respiratory	Resolved	20AUG2015
					30DEC2015	Other Infection	Unknown Organism	unknown	Resolved	13JAN2016
					11FEB2016	Other Infection	Unknown Organism	unknown	Resolved	23MAR2016
1682-001	25OCT2014	29MAR2023		Eculizumab	15MAR2019	Other Infection	Unknown Organism	"Bad" respiratory infection requiring treatment	Ongoing	
				Ravulizumab	15SEP2023	Other Infection	Other Organism	COVID-19 RTI	Resolved	20SEP2023
1722-001	23APR2015	16FEB2023		Eculizumab	24JAN2021	Other Infection	Other Organism	SARS-CoV-2 (PCR)	Resolved	02APR2021

Source: ADAM.ADSL, ADAM.ADPOP, CONV.ALL_SITES, ADAM.ADMEIN
Run Date: 2025-05-14T14:46:27
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ravuema202501/Files/listings/production/programs/l6_infect.sas

Listing 7
Meningococcal Infection
Ravulizumab Study Population

Patient Number	Region	Enrollment Date	Enrollment Status	Ravulizumab Initiation Date	Ravulizumab Discontinuation Date	Reason for Ravulizumab Discontinuation	Treatment Status[a]	Date of Event	Serogroup	Meningococcal Vaccination (Yes/No)	Type of Vaccination
1009-264	Europe	24OCT2013		06AUG2021			Prior Eculizumab Treatment	13JAN2017	Y	Y	Other, please specify
1048-020	Europe	06JAN2014		15MAR2022			Prior Eculizumab Treatment	14JAN2014	B	Y	MenB vaccine (Bexsero® or Trumenba®)
1170-002	Europe	18JAN2010		04JUL2022			Prior Eculizumab Treatment	14JAN2014	Y	Y	Other, please specify

Note: (a) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.

Source: ADAM.ADSL, ADAM.ADPOP, ADAM.ADEX, ADAM.ADMEIN, ADAM.ADCMIN, CONV.ALL_SITES
Run Date: 2025-05-14T14:46:28
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ravuema202501/Files/listings/production/programs/l7_meningo.sas

Listing 8
Impaired Renal Function
Ravulizumab Study Population

Patient Number	Enrollment Date	Ravulizumab Initiation Date	Status	Treatment Exposure At Time of Event	Date of Event	Event Detail	Treatment Required	Outcome	Resolution Date
1009-074	31MAR2009	12JAN2022		Eculizumab	15JAN2010	Iron overload 2010		Ongoing	
	31MAR2009	12JAN2022		Eculizumab	01JUL2011	Impairment		Ongoing	
1009-076	12MAY2009	13AUG2021		Eculizumab	22NOV2016	renal failure		Ongoing	
1009-084	22SEP2009	23FEB2022		Untreated	15OCT2010	Exacerbation of PNH, required fluids		Resolved	30MAR2011
	22SEP2009	23FEB2022		Untreated	02MAY2012	Haemolysis induced renal impairment		Resolved	12MAY2012
1009-115	15JUN2010	19AUG2021		Untreated	15AUG2013	unknown		Resolved	07APR2014
	15JUN2010	19AUG2021		Eculizumab	15AUG2014	unknown		Ongoing	
1009-129	31AUG2010	17JAN2023		Untreated	28NOV2013	This has been presented on and off since 2005 due to ciclosporin		Ongoing	
1009-146	10FEB2011	15NOV2021		Eculizumab	15FEB2012	Acute renal failure			15FEB2012

Source: ADAM.ADSL, ADAM.ADPOP, ADAM.ADMEIN, CONV.ALL_SITES
Run Date: 2025-05-14T14:46:29
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ravuema202501/Files/listings/production/programs/l8_irf.sas

Listing 8
Impaired Renal Function
Ravulizumab Study Population

Patient Number	Enrollment Date	Ravulizumab Initiation Date	Status	Treatment Exposure At Time of Event	Date of Event	Event Detail	Treatment Required	Outcome	Resolution Date
	10FEB2011	15NOV2021		Eculizumab	01MAY2015	Renal tumours		Ongoing	
	10FEB2011	15NOV2021		Eculizumab	01MAR2016	Renal cell carcinoma		Ongoing	
1009-151	10MAR2011	04JAN2022		Untreated	10MAR2011	Impaired Renal Function		Ongoing	
	10MAR2011	04JAN2022		Untreated	15MAR2011	Kidney dysfunction		Ongoing	
1009-161	24MAY2011	05MAY2022		Untreated	17AUG2011	Ongoing renal impairment with increased creatinine due to ciclosporin . CSA on and off in becomes to bad.		Ongoing	
1009-251	11JUN2013	03AUG2021		Eculizumab	06MAY2014	Reduction in GFR		Ongoing	
1009-270	14JAN2014	15OCT2021		Untreated	24NOV2018	acute kidney injury		Ongoing	

Source: ADAM.ADSL, ADAM.ADPOP, ADAM.ADMEIN, CONV.ALL_SITES
Run Date: 2025-05-14T14:46:29
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ravuema202501/Files/listings/production/programs/l8_irf.sas

Listing 8
Impaired Renal Function
Ravulizumab Study Population

Patient Number	Enrollment Date	Ravulizumab Initiation Date	Status	Treatment Exposure At Time of Event	Date of Event	Event Detail	Treatment Required	Outcome	Resolution Date
1009-410	20JUN2017	07MAR2023		Untreated	22FEB2023	Patient showed decreased GFR (between 35 and 58) and increased creatine concentrati on.		Resolved	13MAR2023
1009-420	31OCT2017	16MAR2022		Ravulizumab	03FEB2023	Serum creatine levels above expected range		Ongoing	
1013-028	25OCT2007	08NOV2019	Active	Eculizumab	27MAR2015	renal insufficien cy, macro hematurie, increasing creatinine		Resolved	27MAR2015
1013-046	15AUG2007	03APR2020	Active	Untreated	15MAR2008	Renal Failure		Resolved	25MAR2008
1013-145	13AUG2014	21AUG2019	Discontinued	Eculizumab	24JUL2018	acute on chronic kidney failure		Resolved	31JUL2018

Source: ADAM.ADSL, ADAM.ADPOP, ADAM.ADMEIN, CONV.ALL_SITES
Run Date: 2025-05-14T14:46:29
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ravuema202501/Files/listings/production/programs/l8_irf.sas

Listing 8
Impaired Renal Function
Ravulizumab Study Population

Patient Number	Enrollment Date	Ravulizumab Initiation Date	Status	Treatment Exposure At Time of Event	Date of Event	Event Detail	Treatment Required	Outcome	Resolution Date
1013-216	26MAR2019	23JUL2019	Active	Eculizumab	15JAN2019	Impaired Renal Function		Resolved	15JAN2019
1130-018	14NOV2019	28MAY2020		Ravulizumab	01DEC2021	Rising Cr. The possibility of obstructive uropathy leading to renal dysfunction is not ruled out. - Recommended close follow up with PCP and considerati on of referral to nephrology.		Ongoing	
1134-044	09SEP2009	25MAR2024		Untreated	27APR2010	MDRD GFR <60 still ongoing		Ongoing	
	09SEP2009	25MAR2024		Untreated	05APR2011	MDRD GFR <60 still ongoing		Ongoing	

Listing 8
Impaired Renal Function
Ravulizumab Study Population

Patient Number	Enrollment Date	Ravulizumab Initiation Date	Status	Treatment Exposure At Time of Event	Date of Event	Event Detail	Treatment Required	Outcome	Resolution Date
	09SEP2009	25MAR2024		Untreated	25OCT2011	MDRD GFR <60 still ongoing		Ongoing	
	09SEP2009	25MAR2024		Untreated	24JAN2012	MDRD GFR 30-60		Ongoing	
1134-052	22FEB2010	08FEB2024		Untreated	03AUG2010	Acute Tubulusnecrosis by hemolytic crisis		Resolved	06AUG2010
	22FEB2010	08FEB2024		Untreated	30MAR2011	MDRD GFR <60		Resolved	07OCT2011
1134-111	26SEP2014	02OCT2023		Untreated	04MAY2015	MDRD 49 ml/min/1.73 m2		Ongoing	
	26SEP2014	02OCT2023		Untreated	09NOV2015	MDRD 65 ml/min/1.73 m2		Ongoing	
1151-014	11APR2012	09DEC2020		Eculizumab	11SEP2016	chronic renal failure Grade 1		Ongoing	
1197-020	12JAN2012	10JAN2023		Untreated	08APR2015	Grade 1		Ongoing	

Listing 8
Impaired Renal Function
Ravulizumab Study Population

Patient Number	Enrollment Date	Ravulizumab Initiation Date	Status	Treatment Exposure At Time of Event	Date of Event	Event Detail	Treatment Required	Outcome	Resolution Date
1197-027	21JUN2018	02JAN2023		Ravulizumab	12MAR2023	Non-obstructive acute renal failure, tubulointerstitial nephritis +/- component of hemolysis		Death	13APR2023
1252-002	28SEP2010	08NOV2022		Eculizumab	06MAR2018	Creatinine clearance 50ml/min		Ongoing	
1262-002	02FEB2011	17FEB2023		Eculizumab	16JUL2015	ONE EPISODE OF IMPAIRED RENAL FAILURE DURING HOSPITALIZATION FOR INFECTION		Resolved	21JUL2015
1262-004	14MAR2013	27APR2022		Eculizumab	01SEP2017	IMPAIRED RENAL FUNCTION MAY BE DUE TO DEHYDRATION		Resolved	14SEP2017

Listing 8
Impaired Renal Function
Ravulizumab Study Population

Patient Number	Enrollment Date	Ravulizumab Initiation Date	Status	Treatment Exposure At Time of Event	Date of Event	Event Detail	Treatment Required	Outcome	Resolution Date
1304-002	10MAY2011	15SEP2022		Eculizumab	21AUG2011	créat: 33mg/L		Ongoing	
1351-003	03FEB2017	08SEP2022		Untreated	19AUG2020	Increased creatinine levels.		Ongoing	
1420-004	12JUN2012	09SEP2021		Untreated	15OCT2019	acute kidney infection		Resolved	01NOV2019
1422-022	19MAR2020	03AUG2021		Eculizumab	11JUN2020	Chronic cystitis		Resolved	03SEP2020
1423-002	23AUG2012	24AUG2021		Untreated	11SEP2012	oliguria		Resolved	26SEP2012
1423-008	18JUN2015	10NOV2021		Untreated	04SEP2020	Renal failure		Ongoing	
1423-014	09JUN2017	10NOV2021		Untreated	10OCT2017	Acute kidney injury		Resolved	21OCT2017
1423-017	12NOV2018	24AUG2021		Untreated	06DEC2018	chronic kidney diease		Ongoing	
1425-001	11JAN2013	13JUL2021		Eculizumab	21NOV2016	PNH induced ARF		Ongoing	
1429-001	15NOV2012	20APR2023		Untreated	09NOV2022	acute kidney injury with hemodialysis		Resolved	22DEC2022
1432-005	21JAN2016	10JAN2020		Untreated	21JAN2016	Nephritis		Resolved	05MAR2016

Listing 8
Impaired Renal Function
Ravulizumab Study Population

Patient Number	Enrollment Date	Ravulizumab Initiation Date	Status	Treatment Exposure At Time of Event	Date of Event	Event Detail	Treatment Required	Outcome	Resolution Date
1493-006	25MAR2013	04OCT2019		Untreated	16MAR2015	Cre increased		Ongoing	
1493-020	14MAR2022	03AUG2023		Untreated	18JUL2023	drug induced kidney injury		Ongoing	
1507-002	24APR2013	06JAN2020		Eculizumab	13APR2019	acute kidney injury		Resolved	26APR2019
1507-007	15MAY2013	20AUG2021		Untreated	20OCT2014	Increased creatinine levels(max 1.13 mg/dl)with the low eGFR(50)		Resolved	17DEC2014
	15MAY2013	20AUG2021		Untreated	16MAY2018	acute kidney injury		Resolved	15JUN2018
1667-001	28MAY2014	21JUL2021		Eculizumab	19OCT2015	anemia		Ongoing	

Listing 9
Impaired Hepatic Function
Ravulizumab Study Population

Patient Number	Enrollment Date	Ravulizumab Initiation Date	Status	Treatment Exposure At Time of Event	Date of Event	Event Detail	Treatment Required	Outcome	Resolution Date
1009-074	31MAR2009	12JAN2022		Eculizumab	15MAR2010			Ongoing	
1009-076	12MAY2009	13AUG2021		Eculizumab	22SEP2016			Ongoing	
1009-088	22OCT2009	09FEB2022		Eculizumab	23NOV2010			Ongoing	
1009-272	21JAN2014	05APR2022		Eculizumab	15SEP2014			Ongoing	
1009-409	13JUN2017	02AUG2021		Ravulizumab	30NOV2023			Ongoing	
1009-413	22AUG2017	23AUG2021		Ravulizumab	07OCT2022			Ongoing	
1009-420	31OCT2017	16MAR2022		Ravulizumab	03FEB2023			Ongoing	
	31OCT2017	16MAR2022		Ravulizumab	21NOV2023			Ongoing	
1009-433	13AUG2019	08NOV2021		Ravulizumab	03MAY2022			Ongoing	
1009-443	12MAR2021	08OCT2021		Eculizumab	15JUL2021			Resolved	28JUL2021
1013-076	24MAR2010	15OCT2019	Active	Eculizumab	15MAY2012			Resolved	27SEP2012
1304-002	10MAY2011	15SEP2022		Eculizumab	21AUG2011			Ongoing	
1422-008	30JAN2013	11AUG2021		Eculizumab	21OCT2016			Resolved	28NOV2016
1423-002	23AUG2012	24AUG2021		Untreated	11MAR2014			Resolved	13MAR2014
	23AUG2012	24AUG2021		Untreated	30MAY2014			Resolved	05JUN2014
1462-004	30NOV2012	01NOV2019		Eculizumab	03MAY2017			Ongoing	
	30NOV2012	01NOV2019		Ravulizumab	02AUG2021			Ongoing	
	30NOV2012	01NOV2019		Ravulizumab	31DEC2021			Ongoing	
1462-006	07DEC2012	08NOV2019		Ravulizumab	16NOV2020			Ongoing	

Source: ADAM.ADSL, ADAM.ADPOP, ADAM.ADMEIN, CONV.ALL_SITES
Run Date: 2025-05-14T14:46:32
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ravuema202501/Files/listings/production/programs/l9_ihf.sas

Listing 9
Impaired Hepatic Function
Ravulizumab Study Population

Patient Number	Enrollment Date	Ravulizumab Initiation Date	Status	Treatment Exposure At Time of Event	Date of Event	Event Detail	Treatment Required	Outcome	Resolution Date
1507-002	24APR2013	06JAN2020		Eculizumab	06AUG2014			Ongoing	
1668-001	26MAR2014	17AUG2021		Eculizumab	19AUG2015			Resolved	26AUG2015

Source: ADAM.ADSL, ADAM.ADPOP, ADAM.ADMEIN, CONV.ALL_SITES
Run Date: 2025-05-14T14:46:32
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ravuema202501/Files/listings/production/programs/l9_ihf.sas

Listing 10
Pulmonary Hypertension
Ravulizumab Study Population

Patient Number	Enrollment Date	Ravulizumab Initiation Date	Status	Treatment Exposure At Time of Event	Date of Event	Event Detail	Treatment Required	Outcome	Resolution Date
1009-230	04SEP2012	08OCT2021		Untreated	04SEP2012	Pulmonary Hypertension		Ongoing	
1009-353	12APR2016	24AUG2021		Eculizumab	12APR2016	Pulmonary Hypertension		Ongoing	
1013-087	05JAN2011	01DEC2019	Active	Eculizumab	24MAY2017			Ongoing	
1061-008	23APR2019	27AUG2019		Ravulizumab	07FEB2020			Ongoing	
1214-007	04SEP2014	11MAY2022		Untreated	05JAN2017			Resolved	23JUN2017
1226-001	04JUN2010	18MAY2022		Untreated	01MAY2012			Ongoing	
	04JUN2010	18MAY2022		Untreated	23OCT2012			Ongoing	
1268-167	13APR2016	02SEP2021		Eculizumab	22JAN2019			Ongoing	
1418-009	25OCT2012	24AUG2021		Eculizumab	11JUL2016			Resolved	20MAR2017
1423-008	18JUN2015	10NOV2021		Untreated	03DEC2018			Ongoing	
1423-011	11NOV2015	24AUG2021		Untreated	18AUG2016			Ongoing	
1423-012	07JAN2016	10NOV2021		Untreated	23MAR2016			Resolved	31MAY2016
1423-014	09JUN2017	10NOV2021		Untreated	14JUN2017			Resolved	25JAN2019
1787-003	24MAY2016	14JUL2021		Eculizumab	01JUL2014			Ongoing	
	24MAY2016	14JUL2021		Eculizumab	15DEC2014			Ongoing	

Listing 10
Pulmonary Hypertension
Ravulizumab Study Population

Patient Number	Enrollment Date	Ravulizumab Initiation Date	Status	Treatment Exposure At Time of Event	Date of Event	Event Detail	Treatment Required	Outcome	Resolution Date
1787-005	07JUL2016	04AUG2021		Ravulizumab	14NOV2022			Ongoing	
1787-006	20NOV2017	22MAR2023		Untreated	25JUL2022			Ongoing	

Source: ADAM.ADSL, ADAM.ADPOP, ADAM.ADMEIN, CONV.ALL_SITES
Run Date: 2025-05-14T14:46:03
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ravuema202501/Files/listings/production/programs/l10_ph.sas

Listing 11
Ultomiris Infusion Reactions
Ravulizumab Study Population

Patient Number	Enrollment Date	Ravulizumab Initiation Date	Status	Treatment Exposure At Time of Event	Date of Event	Event Detail	Treatment Required	Outcome	Resolution Date
1009-298	06NOV2014	16SEP2021		Ravulizumab	30AUG2022	Dizziness after Ravulizumab infusion		Resolved	02SEP2022
1013-195	25MAY2016	23AUG2019	Active	Ravulizumab	27JUL2021	headache, Vertigo, Fatigue after infusion		Ongoing	
1093-138	10JUL2015	26JUL2019		Ravulizumab	13NOV2020	pain at the lumbar spine		Resolved	13NOV2020
1134-055	05MAR2010	05OCT2023		Ravulizumab	19OCT2023	Muscle cramps in legs and lower back		Resolved	19OCT2023
	05MAR2010	05OCT2023		Ravulizumab	14DEC2023	Muscle cramps in legs and lower back		Resolved	14DEC2023
	05MAR2010	05OCT2023		Ravulizumab	08FEB2024	Muscle cramps in legs and lower back		Resolved	08FEB2024

Listing 11
Ultomiris Infusion Reactions
Ravulizumab Study Population

Patient Number	Enrollment Date	Ravulizumab Initiation Date	Status	Treatment Exposure At Time of Event	Date of Event	Event Detail	Treatment Required	Outcome	Resolution Date
	05MAR2010	05OCT2023		Ravulizumab	04APR2024	Muscle cramps in legs and lower back		Resolved	04APR2024
1170-009	05JUN2013	11JUL2022		Ravulizumab	07MAR2023	Urticaria		Resolved	12DEC2023
1200-005	27JAN2011	15JUL2020		Ravulizumab	29JUL2020	Nausea, vomiting, diarrhea		Resolved	29JUL2020
1422-008	30JAN2013	11AUG2021		Ravulizumab	25AUG2021	Nausea		Resolved	25AUG2021
1432-003	14JAN2016	30NOV2019		Ravulizumab	19JUL2022	Urticaria		Ongoing	

Listing 12
Pregnancy Outcome
Ravulizumab Study Population

Patient Number	Sex[a]	Enrollment Date	Ravulizumab Initiation Date	Status	Treatment Exposure at time of event	Date of Event	Pregnancy Outcome
1005-029	Female	12MAR2011	09NOV2022		Eculizumab	14MAY2013	Live Birth
	Female	12MAR2011	09NOV2022		Eculizumab	23FEB2015	Live Birth
1009-186	Female	06OCT2011	13OCT2021		Untreated	30NOV2012	Abortion
1009-332	Female	21JUL2015	19OCT2021		Eculizumab	15APR2018	Live Birth
1009-362	Female	02JUN2016	25NOV2021		Eculizumab	13APR2018	Live Birth
1009-431	Female	21JUN2019	07SEP2023		Eculizumab	11MAY2021	Live Birth
1013-046	Female	15AUG2007	03APR2020	Active	Eculizumab	15AUG2012	Abortion
	Female	15AUG2007	03APR2020	Active	Eculizumab	13SEP2013	Live Birth
	Female	15AUG2007	03APR2020	Active	Eculizumab	02OCT2015	Live Birth
1013-117	Female	01MAR2013	01AUG2019	Active	Eculizumab	30OCT2018	Miscarriage /Stillbirth
	Female	01MAR2013	01AUG2019	Active	Ravulizumab	26AUG2019	Miscarriage /Stillbirth
	Female	01MAR2013	01AUG2019	Active	Ravulizumab	30JUL2021	Live Birth
1013-121	Female	21JUN2013	15AUG2019	Active	Eculizumab	20DEC2013	Live Birth
	Female	21JUN2013	15AUG2019	Active	Eculizumab	23DEC2016	Live Birth

(a) Sex indicates the gender of the patient. If the subject is male, the Pregnancy Outcome relates to the spouse.

Source: ADAM.ADSL, ADAM.ADPOP, ADAM.ADPREG, CONV.ALL_SITES
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Listing 12
Pregnancy Outcome
Ravulizumab Study Population

Patient Number	Sex[a]	Enrollment Date	Ravulizumab Initiation Date	Status	Treatment Exposure at time of event	Date of Event	Pregnancy Outcome
1013-122	Female	15JUL2013	10NOV2020	Active	Ravulizumab	23DEC2022	Live Birth
1013-147	Female	30JUL2014	28FEB2023	Active	Eculizumab	14AUG2018	Live Birth
	Female	30JUL2014	28FEB2023	Active	Eculizumab	14OCT2021	Live Birth
1013-150	Female	13AUG2014	17FEB2022	Active	Eculizumab	29JUL2021	Live Birth
1013-163	Female	11JUN2014	15AUG2022	Active	Eculizumab	18SEP2016	Live Birth
	Female	11JUN2014	15AUG2022	Active	Eculizumab	04SEP2019	Miscarriage /Stillbirth
	Female	11JUN2014	15AUG2022	Active	Eculizumab	14OCT2020	Live Birth
1013-215	Female	10AUG2017	10NOV2023	Active	Eculizumab	13SEP2019	Live Birth
	Female	10AUG2017	10NOV2023	Active	Eculizumab	28AUG2021	Abortion
	Female	10AUG2017	10NOV2023	Active	Eculizumab	25JUL2022	Live Birth
1017-009	Female	13SEP2012	01MAR2022		Eculizumab	03MAR2014	Live Birth
1036-001	Female	10JAN2006	03APR2019		Eculizumab	15NOV2009	Live Birth
1048-001	Female	30MAY2006	10MAR2022		Eculizumab	10MAY2011	Live Birth
	Female	30MAY2006	10MAR2022		Eculizumab	15MAY2012	Miscarriage /Stillbirth

(a) Sex indicates the gender of the patient. If the subject is male, the Pregnancy Outcome relates to the spouse.

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Listing 12
Pregnancy Outcome
Ravulizumab Study Population

Patient Number	Sex[a]	Enrollment Date	Ravulizumab Initiation Date	Status	Treatment Exposure at time of event	Date of Event	Pregnancy Outcome
1048-001	Female	30MAY2006	10MAR2022		Eculizumab	23FEB2013	Live Birth
1093-024	Female	17NOV2010	01JUL2020		Eculizumab	10DEC2010	Live Birth
	Female	17NOV2010	01JUL2020		Eculizumab	29OCT2012	Live Birth
1093-030	Female	03NOV2010	14APR2020		Eculizumab	08APR2016	Miscarriage /Stillbirth
1139-013	Female	27JAN2010	12MAY2022		Eculizumab	13JUN2013	Live Birth
	Female	27JAN2010	12MAY2022		Eculizumab	10NOV2015	Live Birth
	Female	27JAN2010	12MAY2022		Eculizumab	11NOV2015	Live Birth
1152-001	Female	16OCT2010	04JAN2021		Eculizumab	07FEB2012	Live Birth
1169-001	Female	17MAR2010	23JUN2022		Eculizumab	03NOV2017	Miscarriage /Stillbirth
	Female	17MAR2010	23JUN2022		Eculizumab	15FEB2019	Live Birth
1169-004	Female	16JUL2010	13JUN2022		Eculizumab	20JUL2010	Live Birth
1170-002	Female	18JAN2010	04JUL2022		Eculizumab	26MAR2011	Live Birth
	Female	18JAN2010	04JUL2022		Eculizumab	08APR2012	Miscarriage /Stillbirth
	Female	18JAN2010	04JUL2022		Eculizumab	17JUN2014	Miscarriage /Stillbirth

(a) Sex indicates the gender of the patient. If the subject is male, the Pregnancy Outcome relates to the spouse.

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Listing 12
Pregnancy Outcome
Ravulizumab Study Population

Patient Number	Sex[a]	Enrollment Date	Ravulizumab Initiation Date	Status	Treatment Exposure at time of event	Date of Event	Pregnancy Outcome
1170-002	Female	18JAN2010	04JUL2022		Eculizumab	04DEC2014	Abortion
1170-009	Female	05JUN2013	11JUL2022		Eculizumab	11DEC2015	Live Birth
1236-002	Female	17FEB2012	21OCT2021		Eculizumab	03DEC2012	Abortion
	Female	17FEB2012	21OCT2021		Eculizumab	31OCT2019	Live Birth
1252-035	Female	08OCT2015	11OCT2022		Untreated	15OCT2017	Live Birth
1268-083	Female	17FEB2014	06AUG2021		Eculizumab	15APR2014	Live Birth
1366-064	Female	18JUN2014	19AUG2021		Untreated	02AUG2014	Miscarriage /Stillbirth
1424-003	Female	31MAR2015	27AUG2021		Eculizumab	31AUG2015	Live Birth
1507-012	Female	10JUL2013	26FEB2020		Eculizumab	15MAR2012	Live Birth

(a) Sex indicates the gender of the patient. If the subject is male, the Pregnancy Outcome relates to the spouse.

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Listing 13
Bone Marrow Transplant
Ravulizumab Study Population

Patient Number	Enrollment Date	Ravulizumab Initiation Date	Ravulizumab Discontinuation Date	Status	Treatment Exposure at time of event	Date of Bone Marrow Transplant
1009-443	12MAR2021	08OCT2021	10FEB2022		Ravulizumab	03MAR2022
1093-131	04MAY2015	31JUL2019	24NOV2020		Ravulizumab	24NOV2020
1214-009	17NOV2020	08FEB2023			Untreated	15JAN2021
1214-009	17NOV2020	08FEB2023			Untreated	05JAN2022
1381-002	15MAR2012	21DEC2019	13SEP2023		Ravulizumab	13SEP2023

Listing 14
All Serious Adverse Events and Special Events
Ravulizumab Study Population

Patient Number	Enrollment status	Treatment Status[a]	Adverse Event Term	Serious Event (Yes/No)	Serious Event Category	Special Event (Yes/No)	Special Event Type	Start Date	End Date	Outcome	Clone Size at Enrollment
1005-006		Prior Eculizumab Treatment	stenosis of the left anterior descending artery	Y	Hospitalization	No		13DEC2023	29JAN2024	Recovered/ Resolved	
1009-006		Prior Eculizumab Treatment	Admitted with viral infection	Y	Hospitalization	No		14APR2022	15APR2022	Recovered/ Resolved	94.98
			Influenza A positive	Y	Hospitalization	No		24MAR2024	29MAR2024	Recovered/ Resolved	94.98
1009-088		Prior Eculizumab Treatment	Admitted with Covid Pneumonitis	Y	Hospitalization	No		22JUL2021	28JUL2021	Recovered/ Resolved	100
			Admitted with acute kidney injury	Y	Hospitalization	No		12DEC2022	14DEC2022	Recovered/ Resolved	100
1009-287		Prior Eculizumab Treatment	Stroke	Y	Death;Life-Threatening;Significant Disability	No		27SEP2023	01OCT2023	Fatal	95.57

Note:
(a) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.

Source: ADAM.ADSL, ADAM.ADPOP, ADAM.ADAE, ADAM.ADLBSUM, CONV.ALL_SITES
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Listing 14
All Serious Adverse Events and Special Events
Ravulizumab Study Population

Patient Number	Enrollment status	Treatment Status[a]	Adverse Event Term	Serious Event (Yes/No)	Serious Event Category	Special Event (Yes/No)	Special Event Type	Start Date	End Date	Outcome	Clone Size at Enrollment
1009-292		Prior Eculizumab Treatment	Admitted with Sepsis, unknown cause.	Y	Hospitalization	No		07SEP2023	11SEP2023	Recovered/ Resolved	92.9
1009-318		Prior Eculizumab Treatment	Infected left ureteric stent site requiring nephrostomy.	Y	Hospitalization	No		05OCT2023	09OCT2023	Recovered/ Resolved	57.99

Note:
(a) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.

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Listing 14
All Serious Adverse Events and Special Events
Ravulizumab Study Population

Patient Number	Enrollment status	Treatment Status[a]	Adverse Event Term	Serious Event (Yes/No)	Serious Event Category	Special Event (Yes/No)	Special Event Type	Start Date	End Date	Outcome	Clone Size at Enrollment
1009-320		Prior Eculizumab Treatment	Epigastric pain	Y	Hospitalization	No		05DEC2023	07DEC2023	Recovered/ Resolved	66.75
			Possible Atypical Pancreatitis	Y	Hospitalization	No		05DEC2023	07DEC2023	Recovered/ Resolved	66.75
			Vomiting	Y	Hospitalization	No		05DEC2023	07DEC2023	Recovered/ Resolved	66.75
			Brachycardia	Y	Hospitalization	No		17JAN2024	30JAN2024	Recovered/ Resolved	66.75
			Dizziness	Y	Hospitalization	No		17JAN2024	30JAN2024	Recovered/ Resolved	66.75
			Headache	Y	Hospitalization	No		17JAN2024	30JAN2024	Recovered/ Resolved	66.75
			Light headedness	Y	Hospitalization	No		17JAN2024	30JAN2024	Recovered/ Resolved	66.75
1009-410		Without Prior Eculizumab Treatment	Gastric adenocarcinoma	Y	Death	No		12FEB2023	09JUN2023	Fatal	11.04

Note:
(a) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.

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Listing 14
All Serious Adverse Events and Special Events
Ravulizumab Study Population

Patient Number	Enrollment status	Treatment Status[a]	Adverse Event Term	Serious Event (Yes/No)	Serious Event Category	Special Event (Yes/No)	Special Event Type	Start Date	End Date	Outcome	Clone Size at Enrollment
1009-420		Without Prior Eculizumab Treatment	Gram negative sepsis	Y	Death;Life-Threatening;Hospitalization	No		04MAR2024	05MAR2024	Fatal	
1009-427		Prior Eculizumab Treatment	Patient transformed from Aplastic Anaemia to acute leukaemia	Y	Death	No		07JUL2022	07JUL2022	Fatal	42.54
1009-431		Prior Eculizumab Treatment	Diarrhoea	Y	Hospitalization	No		25JUN2024	27JUN2024	Recovered/ Resolved	70.73
			Pyrexia	Y	Hospitalization	No		25JUN2024	27JUN2024	Recovered/ Resolved	70.73
			Vomiting	Y	Hospitalization	No		25JUN2024	27JUN2024	Recovered/ Resolved	70.73
1009-433		Prior Eculizumab Treatment	Ischaemic leg	Y	Hospitalization	No		27MAR2024	02APR2024	Recovered/ Resolved	43.94

Note:
(a) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.

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Listing 14
All Serious Adverse Events and Special Events
Ravulizumab Study Population

Patient Number	Enrollment status	Treatment Status[a]	Adverse Event Term	Serious Event (Yes/No)	Serious Event Category	Special Event (Yes/No)	Special Event Type	Start Date	End Date	Outcome	Clone Size at Enrollment
1009-434		Prior Eculizumab Treatment	Breast Cancer	Y	Other	No		08FEB2024		Not Recovered/ Not Resolved	99.19
1013-046	Active	Prior Eculizumab Treatment	cholecystitis	Y	Hospitalization	No		09JAN2023	13JAN2023	Recovered/ Resolved	92.1
1013-058	Active	Prior Eculizumab Treatment	malign melanoma right lower leg	Y	Hospitalization	No		11NOV2019	30NOV2019	Recovered/ Resolved	
1013-061	Active	Prior Eculizumab Treatment	ulcus right foot	Y	Hospitalization	No		02JUN2020	10JUN2020	Recovered/ Resolved	57.68
			acute hemolysis	Y	Hospitalization	No		03AUG2020	13AUG2020	Recovered/ Resolved	57.68
			colitis, acute	Y	Hospitalization	No		12JAN2021	23JAN2021	Recovered/ Resolved	57.68
1013-117	Active	Prior Eculizumab Treatment	Stillbirth	Y	Hospitalization	No		26AUG2019	26AUG2019	Recovered/ Resolved	8.99

Note:
(a) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.

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Listing 14
All Serious Adverse Events and Special Events
Ravulizumab Study Population

Patient Number	Enrollment status	Treatment Status[a]	Adverse Event Term	Serious Event (Yes/No)	Serious Event Category	Special Event (Yes/No)	Special Event Type	Start Date	End Date	Outcome	Clone Size at Enrollment
1013-122	Active	Without Prior Eculizumab Treatment	SARS-Cov-2-infection	Y	Hospitalization	No		04JUL2022	06JUL2022	Recovered/ Resolved	50
1013-145	Discontinued	Prior Eculizumab Treatment	lymph node carcinoma (MALT lymphoma)	Y	Death;Life-Threatening;Hospitalization;Other	No		17FEB2020	16FEB2022	Fatal	88
			pulmonal infection	Y	Death;Hospitalization	No		31JAN2022	16FEB2022	Fatal	88
1013-151	Active	Prior Eculizumab Treatment	hemolytic crisis	Y	Hospitalization	No		21FEB2020	27FEB2020	Recovered/ Resolved	17
1013-155	Active	Prior Eculizumab Treatment	Weber C fracture, left	Y	Hospitalization	No		30JUN2021	02AUG2021	Recovered/ Resolved	
1013-161	Active	Prior Eculizumab Treatment	Dyspnoe	Y	Hospitalization	No		21DEC2020	29DEC2020	Recovered/ Resolved	84

Note:
(a) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.

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Listing 14
All Serious Adverse Events and Special Events
Ravulizumab Study Population

Patient Number	Enrollment status	Treatment Status[a]	Adverse Event Term	Serious Event (Yes/No)	Serious Event Category	Special Event (Yes/No)	Special Event Type	Start Date	End Date	Outcome	Clone Size at Enrollment
1013-163	Active	Prior Eculizumab Treatment	Stillbirth	Y	Hospitalization	No		04SEP2019		Recovered/ Resolved	3
			hospitalization for endomyometritis after abortcurettage	Y	Hospitalization	No		14SEP2019	17SEP2019	Recovered/ Resolved	3
1013-169	Active	Prior Eculizumab Treatment	prostatitis	Y	Hospitalization	No		28JAN2022	17FEB2022	Recovered/ Resolved	
			Perforated sigmoid diverticulus	Y	Hospitalization	No		01JAN2023	10JAN2023	Recovered/ Resolved	
1013-175	Active	Prior Eculizumab Treatment	URINE TRACT INFECTION	Y	Hospitalization	No		29APR2024	03MAY2024	Recovered/ Resolved	86
1013-191	Active	Prior Eculizumab Treatment	hemolytic crisis	Y	Hospitalization	No		05APR2021	15APR2021	Recovered/ Resolved	88
			haemolytic crisis	Y	Hospitalization	No		04OCT2021	13OCT2021	Recovered/ Resolved	88

Note:
(a) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.

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Listing 14
All Serious Adverse Events and Special Events
Ravulizumab Study Population

Patient Number	Enrollment status	Treatment Status[a]	Adverse Event Term	Serious Event (Yes/No)	Serious Event Category	Special Event (Yes/No)	Special Event Type	Start Date	End Date	Outcome	Clone Size at Enrollment
1013-195	Active	Prior Eculizumab Treatment	cholecystitis	Y	Hospitalization	No		25OCT2021	26OCT2021	Recovered/ Resolved	75
1013-205	Active	Prior Eculizumab Treatment	fever of unknown origin	Y	Hospitalization	No		08SEP2020	09SEP2020	Recovered/ Resolved	65.3

Note:
(a) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.

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Listing 14
All Serious Adverse Events and Special Events
Ravulizumab Study Population

Patient Number	Enrollment status	Treatment Status[a]	Adverse Event Term	Serious Event (Yes/No)	Serious Event Category	Special Event (Yes/No)	Special Event Type	Start Date	End Date	Outcome	Clone Size at Enrollment
1013-215	Active	Prior Eculizumab Treatment	abortion because of patient was hospitalized because of Late abortion rising infectious parameters and had to have abortion in pregnancy week 19. further details of Soliris: 900mg i.	Y	Hospitalization	No		28AUG2021	25SEP2021	Recovered/ Resolved	47.2

Note:
(a) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.

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Listing 14
All Serious Adverse Events and Special Events
Ravulizumab Study Population

Patient Number	Enrollment status	Treatment Status[a]	Adverse Event Term	Serious Event (Yes/No)	Serious Event Category	Special Event (Yes/No)	Special Event Type	Start Date	End Date	Outcome	Clone Size at Enrollment
			patient was hospitalized because of hemolysis and had to have abortion in pregnancy week 19. further details of Soliris: 900mg i. v. on 30.08.2021, 13.09.2021	Y	Hospitalization	No		28AUG2021	25SEP2021	Recovered/ Resolved	47.2
			pre-eclampsia	Y	Hospitalization	No		12JUL2022	20JUL2022	Recovered/ Resolved	47.2
1013-243	Discontinued	Prior Eculizumab Treatment	hemolytic crisis	Y	Hospitalization	No		20MAR2022	21MAR2022	Recovered/ Resolved	77

Note:
(a) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.

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Listing 14
All Serious Adverse Events and Special Events
Ravulizumab Study Population

Patient Number	Enrollment status	Treatment Status[a]	Adverse Event Term	Serious Event (Yes/No)	Serious Event Category	Special Event (Yes/No)	Special Event Type	Start Date	End Date	Outcome	Clone Size at Enrollment
1030-007		Without Prior Eculizumab Treatment	Haemolysis	N		No		29JUN2018		Unknown	61.1
			UTI	Y	Hospitalization	No		29JUN2018	04JUL2018	Recovered/ Resolved	61.1
			Urinary Tract Infection	Y	Hospitalization	No		29NOV2022	14DEC2022	Recovered/ Resolved	61.1
			mountain bike accident	Y	Death	No		11NOV2023	11NOV2023	Fatal	61.1
1036-001		Prior Eculizumab Treatment	coronavirus disease 2019 (COVID-19)	N		No		01JAN2021	14JAN2021	Recovered/ Resolved	
1036-002		Prior Eculizumab Treatment	Paroxysmal Noctural hemoglobinuria Flare	Y	Hospitalization	No		28NOV2020	30NOV2020	Recovered/ Resolved	

Note:
(a) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.

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Listing 14
All Serious Adverse Events and Special Events
Ravulizumab Study Population

Patient Number	Enrollment status	Treatment Status[a]	Adverse Event Term	Serious Event (Yes/No)	Serious Event Category	Special Event (Yes/No)	Special Event Type	Start Date	End Date	Outcome	Clone Size at Enrollment
1050-001		Prior Eculizumab Treatment	Acute gastroenteritis with fever	Y	Hospitalization	No		21FEB2018	26FEB2018	Recovered/ Resolved	
			COVID infection	Y	Hospitalization	No		03SEP2020	08SEP2020	Recovered/ Resolved	
1061-004		Prior Eculizumab Treatment	COVID-19 Infection	Y	Hospitalization	No		27JUL2021	29JUL2021	Recovered/ Resolved	
			Hemoptysis	Y	Hospitalization	No		01MAY2022	03MAY2022	Recovered/ Resolved	

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Listing 14
All Serious Adverse Events and Special Events
Ravulizumab Study Population

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1061-008		Prior Eculizumab Treatment	angioectasia	Y	Hospitalization	No		08OCT2020	10OCT2020	Recovered/ Resolved	
			GI Bleed	Y	Hospitalization	No		02NOV2020	03NOV2020	Recovered/ Resolved	
			GI Bleed	Y	Hospitalization	No		11DEC2020	12DEC2020	Recovered/ Resolved	
			GI bleed	Y	Hospitalization	No		21MAY2021	23MAY2021	Recovered/ Resolved	
			GI BLEED	Y	Hospitalization	No		16FEB2022	18FEB2022	Recovered/ Resolved	
			GI Bleed	Y	Hospitalization	No		28FEB2022	01MAR2022	Recovered/ Resolved	
			Acute Blood Loss Anemia	Y	Death;Hospitalization	No		21MAR2022	12APR2022	Fatal	
1093-033		Prior Eculizumab Treatment	gastroscopy in cause of nausea. Send in Error, pls. Please remove from safety	Y	Hospitalization	No		08JAN2019	09JAN2019	Recovered/ Resolved	95.98

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1093-043		Prior Eculizumab Treatment	Influenza B infection	Y	Hospitalization	No		14JAN2018	23JAN2018	Recovered/ Resolved	100
1093-060		Prior Eculizumab Treatment	pyelonephritis	Y	Hospitalization	No		14MAY2019	20MAY2019	Recovered/ Resolved	
1093-089		Without Prior Eculizumab Treatment	Ileus	Y	Hospitalization	No		18FEB2021	27FEB2021	Recovered/ Resolved	
1093-105		Prior Eculizumab Treatment	cholangitis	Y	Hospitalization	No		13AUG2019	15AUG2019	Recovered/ Resolved	99.1
			cholecystolithiasis	Y	Hospitalization	No		13AUG2019	15AUG2019	Recovered/ Resolved	99.1
			cholestasis	Y	Hospitalization	No		13AUG2019	15AUG2019	Recovered/ Resolved	99.1
1093-109		Prior Eculizumab Treatment	absolute arrhythmia in cause of hyperthyreosis	Y	Hospitalization	No		05MAY2019	13MAY2019	Recovered/ Resolved	20.8

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1093-122		Prior Eculizumab Treatment Unknown	urinary tract infection	N		No		19SEP2018		Recovered/ Resolved	29.1
			infection of cysts	Y	Hospitalization	No		02JUL2020	09JUL2020	Recovered/ Resolved	29.1
1093-130		Prior Eculizumab Treatment	brainstem infarction	Y	Life-Threatening;Hospitalization	No		27OCT2017	03NOV2017	Recovered/ Resolved	20.1
			migraine attack	Y	Hospitalization	No		04NOV2018	06NOV2018	Recovered/ Resolved	20.1

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1093-131		Prior Eculizumab Treatment Unknown	Acute Tonsilitis	Y	Hospitalization	No		02NOV2020	13NOV2020	Recovered/ Resolved	
			Urinary tract infection	Y	Hospitalization	No		02NOV2020	13NOV2020	Recovered/ Resolved	
			Conditioning therapy in preparation for Bone Marrow transplantation due to severe aplastic anemia	Y	Hospitalization	No		16NOV2020		Unknown	
1093-137		Prior Eculizumab Treatment Unknown	Infection with Coughing	N		No		14SEP2021	28SEP2021	Recovered/ Resolved	94.5

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1093-138		Prior Eculizumab Treatment Unknown	pseudocysts in Pancreas	N		No		26JUL2019		Not Recovered/ Not Resolved	99.8
			small, multiple ' Gallenkonkremete', I could not find an englisch Translation ...	N		No		26JUL2019		Not Recovered/ Not Resolved	99.8
			Diarrhoe	N		No		25AUG2019	20SEP2019	Recovered/ Resolved	99.8
			Breakthrough Hemolysis	Y	Other	No		30AUG2019	02SEP2019	Recovered/ Resolved	99.8
			Rhinitis	N		No		10OCT2019		Not Recovered/ Not Resolved	99.8

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			cholecystolithiasis	Y	Hospitalization	No		03NOV2019		Not Recovered/ Not Resolved	99.8
1093-140		Without Prior Eculizumab Treatment	prostate carcinoma	Y	Hospitalization	No		02FEB2019	15FEB2019	Recovering /Resolving	1.73
			urinary tract infection	Y	Hospitalization	No		02FEB2019	15FEB2019	Recovered/ Resolved	1.73
1093-153		Without Prior Eculizumab Treatment	Cholecystolithiasis	Y	Hospitalization	No		13JAN2021	15JAN2021	Recovered/ Resolved	93.87
1093-191		Prior Eculizumab Treatment	Sequestered L5/S1 disc herniation on the right	Y	Hospitalization	No		12JUL2018	24JUL2018	Recovered/ Resolved	90.7

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1093-192		Without Prior Eculizumab Treatment	Urolithiasis	N		No		05DEC2021	10DEC2021	Recovered/ Resolved	78.3
			acute cholecystitis	Y	Hospitalization	No		05DEC2021	10DEC2021	Recovered/ Resolved	78.3
			Gall Stones	N		No		07DEC2021		Not Recovered/ Not Resolved	78.3
			Hepatic cyst	N		No		07DEC2021		Not Recovered/ Not Resolved	78.3
			Pleural effusion	N		No		07DEC2021		Not Recovered/ Not Resolved	78.3
			basal atelectasis both sides	N		No		07DEC2021		Not Recovered/ Not Resolved	78.3

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			solitary agiodysplasia	N		No		08DEC2021		Not Recovered/ Not Resolved	78.3
			typ- c gastritis	N		No		08DEC2021		Not Recovered/ Not Resolved	78.3

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1093-222		Without Prior Eculizumab Treatment	local Inflammation due to insect bite	N		No		19MAY2019	28JUN2019	Recovered/ Resolved	2.89
			tooth 18 and 28 extraction unknown origin	Y	Hospitalization	No		12AUG2019	15AUG2019	Recovered/ Resolved	2.89
			Sinus pilonidalis	Y	Hospitalization	No		11OCT2019	12OCT2019	Recovered/ Resolved	2.89
			gastroenteritis	N		No		02JAN2021	12JAN2021	Recovered/ Resolved	2.89
			Coughing	N		No		06FEB2024		Recovering /Resolving	2.89
			Fever 39° Grad. Fever only for one day	N		No		06FEB2024	07FEB2024	Recovered/ Resolved	2.89

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1093-254		Without Prior Eculizumab Treatment	Deep Vein Thrombosis	Y	Hospitalization	No		28SEP2020	28SEP2020	Recovered/ Resolved	71.5
			Liverpunction due to increased liver value	Y	Hospitalization	No		16DEC2022	17DEC2022	Recovered/ Resolved	71.5
			Olecranon bursitis surgery.	Y	Hospitalization	No		30MAY2023	19JUN2023	Recovered/ Resolved	71.5
1130-018		Prior Eculizumab Treatment Unknown	Neutropenia	Y	Hospitalization	No		14MAY2023	20MAY2023	Recovered/ Resolved	38.76
			pneumonia	Y	Hospitalization	No		14MAY2023	20MAY2023	Recovered/ Resolved	38.76
			ureterolithiasis	Y	Hospitalization	No		28MAY2023	31MAY2023	Recovered/ Resolved	38.76
1134-055		Without Prior Eculizumab Treatment	Anemia	Y	Hospitalization	No		24NOV2023	25NOV2023	Recovered/ Resolved	97
			Hemolysis	Y	Hospitalization	No		10APR2024	11APR2024	Recovered/ Resolved	97

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1134-088		Without Prior Eculizumab Treatment	DVT left leg	Y	Other	No		02DEC2020	02DEC2020	Recovered/ Resolved	95
			Malaise	Y	Hospitalization	No		30SEP2023	30SEP2023	Recovered/ Resolved	95
1134-111		Without Prior Eculizumab Treatment	Death NOS	Y	Death	No		31JAN2024	31JAN2024	Fatal	66
1134-140		Without Prior Eculizumab Treatment	DVT right arm, hospitalization in Italy	Y	Hospitalization	No		07JUN2019	07JUN2019	Recovered/ Resolved	92
			Deep trombopenia	N		No		07JUN2019	12JUN2019	Recovered/ Resolved	92

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1139-002		Prior Eculizumab Treatment	Anaemia - reduced haemoglobin levels below patient's baseline	Y	Hospitalization	No		14JUL2021	27JUL2021	Recovered/ Resolved	86
			Adverse drug reaction with deferasirox	Y	Hospitalization	No		17JUL2021	19JUL2021	Recovered/ Resolved	86
1140-002		Prior Eculizumab Treatment	GI bleed	Y	Hospitalization	No		06FEB2024	09FEB2024	Recovered/ Resolved	94
1151-011		Without Prior Eculizumab Treatment	Gastroenteritis	Y	Hospitalization	No		10FEB2024	14FEB2024	Recovered/ Resolved	76

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1151-014		Prior Eculizumab Treatment	Haemolytic Anaemia	Y	Hospitalization	No		21OCT2021	27OCT2021	Recovered/ Resolved	3.5
			Prostate cancer	Y	Other	No		15MAR2022		Not Recovered/ Not Resolved	3.5
			COVID-19 Infection	Y	Hospitalization	No		01OCT2022	06OCT2022	Recovered/ Resolved	3.5
1152-002		Prior Eculizumab Treatment	Diaphragmatic protrusion left side	Y	Hospitalization	No		29OCT2021	02NOV2021	Recovered/ Resolved	68.25
1163-018		Prior Eculizumab Treatment	headache	N		No		02MAY2023	04MAY2023	Recovered/ Resolved	87
1169-006		Prior Eculizumab Treatment	fever	Y	Hospitalization	No		25AUG2023	26AUG2023	Recovered/ Resolved	96

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1197-027		Prior Eculizumab Treatment	bacteriemia	Y	Hospitalization	No		21JAN2020	28JAN2020	Recovered/ Resolved	92
			COLON ADENOCARCINOMA	Y	Hospitalization	No		21JAN2021	10FEB2021	Recovered/ Resolved	92
			Femur fracture	Y	Hospitalization	No		04JUN2021	25JUN2021	Recovered/ Resolved	92
			COVID19	Y	Hospitalization	No		17DEC2022	30DEC2022	Recovered/ Resolved	92
			Acute renal failure (AKIN 3)	Y	Death;Hospitalization	No		11MAR2023	13APR2023	Fatal	92
			Infectious processes	Y	Death;Hospitalization	No		11MAR2023	13APR2023	Fatal	92
			Multifactorial encephalopathy	Y	Death;Hospitalization	No		05APR2023	13APR2023	Fatal	92

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1200-005		Prior Eculizumab Treatment	Acute kidney injury	Y	Hospitalization	No		17DEC2021	09MAR2022	Recovered/ Resolved	
			Nephrolithiasis	Y	Hospitalization	No		17DEC2021	09MAR2022	Recovered/ Resolved	
			Pneumonia	Y	Hospitalization	No		17DEC2021	09MAR2022	Recovered/ Resolved	
			Sepsis	Y	Hospitalization	No		17DEC2021	09MAR2022	Recovered/ Resolved	
			Joint Infection: left shoulder pain and swelling found to have a left septic shoulder	Y	Hospitalization	No		02MAY2022	17MAY2022	Recovered/ Resolved	

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1209-003		Without Prior Eculizumab Treatment	Fracture of the wrist	N		No		11MAY2022	09JUN2022	Recovered/ Resolved	
			Right herniated disc L4-L5	N		No		18NOV2022		Not Recovered/ Not Resolved	
1209-005		Prior Eculizumab Treatment	DYSPHAGIA	N		No		18APR2023		Not Recovered/ Not Resolved	7.7
			Bowel meteorism	N		No		03OCT2023		Not Recovered/ Not Resolved	7.7
1214-005		Prior Eculizumab Treatment	haemolysis	Y	Hospitalization	No		03MAR2019	11MAR2019	Recovered/ Resolved	89.2
			phlegmon lower leg re	Y	Hospitalization	No		03MAR2019	11MAR2019	Recovered/ Resolved	89.2
			hemolytic crisis	Y	Hospitalization	No		17MAY2022	24MAY2022	Recovered/ Resolved	89.2

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Listing 14
All Serious Adverse Events and Special Events
Ravulizumab Study Population

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1219-003		Prior Eculizumab Treatment	RED BLOOD VOMITTING	Y	Hospitalization	No		09FEB2022	10FEB2022	Recovered/ Resolved	27
1226-001		Prior Eculizumab Treatment Unknown	Myocardial infarction	Y	Hospitalization	No		30JUN2022	03JUL2022	Recovered/ Resolved	
1226-003		Prior Eculizumab Treatment Unknown	Covid Infection	N		No		10JUN2022	17JUN2022	Recovered/ Resolved	
			Covid Infection	N		No		27FEB2024	05MAR2024	Recovered/ Resolved	
			Vertigo	N		No		06MAR2024		Recovering /Resolving	
1236-002		Prior Eculizumab Treatment	Sinusitis	N		No		18DEC2023	05JAN2024	Recovered/ Resolved	79.45

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1236-003		Without Prior Eculizumab Treatment	Sinusitis	N		No		01AUG2019	01SEP2019	Recovered/ Resolved	72.44
			Tendon rupture of the right hand	Y	Hospitalization	No		01OCT2019	06NOV2019	Recovered/ Resolved	72.44
			Light pressure in the spleen	N		No		20JUN2020	25JUN2020	Recovered/ Resolved	72.44
			bloated belly	N		No		22JUN2020	25JUN2020	Recovered/ Resolved	72.44
			pain left costal arch/hip-Bone prominence left hip iliac crest	N		No		01JUL2021		Not Recovered/ Not Resolved	72.44
			Covid-19	N		No		16OCT2021	25OCT2021	Recovered/ Resolved	72.44

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1250-003		Without Prior Eculizumab Treatment	cholangitis	Y	Hospitalization	No		10APR2023	17APR2023	Recovered/ Resolved	10
1251-001		Prior Eculizumab Treatment	fever	Y	Hospitalization	No		12DEC2020	14DEC2020	Recovered/ Resolved	
			INFECTION	Y	Hospitalization	No		26JAN2022	28JAN2022	Recovered/ Resolved	
1251-005		Prior Eculizumab Treatment	INFILTRATING LOBULAR CARCINOMA RIGHT BREAST	Y	Hospitalization	No		05JUL2022	07JUL2022	Recovered/ Resolved	48

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1251-009		Prior Eculizumab Treatment	HEMOLYSIS	Y	Hospitalization	No		24MAY2022	30MAY2022	Recovered/ Resolved	62.31
			Pancreatitis	Y	Hospitalization	No		09DEC2022	15DEC2022	Recovered/ Resolved	62.31
			cholelithiasis	Y	Hospitalization	No		09MAR2023	10MAR2023	Recovered/ Resolved	62.31
			FEBRILE SYNDROME	Y	Hospitalization	No		24APR2024	03MAY2024	Recovered/ Resolved	62.31
			CERVICAL INFECTIOUS SPONDYLODISCITIS	Y	Hospitalization	No		06MAY2024	13MAY2024	Recovered/ Resolved	62.31
1252-002		Prior Eculizumab Treatment	Basal Cell Carcinoma	Y	Life-Threatening	No		15OCT2019	28OCT2019	Recovered/ Resolved	87.69
1262-002		Prior Eculizumab Treatment	FEVER AT END OF ERHYTROCYTE TRANSFUSION	Y	Hospitalization	No		14AUG2018	15AUG2018	Recovered/ Resolved	

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1266-005		Without Prior Eculizumab Treatment	GOUT ATTACK	N		No		13JUL2023		Recovered/ Resolved	82
1269-003		Prior Eculizumab Treatment	Hemolytic crisis	Y	Hospitalization	No		12JAN2020	16JAN2020	Recovered/ Resolved	95.6
1275-002		Prior Eculizumab Treatment	FEBRILE hemolysis	Y	Hospitalization	No		04JAN2018	13JAN2018	Recovered/ Resolved with Sequelae	

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1304-001		Prior Eculizumab Treatment	Covid-19	Y	Hospitalization	No		24SEP2020	28SEP2020	Recovered/ Resolved	
			SINUSITIS	N		No		10OCT2020	28OCT2020	Recovered/ Resolved	
			ACUTE RENAL FAILURE	Y	Hospitalization	No		22MAY2021	27MAY2021	Recovered/ Resolved	
			Urinary infection	Y	Hospitalization	No		22MAY2021	27MAY2021	Recovered/ Resolved	
			bronchial infection	Y	Hospitalization	No		25JUL2021	09AUG2021	Recovered/ Resolved	
			ACUTE GOUT EPISODIS	N		No		22JUN2022	06JUL2022	Recovered/ Resolved	
			hypoglycemia	Y	Hospitalization	No		25APR2023	03SEP2023	Recovered/ Resolved	
			cardiac decompensation	Y	Hospitalization	No		25AUG2023	03SEP2023	Recovered/ Resolved	
1304-002		Prior Eculizumab Treatment	SARS COV2 INFECTION	N		No		04MAR2021		Recovered/ Resolved	
			SARS COV2 INFECTION	N		No		02FEB2022		Recovered/ Resolved	

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1319-001		Prior Eculizumab Treatment	Admitted with Urinary Tract Infection	Y	Hospitalization	No		06FEB2023	12FEB2023	Recovered/ Resolved	99.7
1351-013		Prior Eculizumab Treatment	Admitted with Chest pain and shortness of breath. CTPA confirmed large pulmonary embolism.	Y	Hospitalization	No		25FEB2021	01MAR2021	Recovered/ Resolved	59
1358-001		Prior Eculizumab Treatment Unknown	appendecitis	Y	Hospitalization	No		15FEB2024	16FEB2024	Recovered/ Resolved	
			cholecystitis	Y	Hospitalization	No		15FEB2024	16FEB2024	Recovered/ Resolved	
1366-024		Without Prior Eculizumab Treatment	Traumatic Subdural hemorrhage	Y	Hospitalization	No		05MAR2023	14MAR2023	Recovered/ Resolved	68.8

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1366-036		Prior Eculizumab Treatment	COVID-19 infection	Y	Hospitalization	No		14AUG2022	03SEP2022	Recovered/ Resolved	99.9
1366-097		Prior Eculizumab Treatment	phyngitis	N		No		25JAN2018	08FEB2018	Recovered/ Resolved	81.2
			Dysuria	N		No		08FEB2018	22FEB2018	Recovered/ Resolved	81.2
1366-108		Prior Eculizumab Treatment	DVT	Y	Hospitalization	No		13MAR2019	23MAR2019	Recovered/ Resolved	43.8
			Metastases to lymph nodes	Y	Hospitalization	No		05APR2021	01MAY2021	Recovered/ Resolved	43.8
			enterocolitis	Y	Hospitalization	No		18JUL2022	19JUL2022	Recovered/ Resolved	43.8
1366-162		Without Prior Eculizumab Treatment	Pneumonia	Y	Hospitalization	No		17MAR2023	01APR2023	Recovered/ Resolved	92.98

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1381-002		Prior Eculizumab Treatment	Acute ST elevation myocardial infarction (STEMI)	Y	Hospitalization	No		12SEP2023	15SEP2023	Recovered/ Resolved	

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1381-003		Prior Eculizumab Treatment	Failed kidney transplant	Y	Hospitalization	No		02MAR2022		Recovering /Resolving	
			Vancomycin-Resistant Enterococcus bacteremia	Y	Hospitalization	No		10APR2022	20APR2022	Recovered/ Resolved	
			COVID-19 infection	Y	Hospitalization	No		01DEC2022	08DEC2022	Recovered/ Resolved	
			right inguinal fossa abscess	Y	Hospitalization	No		01DEC2022		Recovering /Resolving	
			failed kidney transplant	Y	Hospitalization	No		25JAN2023		Not Recovered/ Not Resolved	
			non-healing RLQ wound	Y	Hospitalization	No		25JAN2023	01FEB2023	Recovered/ Resolved with Sequelae	

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			COVID 19 infection	Y	Hospitalization	No		03AUG2023	15AUG2023	Recovered/ Resolved	
			sever anima	Y	Hospitalization	No		03AUG2023	04AUG2023	Recovered/ Resolved	
1381-008		Prior Eculizumab Treatment	Odontogenic abscess infection	Y	Hospitalization	No		15JUL2021	19JUL2021	Recovered/ Resolved	
			PNH crisis, precipitated by infection	Y	Hospitalization	No		15JUL2021	19JUL2021	Recovered/ Resolved	
			Right facial cellulitis	Y	Hospitalization	No		15JUL2021	19JUL2021	Recovered/ Resolved	
			Sepsis	Y	Hospitalization	No		15JUL2021	19JUL2021	Recovered/ Resolved	

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1381-014		Without Prior Eculizumab Treatment	Fatigue 1 day after each Ultomiris infusion	N		No		11JUL2020	09JAN2021	Recovered/ Resolved	23.4
			Headache 1 day after each Ultomiris infusion	N		No		11JUL2020	09JAN2021	Recovered/ Resolved	23.4
			Closed Colles fracture	Y	Significant Disability;Hospitalization	No		22JAN2021		Recovering /Resolving	23.4
1381-017		Prior Eculizumab Treatment	recurrent DVT	N		No		12DEC2021		Recovering /Resolving	40.9
			fatigue	Y	Hospitalization	No		07DEC2023		Recovering /Resolving	40.9
			light-headedness	Y	Hospitalization	No		07DEC2023	07DEC2023	Recovered/ Resolved	40.9
			short of breath	Y	Hospitalization	No		07DEC2023	08DEC2023	Recovered/ Resolved	40.9

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1418-042		Without Prior Eculizumab Treatment	Abdominal pain	N		No		06SEP2017	14NOV2017	Recovered/ Resolved	68.31
1418-045		Prior Eculizumab Treatment	FEVER	N		No		24MAR2019	30MAR2019	Recovered/ Resolved	94.46
			Headache	N		No		24MAR2019	30MAR2019	Recovered/ Resolved	94.46
			diarrhea	N		No		24MAR2019	30MAR2019	Recovered/ Resolved	94.46
			hypokalemia	N		No		25MAR2019	26MAR2019	Recovered/ Resolved	94.46
1420-004		Prior Eculizumab Treatment	Acute kidney injury	Y	Hospitalization	No		15OCT2019	01NOV2019	Recovered/ Resolved	
1421-031		Without Prior Eculizumab Treatment	HIP FRACTURE	Y	Hospitalization	No		23APR2022	04MAY2022	Recovered/ Resolved	91.5

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1422-004		Prior Eculizumab Treatment	fracture of distal radius, Rt	Y	Hospitalization	No		28OCT2018	30OCT2018	Recovered/ Resolved	48.9
			Acute cholecystitis	Y	Hospitalization	No		24MAR2021	04APR2021	Recovered/ Resolved	48.9
			Iron overload	N		No		19OCT2021		Not Recovered/ Not Resolved	48.9
			COVID-19 infection	Y	Hospitalization	No		20DEC2022	27DEC2022	Recovered/ Resolved	48.9
			AST increased	N		No		21DEC2022	26DEC2022	Recovered/ Resolved	48.9
			fatigue	Y	Hospitalization	No		12JUL2023	24JUL2023	Recovered/ Resolved	48.9
1422-008		Prior Eculizumab Treatment	Nausea	N		No		25AUG2021	25AUG2021	Recovered/ Resolved	32.7
			acute calculous cholecystitis	Y	Hospitalization	No		22SEP2023	25SEP2023	Recovered/ Resolved	32.7

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1422-011		Prior Eculizumab Treatment	Weakness	N		No		26JUN2017	05JUL2017	Recovered/ Resolved	36.7
			Retinal detachment	Y	Hospitalization	No		21JUN2019	04JUL2019	Recovered/ Resolved	36.7
			right eye cataract	Y	Hospitalization	No		27APR2020	27APR2020	Recovered/ Resolved	36.7
1422-022		Prior Eculizumab Treatment	Chronic cysititis	N		No		11JUN2020	03SEP2020	Recovered/ Resolved	89.8
1423-002		Prior Eculizumab Treatment	Cholecystitis	Y	Hospitalization	No		09OCT2023	12OCT2023	Recovered/ Resolved	

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1423-006		Prior Eculizumab Treatment	upper respiratory infection	N		No		20APR2016	22APR2016	Recovered/ Resolved	
			Osteoporosis	N		No		01JUN2016		Recovering /Resolving	
			tsutsugamushi	Y	Hospitalization	No		25SEP2017	02OCT2017	Recovered/ Resolved	
			Infectious spondylitis of L3-4	Y	Other	No		23AUG2019	08OCT2019	Recovered/ Resolved	
			Right hip osteoarthritis	Y	Hospitalization	No		22APR2020	04MAY2020	Recovered/ Resolved	

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Listing 14
All Serious Adverse Events and Special Events
Ravulizumab Study Population

Patient Number	Enrollment status	Treatment Status[a]	Adverse Event Term	Serious Event (Yes/No)	Serious Event Category	Special Event (Yes/No)	Special Event Type	Start Date	End Date	Outcome	Clone Size at Enrollment
1423-008		Prior Eculizumab Treatment	Hematuria	Y	Hospitalization	No		20NOV2018	24NOV2018	Recovered/ Resolved	89.9
			Cryptococcus CNS infection	Y	Hospitalization	No		06MAR2020	27MAR2020	Recovered/ Resolved	89.9
			Cellulitis	Y	Hospitalization	No		30MAR2020	15APR2020	Recovered/ Resolved	89.9
			Cryptococcus CNS infection	Y	Hospitalization	No		12JUN2020	04AUG2020	Recovered/ Resolved with Sequelae	89.9
			Myalgia	N		No		14APR2021		Recovering /Resolving	89.9
			joint pain	N		No		28APR2021		Recovering /Resolving	89.9
			headache	N		No		23JUN2021	12OCT2021	Recovered/ Resolved	89.9
			heel pain	N		No		21JUL2021	12OCT2021	Recovered/ Resolved	89.9
			Influenza infection	Y	Hospitalization	No		05NOV2023	09NOV2023	Recovered/ Resolved	89.9

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1423-011		Prior Eculizumab Treatment	Gastric dysplasia	Y	Hospitalization	No		15JUL2020	18JUL2020	Recovered/ Resolved	46.8
			Hyperplasia of prostate	Y	Hospitalization	No		24APR2023	27APR2023	Recovered/ Resolved	46.8
			Infectious spondylitis	Y	Hospitalization	No		31JUL2023	03AUG2023	Recovered/ Resolved with Sequelae	46.8
			Infectious spondylitis	Y	Hospitalization	No		18AUG2023	15SEP2023	Recovered/ Resolved	46.8
			Klebsiella pneumoniae bacteremia	Y	Hospitalization	No		28AUG2023	15SEP2023	Recovered/ Resolved	46.8
			Urinary tract infection	Y	Hospitalization	No		28AUG2023	15SEP2023	Recovered/ Resolved	46.8

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1423-012		Prior Eculizumab Treatment	Cold	N		No		02DEC2016	04DEC2016	Recovered/ Resolved	93.2
			Cold	N		No		30DEC2016	03JAN2017	Recovered/ Resolved	93.2
			urinary tract infection	Y	Hospitalization	No		26AUG2017	11SEP2017	Recovered/ Resolved	93.2
			Pneumonia	Y	Hospitalization	No		25APR2019	03MAY2019	Recovered/ Resolved	93.2
			Atrial fibrillation	Y	Hospitalization	No		25MAY2020	22JUN2020	Recovered/ Resolved	93.2
			mitral regurgitation	Y	Hospitalization	No		28MAY2020	22JUN2020	Recovered/ Resolved	93.2
			tricuspid regurgitation	Y	Hospitalization	No		28MAY2020	22JUN2020	Recovered/ Resolved	93.2
			Zoster	Y	Hospitalization	No		11MAY2022	04JUN2022	Recovered/ Resolved	93.2

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			bacteremia	Y	Hospitalization	No		29MAR2023	11APR2023	Recovered/ Resolved	93.2
			Escherichia coli bacteremia	Y	Hospitalization	No		03MAY2023	19MAY2023	Recovered/ Resolved	93.2
			Exacerbation of prostate hyperplasia	Y	Hospitalization	No		13JUN2023	28JUN2023	Recovered/ Resolved	93.2

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1423-014		Prior Eculizumab Treatment	Myoclonic movement	Y	Hospitalization	No		03AUG2017	22AUG2017	Recovered/ Resolved	93.5
			worse headache	Y	Hospitalization	No		03AUG2017	31OCT2017	Recovered/ Resolved	93.5
			Myoclonic movement	N		No		23AUG2017	29AUG2017	Recovered/ Resolved	93.5
			acute kidney injury	Y	Hospitalization	No		10OCT2017	21OCT2017	Recovered/ Resolved	93.5
			General weakness	N		No		21NOV2017	21NOV2017	Recovered/ Resolved	93.5
			chill	N		No		29NOV2017	11DEC2017	Recovered/ Resolved	93.5
			scapular area pain	N		No		13DEC2017	08JAN2018	Recovered/ Resolved	93.5
			general weakness	N		No		06FEB2018	06MAR2018	Recovered/ Resolved	93.5
			general pain	N		No		07MAR2018	03APR2018	Recovered/ Resolved	93.5
			facial flushing	N		No		22MAR2018	01MAY2018	Recovered/ Resolved	93.5

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			headache	N		No		22MAR2018	01MAY2018	Recovered/ Resolved	93.5
			scapular area pain	N		No		02MAY2018	24JUL2018	Recovered/ Resolved	93.5
1423-017		Prior Eculizumab Treatment	gingivitis	Y	Hospitalization	No		12NOV2018	15NOV2018	Recovered/ Resolved	86.4
			Urinary tract infection	Y	Hospitalization	No		31JAN2019	07FEB2019	Recovered/ Resolved	86.4
			Menorrhagia	N		No		03JUN2019	09JUN2019	Recovered/ Resolved	86.4
			cold	N		No		24OCT2019	07NOV2019	Recovered/ Resolved	86.4
1423-018		Prior Eculizumab Treatment	Abdominal pain	Y	Hospitalization	No		03NOV2019	12NOV2019	Recovered/ Resolved	77.6
			Abdominal pain	Y	Hospitalization	No		12DEC2019	18DEC2019	Recovered/ Resolved	77.6

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1425-003		Prior Eculizumab Treatment	Faecal incontinence	N		No		17APR2019	07MAY2019	Recovered/ Resolved	85.94
			Plueral effusion	N		No		08OCT2019	22NOV2019	Recovered/ Resolved	85.94
			Pleural Effusion	Y	Hospitalization	No		10AUG2021	13AUG2021	Recovered/ Resolved	85.94
1429-001		Prior Eculizumab Treatment Unknown	abdominal pain	N		No		02MAR2017		Not Recovered/ Not Resolved	
			Sore throat	N		No		20APR2017	30APR2017	Recovered/ Resolved	
			Common cold	N		No		10OCT2017	20OCT2017	Recovered/ Resolved	
			headache	N		No		27AUG2018		Not Recovered/ Not Resolved	

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1429-011		Without Prior Eculizumab Treatment	Neutropenic fever	Y	Hospitalization	No		20FEB2022	11MAR2022	Recovered/ Resolved with Sequelae	94.64
			Intracerebral hemorrhage	Y	Death	No		11MAR2022	11MAR2022	Fatal	94.64
1432-003		Prior Eculizumab Treatment	Hemolysis	Y	Other	No		05JUL2021	17AUG2021	Recovered/ Resolved	
1432-004		Without Prior Eculizumab Treatment	Hematuria	N		No		12JAN2019	14JAN2019	Recovered/ Resolved	
			Infection	N		No		12JAN2019	14JAN2019	Recovered/ Resolved	
1432-009		Prior Eculizumab Treatment Unknown	septicaemia	Y	Hospitalization	No		26JAN2020		Recovering /Resolving	
			septicemia	Y	Hospitalization	No		27MAR2020		Recovering /Resolving	
			sepsis	Y	Hospitalization	No		06JUL2020		Recovering /Resolving	

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1462-004		Prior Eculizumab Treatment	Rib fracture Th6-8	Y	Hospitalization	No		21JUL2019	24JUL2019	Recovered/ Resolved	
			Hepatocellular carcinoma	Y	Hospitalization	No		20JUL2020		Not Recovered/ Not Resolved	
			Hepatic encephalopathy	Y	Hospitalization	No		02AUG2021		Recovering /Resolving	
			Infectious enteritis	Y	Hospitalization	No		04SEP2021	10SEP2021	Recovered/ Resolved	
			enteritis	Y	Hospitalization	No		24SEP2021	02OCT2021	Recovered/ Resolved	
			Gastric hemorrhage (post biopsy)	Y	Hospitalization	No		25MAY2022	29MAY2022	Recovered/ Resolved	
			hepatic encephalopathy	Y	Hospitalization	No		20DEC2022	28DEC2022	Recovered/ Resolved	

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			Fever post FFP administration	Y	Hospitalization	No		06MAR2023	15MAR2023	Recovered/ Resolved	
			Radiofrequency ablation for hepatocellular carcinoma	Y	Hospitalization	No		22MAR2023		Recovering /Resolving	
			Radiofrequency ablation for hepatocellular carcinoma	Y	Hospitalization	No		19JUL2023		Recovering /Resolving	

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1462-006		Prior Eculizumab Treatment	Disseminated gonococcal infection	Y	Hospitalization	No		05FEB2020	03MAR2020	Recovered/ Resolved	
			infectious vasculitis	Y	Other	No		06FEB2020		Recovering /Resolving	
			Exacerbation of PNH	Y	Hospitalization	No		07FEB2020		Recovering /Resolving	
			Septic Shock	Y	Other	No		07FEB2020	03MAR2020	Recovered/ Resolved	
			gallstones	Y	Hospitalization	No		20MAY2022	08JUL2022	Recovered/ Resolved	
			gallstones	Y	Hospitalization	No		04JUL2022	08JUL2022	Recovered/ Resolved	
			COVID-19 infection	Y	Hospitalization	No		22DEC2022	28DEC2022	Recovered/ Resolved	

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1462-008		Prior Eculizumab Treatment	Gallbladder swelling	Y	Other	No		21AUG2020	25AUG2020	Recovered/ Resolved	
			deep vein thrombosis	Y	Hospitalization	No		10JAN2024		Recovering /Resolving	
			pulmonary embolism	Y	Hospitalization	No		10JAN2024		Recovering /Resolving	
1462-009		Prior Eculizumab Treatment	Influenza a virus infection	N		No		25JAN2019	01FEB2019	Recovered/ Resolved	
			colon polyps	Y	Hospitalization	No		15MAR2023	17MAR2023	Recovered/ Resolved	
			retroperitoneal haematoma	Y	Hospitalization	No		10DEC2023	18DEC2023	Recovered/ Resolved	
1507-002		Prior Eculizumab Treatment	COVID-19 infection	Y	Hospitalization	No		24JAN2023	01FEB2023	Recovered/ Resolved	99.28

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1507-003		Prior Eculizumab Treatment	Hemolysis	Y	Other	No		17AUG2021	18AUG2021	Recovered/ Resolved	
			anemia	Y	Other	No		17AUG2021	18AUG2021	Recovered/ Resolved	
			fatigue	Y	Other	No		17AUG2021	18AUG2021	Recovered/ Resolved	
			pneumonia	Y	Hospitalization	No		20JUL2023	29JUL2023	Recovered/ Resolved	

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1558-002		Prior Eculizumab Treatment	Upper respiratory tract infection	N		No		06JAN2019	16JAN2019	Recovered/ Resolved	
			Hemolytic crisis	Y	Hospitalization	No		13JAN2019	18JAN2019	Recovered/ Resolved	
			Parotid primary carcinoma	Y	Other	No		15JAN2019		Not Recovered/ Not Resolved	
			Acute confusional syndrome	Y	Hospitalization	No		28APR2019	06MAY2019	Recovered/ Resolved	
			HEMOLYTIC CRISIS	Y	Other	Yes	Lack of Therapeutic Efficacy	18AUG2020	08SEP2020	Recovered/ Resolved	
1612-001		Prior Eculizumab Treatment	cholecystitis	Y	Hospitalization	No		15DEC2019	17DEC2019	Recovered/ Resolved	92.4

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1667-004		Prior Eculizumab Treatment	diarrhea	N		No		13MAY2020	27MAY2020	Recovered/ Resolved	
			alopecia	N		No		27MAY2020	10JUN2020	Recovered/ Resolved	
1668-001		Prior Eculizumab Treatment	Pneumonia	Y	Hospitalization	No		25MAR2017	28MAR2017	Recovered/ Resolved	
1670-002		Prior Eculizumab Treatment	covid-19 infection	Y	Hospitalization	No		26MAR2022	30MAR2022	Recovered/ Resolved	98.2
			covid-19 infection	Y	Hospitalization	No		31JUL2023	05AUG2023	Recovered/ Resolved	98.2

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1682-001		Prior Eculizumab Treatment	Post-concussion syndrome	N		No		07APR2021		Recovering/Resolving	87.16
			Syncopal episode	N		No		07APR2021		Recovering/Resolving	87.16
			pre-syncope, suspected cardiogenic reflexive vasovagal syncope	N		No		02JUN2021	02JUN2021	Recovered/Resolved	87.16
			Pruritus	N		No		25JAN2022		Not Recovered/Not Resolved	87.16
1787-003		Prior Eculizumab Treatment	Rt.wrist osteomyelitis	Y	Hospitalization	No		25FEB2018	20MAR2018	Recovered/Resolved	96.7
1787-005		Prior Eculizumab Treatment	Jaundice	Y	Hospitalization	No		14FEB2018	19FEB2018	Recovered/Resolved	100
			Jaundice	Y	Hospitalization	No		26OCT2018	31OCT2018	Recovered/Resolved	100

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(a) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.

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Run Date: 2025-05-14T14:46:12
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ravuema202501/Files/listings/production/programs/l14_sae.sas

Listing 14
All Serious Adverse Events and Special Events
Ravulizumab Study Population

Patient Number	Enrollment status	Treatment Status[a]	Adverse Event Term	Serious Event (Yes/No)	Serious Event Category	Special Event (Yes/No)	Special Event Type	Start Date	End Date	Outcome	Clone Size at Enrollment
1796-001		Prior Eculizumab Treatment	mild nausea	N		No		02MAR2017	12APR2017	Recovered/ Resolved	80
			Dyspepsia	N		No		21SEP2017	12OCT2017	Recovered/ Resolved	80
			Nausea	N		No		21SEP2017	12OCT2017	Recovered/ Resolved	80
			aggravation of hemolytic anemia	Y	Hospitalization	No		07MAY2020	10MAY2020	Recovered/ Resolved	80

Note:
(a) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.

Source: ADAM.ADSL, ADAM.ADPOP, ADAM.ADAE, ADAM.ADLBSUM, CONV.ALL_SITES
Run Date: 2025-05-14T14:46:12
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ravuema202501/Files/listings/production/programs/l14_sae.sas

Listing 15
Patient Information and Treatment Information
Frequent Treatment Switchers

Patient Number: 1008-062
Enrollment Date: 16DEC2016
Age at First Treatment Initiation: 45.2

Treatment	Initiation Date	Discontinuation Date	Reason for Treatment Discontinuation
ECU	15SEP2014	06FEB2019	
RVU	06FEB2019	04MAR2019	
ECU	04MAR2019	01APR2019	Switch to ravulizumab IV

Source: ADAM.ADSL, ADAM.ADPOP, ADAM.ADEX2, ADAM.ADEX
Run Date: 2025-05-14T14:46:13
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ravuema202501/Files/listings/production/programs/l15_patinfo.sas

Listing 15
Patient Information and Treatment Information
Frequent Treatment Switchers

Patient Number: 1009-030
Enrollment Date: 24OCT2005
Age at First Treatment Initiation: 27.9

Treatment	Initiation Date	Discontinuation Date	Reason for Treatment Discontinuation
ECU	10JUN2013	21OCT2021	
RVU	21OCT2021	24FEB2022	Patient choice
ECU	24FEB2022	29NOV2024	Switch to ravulizumab IV

Source: ADAM.ADSL, ADAM.ADPOP, ADAM.ADEX2, ADAM.ADEX
Run Date: 2025-05-14T14:46:13
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ravuema202501/Files/listings/production/programs/l15_patinfo.sas

Listing 15
Patient Information and Treatment Information
Frequent Treatment Switchers

Patient Number: 1009-296
Enrollment Date: 30OCT2014
Age at First Treatment Initiation: 38.1

Treatment	Initiation Date	Discontinuation Date	Reason for Treatment Discontinuation
ECU	15AUG2014	13JAN2015	
RVU	13JUL2022	10JAN2023	Switch to eculizumab IV
ECU	10JAN2023	03JUN2024	Physician decision

Listing 15
Patient Information and Treatment Information
Frequent Treatment Switchers

Patient Number: 1009-417
Enrollment Date: 24OCT2017
Age at First Treatment Initiation: 57.6

Treatment	Initiation Date	Discontinuation Date	Reason for Treatment Discontinuation
ECU	01FEB2018	18MAY2022	
RVU	18MAY2022	03MAY2023	Switch to eculizumab IV
ECU	03MAY2023	27AUG2024	Switch to ravulizumab IV

Source: ADAM.ADSL, ADAM.ADPOP, ADAM.ADEX2, ADAM.ADEX
Run Date: 2025-05-14T14:46:13
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ravuema202501/Files/listings/production/programs/l15_patinfo.sas

Listing 15
Patient Information and Treatment Information
Frequent Treatment Switchers

Patient Number: 1013-039
Enrollment Date: 30MAY2007
Age at First Treatment Initiation: 17.5

Treatment	Initiation Date	Discontinuation Date	Reason for Treatment Discontinuation
ECU	29DEC2008	19SEP2019	
RVU	19SEP2019	30OCT2020	
ECU	30OCT2020	15FEB2021	Switch to other anti-complement treatment
RVU	15FEB2021	02MAY2024	Switch to ravulizumab SC

Source: ADAM.ADSL, ADAM.ADPOP, ADAM.ADEX2, ADAM.ADEX
Run Date: 2025-05-14T14:46:13
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ravuema202501/Files/listings/production/programs/l15_patinfo.sas

Listing 15
Patient Information and Treatment Information
Frequent Treatment Switchers

Patient Number: 1013-060
Enrollment Date: 06JUL2009
Age at First Treatment Initiation: 28.7

Treatment	Initiation Date	Discontinuation Date	Reason for Treatment Discontinuation
ECU	04MAR2008	10SEP2020	
RVU	10SEP2020	08DEC2020	Adverse Event
ECU	08DEC2020	08DEC2020	Switch to other anti-complement treatment
RVU	08DEC2020	30MAR2021	Adverse Event

Listing 15
Patient Information and Treatment Information
Frequent Treatment Switchers

Patient Number: 1013-107
Enrollment Date: 06SEP2012
Age at First Treatment Initiation: 44

Treatment	Initiation Date	Discontinuation Date	Reason for Treatment Discontinuation
ECU	19JUN2012	15AUG2019	
RVU	15AUG2019	06JUN2020	Switch to eculizumab IV
ECU	18AUG2020	15JUL2022	Switch to other anti-complement treatment
OAC	15JUL2022	12JAN2024	

Listing 15
Patient Information and Treatment Information
Frequent Treatment Switchers

Patient Number: 1013-113
Enrollment Date: 17OCT2012
Age at First Treatment Initiation: 44.3

Treatment	Initiation Date	Discontinuation Date	Reason for Treatment Discontinuation
ECU	17OCT2012	11APR2017	
RVU	15AUG2019	30SEP2020	Switch to eculizumab IV
ECU	30SEP2020	18APR2024	Switch to other anti-complement treatment

Source: ADAM.ADSL, ADAM.ADPOP, ADAM.ADEX2, ADAM.ADEX
Run Date: 2025-05-14T14:46:13
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ravuema202501/Files/listings/production/programs/l15_patinfo.sas

Listing 15
Patient Information and Treatment Information
Frequent Treatment Switchers

Patient Number: 1013-164
Enrollment Date: 22APR2015
Age at First Treatment Initiation: 72

Treatment	Initiation Date	Discontinuation Date	Reason for Treatment Discontinuation
ECU	08JUL2015	02JAN2020	
RVU	02JAN2020	16JAN2020	
ECU	16JAN2020	16JAN2020	Switch to other anti-complement treatment
RVU	16JAN2020	15MAR2024	

Listing 15
Patient Information and Treatment Information
Frequent Treatment Switchers

Patient Number: 1013-184
Enrollment Date: 29FEB2016
Age at First Treatment Initiation: 31.1

Treatment	Initiation Date	Discontinuation Date	Reason for Treatment Discontinuation
ECU	15AUG2016	15OCT2019	
RVU	15OCT2019	01JUN2020	Switch to other anti-complement treatment
ECU	01JUN2020	26APR2022	Switch to other anti-complement treatment
OAC	26APR2022	25JAN2024	

Listing 15
Patient Information and Treatment Information
Frequent Treatment Switchers

Patient Number: 1039-008
Enrollment Date: 04OCT2016
Age at First Treatment Initiation: 19.1

Treatment	Initiation Date	Discontinuation Date	Reason for Treatment Discontinuation
ECU	23AUG2016	20NOV2019	
RVU	20NOV2019	11MAY2020	Switch to eculizumab IV
ECU	11MAY2020	29MAY2020	Death

Source: ADAM.ADSL, ADAM.ADPOP, ADAM.ADEX2, ADAM.ADEX
Run Date: 2025-05-14T14:46:13
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ravuema202501/Files/listings/production/programs/l15_patinfo.sas

Listing 15
Patient Information and Treatment Information
Frequent Treatment Switchers

Patient Number: 1093-106
Enrollment Date: 21OCT2014
Age at First Treatment Initiation: 61.1

Treatment	Initiation Date	Discontinuation Date	Reason for Treatment Discontinuation
RVU	07AUG2012	27AUG2014	
ECU	27AUG2014	07AUG2019	Switch to other anti-complement treatment
OAC	07AUG2019	08OCT2019	
RVU	08OCT2019	17MAY2023	Adverse Event

Listing 15
Patient Information and Treatment Information
Frequent Treatment Switchers

Patient Number: 1093-134
Enrollment Date: 05JUN2015
Age at First Treatment Initiation: 37

Treatment	Initiation Date	Discontinuation Date	Reason for Treatment Discontinuation
ECU	15JUN2015	13OCT2019	
RVU	13OCT2019	15OCT2019	
ECU	15OCT2019	12NOV2019	Switch to other anti-complement treatment
RVU	15NOV2019	15JAN2020	Physician decision

Listing 15
Patient Information and Treatment Information
Frequent Treatment Switchers

Patient Number: 1093-177
Enrollment Date: 07MAR2017
Age at First Treatment Initiation: 79.1

Treatment	Initiation Date	Discontinuation Date	Reason for Treatment Discontinuation
ECU	19JUL2018	15NOV2019	
RVU	15NOV2019	15MAR2020	
ECU	15MAR2020	12APR2020	Switch to other anti-complement treatment

Listing 15
Patient Information and Treatment Information
Frequent Treatment Switchers

Patient Number: 1093-255
Enrollment Date: 14JUL2020
Age at First Treatment Initiation: 12.8

Treatment	Initiation Date	Discontinuation Date	Reason for Treatment Discontinuation
ECU	15APR2014	06AUG2019	
RVU	06AUG2019	17APR2024	
ECU	25JUN2020	23JUL2020	Switch to other anti-complement treatment

Listing 15
Patient Information and Treatment Information
Frequent Treatment Switchers

Patient Number: 1093-283
Enrollment Date: 05OCT2021
Age at First Treatment Initiation: 26

Treatment	Initiation Date	Discontinuation Date	Reason for Treatment Discontinuation
ECU	15JUN2019	15FEB2020	
RVU	15FEB2020	25MAY2021	
ECU	25MAY2021	22JUN2021	Switch to ravulizumab IV

Listing 15
Patient Information and Treatment Information
Frequent Treatment Switchers

Patient Number: 1147-001
Enrollment Date: 08OCT2009
Age at First Treatment Initiation: 33.3

Treatment	Initiation Date	Discontinuation Date	Reason for Treatment Discontinuation
ECU	08OCT2007	08APR2019	
RVU	08APR2019	12SEP2019	Switch to eculizumab IV
ECU	12SEP2019	22MAY2024	

Source: ADAM.ADSL, ADAM.ADPOP, ADAM.ADEX2, ADAM.ADEX
Run Date: 2025-05-14T14:46:13
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ravuema202501/Files/listings/production/programs/l15_patinfo.sas

Listing 15
Patient Information and Treatment Information
Frequent Treatment Switchers

Patient Number: 1252-048
Enrollment Date: 15FEB2022
Age at First Treatment Initiation: 53

Treatment	Initiation Date	Discontinuation Date	Reason for Treatment Discontinuation
ECU	01JUL2016	15JAN2022	
RVU	15JAN2022	15JAN2023	
ECU	15JAN2023	12FEB2023	Switch to ravulizumab IV

Listing 15
Patient Information and Treatment Information
Frequent Treatment Switchers

Patient Number: 1268-067
Enrollment Date: 07JAN2013
Age at First Treatment Initiation: 27.1

Treatment	Initiation Date	Discontinuation Date	Reason for Treatment Discontinuation
ECU	20JUL2015	18AUG2021	
RVU	18AUG2021	25AUG2021	
ECU	25AUG2021	01SEP2021	Switch to ravulizumab IV
RVU	01SEP2021	04JUL2024	

Source: ADAM.ADSL, ADAM.ADPOP, ADAM.ADEX2, ADAM.ADEX
Run Date: 2025-05-14T14:46:13
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ravuema202501/Files/listings/production/programs/l15_patinfo.sas

Listing 15
Patient Information and Treatment Information
Frequent Treatment Switchers

Patient Number: 1268-201
Enrollment Date: 30JAN2018
Age at First Treatment Initiation: 20.6

Treatment	Initiation Date	Discontinuation Date	Reason for Treatment Discontinuation
ECU	30JAN2018	18AUG2021	
RVU	18AUG2021	23AUG2021	
ECU	23AUG2021	01SEP2021	Switch to ravulizumab IV
RVU	01SEP2021	04JUL2024	Switch to eculizumab IV

Source: ADAM.ADSL, ADAM.ADPOP, ADAM.ADEX2, ADAM.ADEX
Run Date: 2025-05-14T14:46:13
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ravuema202501/Files/listings/production/programs/l15_patinfo.sas

Listing 15
Patient Information and Treatment Information
Frequent Treatment Switchers

Patient Number: 1275-003
Enrollment Date: 29JAN2011
Age at First Treatment Initiation: 59.7

Treatment	Initiation Date	Discontinuation Date	Reason for Treatment Discontinuation
ECU	26MAR2007	31OCT2022	
RVU	31OCT2022	03JUL2023	Switch to eculizumab IV
ECU	03JUL2023	18SEP2023	
OAC	18SEP2023	01FEB2024	
ECU	01FEB2024	01MAR2024	Switch to ravulizumab IV

Listing 15
Patient Information and Treatment Information
Frequent Treatment Switchers

Patient Number: 1275-005
Enrollment Date: 25APR2019
Age at First Treatment Initiation: 28.9

Treatment	Initiation Date	Discontinuation Date	Reason for Treatment Discontinuation
ECU	20MAY2019	15NOV2022	
RVU	15NOV2022	21MAR2023	Switch to eculizumab IV
ECU	21MAR2023	23FEB2024	Switch to ravulizumab IV

Listing 15
Patient Information and Treatment Information
Frequent Treatment Switchers

Patient Number: 1381-005
Enrollment Date: 20AUG2012
Age at First Treatment Initiation: 41.9

Treatment	Initiation Date	Discontinuation Date	Reason for Treatment Discontinuation
ECU	08MAY2018	07MAY2019	
RVU	07MAY2019	06NOV2020	
ECU	06NOV2020	04DEC2020	Switch to other anti-complement treatment

Listing 15
Patient Information and Treatment Information
Frequent Treatment Switchers

Patient Number: 1381-010
Enrollment Date: 09DEC2016
Age at First Treatment Initiation: 21.9

Treatment	Initiation Date	Discontinuation Date	Reason for Treatment Discontinuation
ECU	26MAY2016	11JAN2019	
RVU	11JAN2019	10JAN2020	
ECU	10JAN2020	23JUL2020	Physician decision
RVU	23JUL2020	07SEP2020	Switch to eculizumab IV

Listing 15
Patient Information and Treatment Information
Frequent Treatment Switchers

Patient Number: 1454-003
Enrollment Date: 18MAR2013
Age at First Treatment Initiation: 44.7

Treatment	Initiation Date	Discontinuation Date	Reason for Treatment Discontinuation
ECU	05MAR2008	21FEB2022	
RVU	21FEB2022	29JUN2022	Switch to eculizumab IV
ECU	29JUN2022	29FEB2024	Switch to ravulizumab IV

Source: ADAM.ADSL, ADAM.ADPOP, ADAM.ADEX2, ADAM.ADEX
Run Date: 2025-05-14T14:46:13
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ravuema202501/Files/listings/production/programs/l15_patinfo.sas

Listing 15
Patient Information and Treatment Information
Frequent Treatment Switchers

Patient Number: 1462-005
Enrollment Date: 30NOV2012
Age at First Treatment Initiation: 35.5

Treatment	Initiation Date	Discontinuation Date	Reason for Treatment Discontinuation
ECU	22DEC2010	06DEC2019	
RVU	06DEC2019	15FEB2023	
ECU	15FEB2023	03MAR2023	Switch to ravulizumab IV
RVU	03MAR2023	08FEB2024	Physician decision

Listing 15
Patient Information and Treatment Information
Frequent Treatment Switchers

Patient Number: 1462-007
Enrollment Date: 07DEC2012
Age at First Treatment Initiation: 61.5

Treatment	Initiation Date	Discontinuation Date	Reason for Treatment Discontinuation
ECU	12JAN2011	08NOV2019	
RVU	08NOV2019	29SEP2023	Physician decision
ECU	29SEP2023	12JAN2024	Switch to ravulizumab IV
OAC	12JAN2024	08FEB2024	

Source: ADAM.ADSL, ADAM.ADPOP, ADAM.ADEX2, ADAM.ADEX
Run Date: 2025-05-14T14:46:13
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ravuema202501/Files/listings/production/programs/l15_patinfo.sas

Listing 15
Patient Information and Treatment Information
Frequent Treatment Switchers

Patient Number: 1508-001
Enrollment Date: 18JUN2013
Age at First Treatment Initiation: 29.7

Treatment	Initiation Date	Discontinuation Date	Reason for Treatment Discontinuation
ECU	29MAR2011	19NOV2019	
RVU	19NOV2019	12FEB2021	Physician decision
ECU	12FEB2021	12APR2022	Physician decision

Listing 15
Patient Information and Treatment Information
Frequent Treatment Switchers

Patient Number: 1610-006
Enrollment Date: 27NOV2019
Age at First Treatment Initiation: 54.5

Treatment	Initiation Date	Discontinuation Date	Reason for Treatment Discontinuation
ECU	16DEC2019	22OCT2020	
RVU	22OCT2020	11FEB2021	Adverse Event
ECU	21JUN2023	19JUL2023	Switch to other anti-complement treatment
OAC	05SEP2023	05SEP2023	

Listing 15
Patient Information and Treatment Information
Frequent Treatment Switchers

Patient Number: 1743-007
Enrollment Date: 19JAN2016
Age at First Treatment Initiation: 39.1

Treatment	Initiation Date	Discontinuation Date	Reason for Treatment Discontinuation
ECU	15AUG2011	01JAN2023	
RVU	01JAN2023	15FEB2024	Adverse Event
ECU	15FEB2024	14MAY2024	Switch to ravulizumab IV

Listing 16
All Serious Adverse Events and Special Events
Frequent Treatment Switchers

Patient Number	Status	Treatment Status[a]	Adverse Event Term	Serious Event (Yes/No)	Serious Event Category	Special Event (Yes/No)	Special Event Type	Start Date	End Date	Outcome
1013-039	Active		influenca B Virus infection	Y	Hospitalization	No		28FEB2020	24MAR2020	Recovered/ Resolved
1013-060	Discontinued		fever, viral infection	Y	Hospitalization	No		04JAN2020	13JAN2020	Recovered/ Resolved
1013-107	Discontinued		Hemolysis	Y	Hospitalization	No		09OCT2017	14OCT2017	Recovered/ Resolved
			bone marrow failure	Y	Death	No		15NOV2023	12JAN2024	Fatal
1013-184	Active		Caesarean section due to child birth	Y	Hospitalization	No		24MAY2021	28MAY2021	Recovered/ Resolved
1039-008			Encephalitis	Y	Hospitalization	No		21MAY2019	24MAY2019	Recovered/ Resolved
			Seizures	Y	Hospitalization	No		28MAY2019	31MAY2019	Recovered/ Resolved
			Severe sepsis with acute organ dysfunction due to Neisseria meningitis	Y	Death	No		27MAY2020	29MAY2020	Fatal

Note:
(a) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.

Source: ADAM.ADSL, ADAM.ADPOP, ADAM.ADAE, CONV.ALL_SITES
Run Date: 2025-05-14T14:46:14
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ravuema202501/Files/listings/production/programs/l16_sae_fswitch.sas

Listing 16
All Serious Adverse Events and Special Events
Frequent Treatment Switchers

Patient Number	Status	Treatment Status[a]	Adverse Event Term	Serious Event (Yes/No)	Serious Event Category	Special Event (Yes/No)	Special Event Type	Start Date	End Date	Outcome
1093-106			Multiple bone or spinal metastases in prostate cancer (Dec/2020) / See above # 5	N		No		26APR2022		Not Recovered/ Not Resolved
			abscess lower leg left	Y	Hospitalization	No		22SEP2022		Recovering /Resolving
			febrile infection	N		No				Recovered/ Resolved
			prostate adenocarcinoma	N		No		09DEC2020		Not Recovered/ Not Resolved
			respiratory tract infection	N		No				Recovered/ Resolved
			sanguineous urine	N		No				Recovered/ Resolved
			sinusitis	N		No				Recovered/ Resolved
			soft tissue infection left lower leg	Y	Hospitalization	No		22SEP2022		Recovering /Resolving

Note:
(a) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.

Source: ADAM.ADSL, ADAM.ADPOP, ADAM.ADAE, CONV.ALL_SITES
Run Date: 2025-05-14T14:46:14
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ravuema202501/Files/listings/production/programs/l16_sae_fswitch.sas

Listing 16
All Serious Adverse Events and Special Events
Frequent Treatment Switchers

Patient Number	Status	Treatment Status[a]	Adverse Event Term	Serious Event (Yes/No)	Serious Event Category	Special Event (Yes/No)	Special Event Type	Start Date	End Date	Outcome
1093-134			Leocozytosis du to prednisolon intake	N		No		15JAN2020		Not Recovered/ Not Resolved
			Vitamin B 12 deficiency	N		No		15JAN2020		Not Recovered/ Not Resolved
			abdominal pain	Y	Hospitalization	No		27MAR2018	06APR2018	Recovered/ Resolved
			frontotemporale Cephalien with eye pain	Y	Hospitalization	No		27MAR2018	06APR2018	Recovered/ Resolved
			preileus	Y	Hospitalization	No		09MAR2019	12MAR2019	Unknown
1093-283			Corona Virus Infection	N		No				Recovered/ Resolved

Note:
(a) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.

Source: ADAM.ADSL, ADAM.ADPOP, ADAM.ADAE, CONV.ALL_SITES
Run Date: 2025-05-14T14:46:14
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ravuema202501/Files/listings/production/programs/l16_sae_fswitch.sas

Listing 16
All Serious Adverse Events and Special Events
Frequent Treatment Switchers

Patient Number	Status	Treatment Status[a]	Adverse Event Term	Serious Event (Yes/No)	Serious Event Category	Special Event (Yes/No)	Special Event Type	Start Date	End Date	Outcome
1275-003			Alteration of general condition	Y	Hospitalization	No		07OCT2019	10OCT2019	Recovered/ Resolved with Sequelae
			Anemia	Y	Hospitalization	No		07OCT2019	10OCT2019	Recovered/ Resolved
			Health deterioration	Y	Hospitalization	No		11DEC2023	28DEC2023	Recovered/ Resolved
			arthritis	Y	Hospitalization	No		17NOV2022	29NOV2022	Recovered/ Resolved
			fever	Y	Hospitalization	No		25JAN2018	30JAN2018	Recovered/ Resolved
			fever (39°C)	Y	Hospitalization	No		07OCT2019	08OCT2019	Recovered/ Resolved

Note:
(a) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.

Source: ADAM.ADSL, ADAM.ADPOP, ADAM.ADAE, CONV.ALL_SITES
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Listing 16
All Serious Adverse Events and Special Events
Frequent Treatment Switchers

Patient Number	Status	Treatment Status[a]	Adverse Event Term	Serious Event (Yes/No)	Serious Event Category	Special Event (Yes/No)	Special Event Type	Start Date	End Date	Outcome
1381-005			COVID-19 pneumonia	Y	Hospitalization	No		25OCT2020		Not Recovered/ Not Resolved
			Cough	N		No				Recovering /Resolving
			Headache	N		No		17MAY2019		Not Recovered/ Not Resolved
			Lethargy	N		No				Not Recovered/ Not Resolved
			Shingles	N		No		05OCT2020		Recovering /Resolving
			Tinnitus	N		No		08MAY2018		Not Recovered/ Not Resolved
			palpitations	N		No		30DEC2019	30DEC2019	Recovered/ Resolved
			relapsed idiopathic thrombocytopenic purpura	Y	Hospitalization	No		26OCT2020		Not Recovered/ Not Resolved
			rupture of ovarian cyst	Y	Hospitalization	No		31JAN2018	01FEB2018	Recovered/ Resolved

Note:
(a) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.

Source: ADAM.ADSL, ADAM.ADPOP, ADAM.ADAE, CONV.ALL_SITES
Run Date: 2025-05-14T14:46:14
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ravuema202501/Files/listings/production/programs/l16_sae_fswitch.sas

Listing 16
All Serious Adverse Events and Special Events
Frequent Treatment Switchers

Patient Number	Status	Treatment Status[a]	Adverse Event Term	Serious Event (Yes/No)	Serious Event Category	Special Event (Yes/No)	Special Event Type	Start Date	End Date	Outcome
1381-010			AV fistula	Y	Hospitalization	No		28MAR2018	28MAR2018	Unknown
			Abdominal pain	Y	Hospitalization	No		30JAN2020	31JAN2020	Recovered/ Resolved
			Acute on chronic renal failure	Y	Hospitalization	No		31JAN2018	22FEB2018	Recovered/ Resolved
			Anemia	Y	Hospitalization	No		11DEC2019	20DEC2019	Recovered/ Resolved
								31OCT2019	02NOV2019	Recovered/ Resolved
			Bacteremia	Y	Hospitalization	No		05MAY2018	26MAY2018	Recovered/ Resolved
			Bleeding	Y	Hospitalization	No		29DEC2017	03JAN2018	Recovered/ Resolved
			CHF exacerbation	Y	Hospitalization	No		02JUL2019	27JUL2019	Recovered/ Resolved
			Chronic renal failure requiring dialysis	Y	Hospitalization	No		28MAR2018	29MAR2018	Recovered/ Resolved
			Death- unknown cause	Y	Death	No		07SEP2020	07SEP2020	Fatal
			Diarrhea	Y	Hospitalization	No		28NOV2017	30NOV2017	Recovered/ Resolved
			End stage renal disease	Y	Hospitalization	No		06SEP2019	29OCT2019	Recovered/ Resolved with Sequelae
			Enterococcus Meningitis	Y	Hospitalization	No		07OCT2017	22NOV2017	Recovered/ Resolved

Note:
(a) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.

Source: ADAM.ADSL, ADAM.ADPOP, ADAM.ADAE, CONV.ALL_SITES
Run Date: 2025-05-14T14:46:14
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ravuema202501/Files/listings/production/programs/l16_sae_fswitch.sas

Listing 16
All Serious Adverse Events and Special Events
Frequent Treatment Switchers

Patient Number	Status	Treatment Status[a]	Adverse Event Term	Serious Event (Yes/No)	Serious Event Category	Special Event (Yes/No)	Special Event Type	Start Date	End Date	Outcome
			Epistaxis	Y	Hospitalization	No		08JUN2019	11JUN2019	Recovered/ Resolved
			Fatigue secondary to deconditioning	Y	Significant Disability;Hospitalization	No		06MAY2017	09MAY2017	Recovered/ Resolved
			Fungal peritonitis	Y	Hospitalization	No		01APR2020	08APR2020	Recovered/ Resolved
			Fungemia	Y	Hospitalization	No		01APR2020	08APR2020	Recovered/ Resolved
			Green diarrhea	Y	Hospitalization	No		06MAY2017	09MAY2017	Recovered/ Resolved with Sequelae
			Hyperkalemia	Y	Hospitalization	No		02JUL2019	27JUL2019	Recovered/ Resolved
			Hypertension	Y	Hospitalization	No		31OCT2019	02NOV2019	Recovered/ Resolved
			Hypervolemia	Y	Hospitalization	No		01SEP2017	11SEP2017	Recovered/ Resolved
								08JAN2020	13JAN2020	Recovered/ Resolved
								19JAN2020	24JAN2020	Recovered/ Resolved
								19SEP2017	04OCT2017	Recovered/ Resolved
			Hypokalemia	Y	Hospitalization	No		11DEC2019	20DEC2019	Recovered/ Resolved

Note:
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Frequent Treatment Switchers

Patient Number	Status	Treatment Status[a]	Adverse Event Term	Serious Event (Yes/No)	Serious Event Category	Special Event (Yes/No)	Special Event Type	Start Date	End Date	Outcome
			Hyponatremia	Y	Hospitalization	No		24DEC2016	01JAN2017	Recovered/ Resolved
			MRSA bacteremia	Y	Hospitalization	No		27MAY2020	31MAY2020	Recovered/ Resolved
			MSSA bacteremia	Y	Hospitalization	No		15MAR2018	24MAR2018	Recovered/ Resolved
			Methicillin resistant staph aureas bacteremia	Y	Hospitalization	No		13APR2017	04MAY2017	Recovered/ Resolved
			Nephrotic syndrome	Y	Hospitalization	No		07OCT2017	22NOV2017	Recovered/ Resolved
			Nephrotic syndrome secondary to minimal change disease	Y	Hospitalization	No		13APR2017	04MAY2017	Recovered/ Resolved
			PNH flare	Y	Hospitalization	No		07OCT2017	22NOV2017	Recovered/ Resolved
			Parainfluenza pneumonia	Y	Hospitalization	No		16DEC2017	20DEC2017	Recovered/ Resolved
			Parvovirus B19 test positive	Y	Hospitalization	No		29APR2017	04MAY2017	Recovered/ Resolved
			Peritonitis	Y	Hospitalization;Other	No		06SEP2019	29OCT2019	Recovered/ Resolved
			Pneumonia	Y	Hospitalization	No		07OCT2017	22NOV2017	Recovered/ Resolved
								08FEB2020	04MAR2020	Recovered/ Resolved

Note:
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Listing 16
All Serious Adverse Events and Special Events
Frequent Treatment Switchers

Patient Number	Status	Treatment Status[a]	Adverse Event Term	Serious Event (Yes/No)	Serious Event Category	Special Event (Yes/No)	Special Event Type	Start Date	End Date	Outcome
								18AUG2017	24AUG2017	Recovered/ Resolved
			Pseudomonas bacteremia	Y	Hospitalization	No		06MAY2019	19MAY2019	Recovered/ Resolved
			Sepsis	Y	Hospitalization	No		08FEB2020	04MAR2020	Recovered/ Resolved
								30MAY2019	07JUN2019	Recovered/ Resolved
			Septic cardiomyopathy	Y	Hospitalization	No		15MAR2018	24MAR2018	Recovered/ Resolved
			Sinusitis	Y	Hospitalization	No		29DEC2017	03JAN2018	Recovered/ Resolved
			Strep pneumonia	Y	Hospitalization	No		16DEC2017	20DEC2017	Recovered/ Resolved
			Uremia	Y	Hospitalization	No		31OCT2019	02NOV2019	Recovered/ Resolved
			abdominal pain	Y	Hospitalization	No		06MAY2017	09MAY2017	Recovered/ Resolved with Sequelae
								27JUN2018	29JUN2018	Recovered/ Resolved
			acute CVA	Y	Hospitalization	No		06SEP2019	29OCT2019	Recovered/ Resolved with Sequelae
			acute blood loss (epistaxis)	Y	Hospitalization	No		01JUN2018	07JUN2018	Recovered/ Resolved

Note:
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Listing 16
All Serious Adverse Events and Special Events
Frequent Treatment Switchers

Patient Number	Status	Treatment Status[a]	Adverse Event Term	Serious Event (Yes/No)	Serious Event Category	Special Event (Yes/No)	Special Event Type	Start Date	End Date	Outcome
			acute kidney injury	Y	Hospitalization	No		06MAY2017	09MAY2017	Recovered/ Resolved with Sequelae
			acute liver failure	Y	Hospitalization	No		02JUL2019	27JUL2019	Recovered/ Resolved
			acute renal failure	Y	Hospitalization	No		07OCT2017	22NOV2017	Recovered/ Resolved
			anion gap metabolic acidosis	Y	Hospitalization	No		31OCT2019	02NOV2019	Recovered/ Resolved
			atypical chest pain	N		No		26MAR2018	26MAR2018	Recovered/ Resolved
			bleeding from Tunneled Dialysis Catheter	Y	Hospitalization	No		27MAY2020	31MAY2020	Recovered/ Resolved
			calf calciphylaxis	Y	Other	No		08FEB2020	04MAR2020	Recovered/ Resolved
			cellulitis	Y	Hospitalization	No		01MAY2020	03MAY2020	Recovered/ Resolved
								22NOV2019	30NOV2019	Recovered/ Resolved
			chest pain	N		No		27MAR2018	27MAR2018	Recovered/ Resolved
								31MAR2018	31MAR2018	Recovered/ Resolved
			chest wall pain	N		No		13MAR2018	13MAR2018	Recovered/ Resolved

Note:
(a) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.

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All Serious Adverse Events and Special Events
Frequent Treatment Switchers

Patient Number	Status	Treatment Status[a]	Adverse Event Term	Serious Event (Yes/No)	Serious Event Category	Special Event (Yes/No)	Special Event Type	Start Date	End Date	Outcome
			chronic pain	Y	Hospitalization	No		11DEC2019	20DEC2019	Recovered/ Resolved
			complication associated with device	Y	Hospitalization	No		24APR2018	27APR2018	Recovered/ Resolved
			electrolyte imbalance	Y	Hospitalization	No		27DEC2019	02JAN2020	Recovered/ Resolved
			elevated liver enzymes	Y	Hospitalization	No		11DEC2019	20DEC2019	Recovered/ Resolved
			epistaxis	N		No		06SEP2019	29OCT2019	Recovered/ Resolved
				Y	Hospitalization	No		30MAY2019	07JUN2019	Recovered/ Resolved
								31OCT2019	02NOV2019	Recovered/ Resolved
			generalized weakness	Y	Hospitalization	No		06NOV2018	10NOV2018	Recovered/ Resolved
								11JUL2018	24JUL2018	Recovered/ Resolved
			headache	N		No		31MAR2018	31MAR2018	Recovered/ Resolved
			hyperkalemia	Y	Hospitalization	No		31OCT2019	02NOV2019	Recovered/ Resolved
			hypervolemia	Y	Hospitalization	No		07MAR2018	13MAR2018	Recovered/ Resolved
								24FEB2018	27FEB2018	Recovered/ Resolved

Note:
(a) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.

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All Serious Adverse Events and Special Events
Frequent Treatment Switchers

Patient Number	Status	Treatment Status[a]	Adverse Event Term	Serious Event (Yes/No)	Serious Event Category	Special Event (Yes/No)	Special Event Type	Start Date	End Date	Outcome
			hypokalemia	Y	Hospitalization	No		07OCT2017	22NOV2017	Recovered/ Resolved
					Life-Threatening; Hospitalization	No		06SEP2019	08SEP2019	Recovered/ Resolved
			hypomagnesemia	Y	Hospitalization	No		07OCT2017	22NOV2017	Recovered/ Resolved
			hyponatremia	Y	Hospitalization	No		31OCT2019	02NOV2019	Recovered/ Resolved
			leukocytosis	Y	Hospitalization	No		06MAY2017	09MAY2017	Recovered/ Resolved with Sequelae
								31OCT2019	02NOV2019	Recovered/ Resolved
			malfunctioning hemodialysis catheter	Y	Hospitalization	No		01APR2020	08APR2020	Recovered/ Resolved
			metabolic acidosis	Y	Hospitalization	No		11DEC2019	20DEC2019	Recovered/ Resolved
			musculoskeletal neck pain	Y	Hospitalization	No		06MAY2017	09MAY2017	Recovered/ Resolved
			myocardial infarction	Y	Hospitalization	No		06SEP2019	29OCT2019	Recovered/ Resolved with Sequelae
			nose Bleeding	Y	Hospitalization	No		26DEC2017	29DEC2017	Recovered/ Resolved

Note:
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Frequent Treatment Switchers

Patient Number	Status	Treatment Status[a]	Adverse Event Term	Serious Event (Yes/No)	Serious Event Category	Special Event (Yes/No)	Special Event Type	Start Date	End Date	Outcome
			peritonitis	Y	Hospitalization	No		11JUL2018	24JUL2018	Recovered/ Resolved
			pneumonia	Y	Hospitalization	No		02JUL2019	27JUL2019	Recovered/ Resolved
								24FEB2018	27FEB2018	Recovered/ Resolved
			poorly functioning tunneled dialysis catheter	Y	Significant Disability	No		24APR2018		Not Recovered/ Not Resolved
			presyncope	Y	Hospitalization	No		03NOV2018	04NOV2018	Recovered/ Resolved
			protein calorie malnutrition	Y	Hospitalization	No		31OCT2019	02NOV2019	Recovered/ Resolved
			recurrent mechanical epistaxis	Y	Hospitalization	No		11DEC2019	20DEC2019	Recovered/ Resolved
			right atrial thrombus	Y	Hospitalization	No		23AUG2018	31AUG2018	Recovered/ Resolved
			right leg cellulitis	Y	Hospitalization	No		06APR2019	17APR2019	Recovered/ Resolved
			sepsis due to staph bacteremia	Y	Hospitalization	No		11SEP2018	19SEP2018	Recovered/ Resolved
			spongiotic dermitis	N		No		07FEB2018	13MAR2018	Recovered/ Resolved
			thrombocytopenia	Y	Hospitalization	No		31OCT2019	02NOV2019	Recovered/ Resolved

Note:
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All Serious Adverse Events and Special Events
Frequent Treatment Switchers

Patient Number	Status	Treatment Status[a]	Adverse Event Term	Serious Event (Yes/No)	Serious Event Category	Special Event (Yes/No)	Special Event Type	Start Date	End Date	Outcome
1454-003			colon cancer	Y	Hospitalization	No		09MAY2022	24JUL2022	Recovered/ Resolved
1462-005			appendicitis	Y	Hospitalization	No		06FEB2023	23FEB2023	Recovered/ Resolved
			gallstones (Stand by laparoscopic cholecystectomy)	Y	Hospitalization	No		12SEP2023	15SEP2023	Recovered/ Resolved
1462-007			Anemia	Y	Hospitalization	No		21AUG2020		Recovering /Resolving
			Cellulitis of left leg	Y	Hospitalization	No		09OCT2018	20OCT2018	Recovered/ Resolved
								15AUG2018	19AUG2018	Recovered/ Resolved
			Epicarditis	Y	Hospitalization	No		27FEB2019	04MAR2019	Recovered/ Resolved
			Fever	Y	Hospitalization	No		06SEP2019	14SEP2019	Recovered/ Resolved
			Pericardial effusion	Y	Hospitalization	No		18JUN2020	06JUL2020	Recovered/ Resolved
			hypothyroidism	Y	Hospitalization	No		26MAR2021		Recovering /Resolving

Note:
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Frequent Treatment Switchers

Patient Number	Status	Treatment Status[a]	Adverse Event Term	Serious Event (Yes/No)	Serious Event Category	Special Event (Yes/No)	Special Event Type	Start Date	End Date	Outcome
1462-007			Pericardial effusion	Y	Hospitalization	No		27OCT2021		Recovering /Resolving
			Renal function worsening	Y	Hospitalization	No		15AUG2022	20AUG2022	Recovered/ Resolved
			angina pectoris	Y	Hospitalization	No		12JAN2022		Recovering /Resolving
			cellulitis	Y	Hospitalization	No		15MAR2023	30MAR2023	Recovered/ Resolved
			coronary angiography for diagnosis and evaluation of exertional angina	Y	Hospitalization	No		17JAN2022	12FEB2022	Recovered/ Resolved
			percutaneous coronary intervention for the treatment of exertional angina	Y	Hospitalization	No		07FEB2022	12FEB2022	Recovered/ Resolved
			pericarditis	Y	Hospitalization	No		01NOV2021		Recovering /Resolving
1508-001			MDS	Y	Other	No		27APR2021		Not Recovered/ Not Resolved

Note:
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Table 1
Study Population
IPIG PNH Registry

	N
Patients ever enrolled in IPIG PNH Registry as of 13JAN2025	123
IPIG PNH Registry patients also present in Alexion PNH Registry[a]	81
Ravulizumab Study Population[b]	62
Alexion PNH Registry Study Population[d]	56
Prior eculizumab treatment[c]	46
Without prior eculizumab treatment	9
Prior eculizumab treatment unknown	1
IPIG PNH Registry Study Population[e]	6
Prior eculizumab treatment[c]	1
Without prior eculizumab treatment	5
Prior eculizumab treatment unknown	0
Frequent treatment switchers[f]	0

Notes: (a) Based on matching participant IDs provided in both Registries. (b) If the participant was enrolled in the Alexion PNH Registry and initiated ravulizumab in the Alexion PNH Registry, then the information regarding enrollment date and ravulizumab initiation date is based on the Alexion PNH Registry data. Otherwise, if ravulizumab is initiated in the IPIG PNH Registry, then information is based on the IPIG PNH Registry data.
(c) Prior eculizumab treatment indicates that eculizumab was discontinued within 28 days of ravulizumab initiation. Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation. Participants were classified into the Prior Eculizumab Treatment Unknown group due to unknown prior eculizumab treatment history or because of a missing eculizumab discontinuation date.
(d) Participants enrolled in the Alexion PNH Registry and initiated ravulizumab in the Alexion PNH Registry on or after enrollment. (e) Participants who initiated ravulizumab on or after enrollment in the IPIG PNH irrespective of their participation in the Alexion PNH Registry. (f) Frequent treatment switchers refer to patients who switched between eculizumab and ravulizumab treatment more than once in either of the registries. These patients will not be included in the analysis.

Source: ADAM.ADSLI
Run Date: 2025-05-13T15:40:33
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Table 2
Patient Demographics, by Treatment Status
IPIG PNH Registry Study Population

	All Ravulizumab Patients[b] (N=6)	Prior Eculizumab Treatment[c] (N=1)	Without Prior Eculizumab Treatment[d] (N=5)	Prior Eculizumab Treatment Unknown (N=0)
Gender, n (%)				
n	6	1	5	0
Male	3 (50.0)	0 (0.0)	3 (60.0)	0 (0.0)
Female	3 (50.0)	1 (100.0)	2 (40.0)	0 (0.0)
Ethnicity, n (%)				
n	6	1	5	0
Not Hispanic or Latino	5 (83.3)	0 (0.0)	5 (100.0)	0 (0.0)
Unknown	1 (16.7)	1 (100.0)	0 (0.0)	0 (0.0)
Race, n (%)				
n	6	1	5	0
White	4 (66.7)	0 (0.0)	4 (80.0)	0 (0.0)
Asian	1 (16.7)	0 (0.0)	1 (20.0)	0 (0.0)
Not known	1 (16.7)	1 (100.0)	0 (0.0)	0 (0.0)
Age at enrollment (years)				

Notes: Q1 = first quartile; Q3 = third quartile; SD = standard deviation.
(a) PNH disease start is defined as the earliest date among date of PNH diagnosis, date of first PNH symptom, and date of first detected PNH clone.
(b) Patients were classified into the Prior Eculizumab Treatment Unknown group due to unknown prior eculizumab treatment history or because of a missing eculizumab discontinuation date.
(c) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation.
(d) Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.

Source: ADAM.ADSLI
Run Date: 2025-05-13T15:40:34
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Table 2
Patient Demographics, by Treatment Status
IPIG PNH Registry Study Population

	All Ravulizumab Patients[b] (N=6)	Prior Eculizumab Treatment[c] (N=1)	Without Prior Eculizumab Treatment[d] (N=5)	Prior Eculizumab Treatment Unknown (N=0)
n	6	1	5	0
Mean (SD)	48.3 (19.93)	32.0 (---)	51.6 (20.40)	-- (---)
Median (Q1, Q3)	39.5 (32.0, 70.0)	32.0 (32.0, 32.0)	41.0 (38.0, 70.0)	-- (--, --)
Age group at enrollment, n (%)				
n	6	1	5	0
<2 years	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
2 to <12 years	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
12 to <18 years	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
18 to <30 years	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
30 to <50 years	4 (66.7)	1 (100.0)	3 (60.0)	0 (0.0)
50 to <65 years	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
65+ years	2 (33.3)	0 (0.0)	2 (40.0)	0 (0.0)
Age at PNH disease start (years)[a]				
n	6	1	5	0

Notes: Q1 = first quartile; Q3 = third quartile; SD = standard deviation.
(a) PNH disease start is defined as the earliest date among date of PNH diagnosis, date of first PNH symptom, and date of first detected PNH clone.
(b) Patients were classified into the Prior Eculizumab Treatment Unknown group due to unknown prior eculizumab treatment history or because of a missing eculizumab discontinuation date.
(c) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation.
(d) Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.

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Table 2
Patient Demographics, by Treatment Status
IPIG PNH Registry Study Population

	All Ravulizumab Patients[b] (N=6)	Prior Eculizumab Treatment[c] (N=1)	Without Prior Eculizumab Treatment[d] (N=5)	Prior Eculizumab Treatment Unknown (N=0)
Mean (SD)	44.7 (23.42)	14.0 (---)	50.8 (20.09)	-- (---)
Median (Q1, Q3)	38.5 (32.0, 70.0)	14.0 (14.0, 14.0)	40.0 (37.0, 70.0)	-- (--, --)
Age group at PNH disease start, n (%)				
n	6	1	5	0
<2 years	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
2 to <12 years	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
12 to <18 years	1 (16.7)	1 (100.0)	0 (0.0)	0 (0.0)
18 to <30 years	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
30 to <50 years	3 (50.0)	0 (0.0)	3 (60.0)	0 (0.0)
50 to <65 years	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
65+ years	2 (33.3)	0 (0.0)	2 (40.0)	0 (0.0)
Years from PNH disease start to enrollment				
n	6	1	5	0
Mean (SD)	3.9 (7.42)	19.0 (---)	0.9 (0.65)	-- (---)

Notes: Q1 = first quartile; Q3 = third quartile; SD = standard deviation.
(a) PNH disease start is defined as the earliest date among date of PNH diagnosis, date of first PNH symptom, and date of first detected PNH clone.
(b) Patients were classified into the Prior Eculizumab Treatment Unknown group due to unknown prior eculizumab treatment history or because of a missing eculizumab discontinuation date.
(c) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation.
(d) Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.

Source: ADAM.ADSLI
Run Date: 2025-05-13T15:40:34
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ipig/Files/tables/production/programs/t2_demo_i.sas

Table 2
Patient Demographics, by Treatment Status
IPIG PNH Registry Study Population

	All Ravulizumab Patients[b] (N=6)	Prior Eculizumab Treatment[c] (N=1)	Without Prior Eculizumab Treatment[d] (N=5)	Prior Eculizumab Treatment Unknown (N=0)
Median (Q1, Q3)	1.1 (0.3, 1.8)	19.0 (19.0, 19.0)	1.1 (0.3, 1.1)	-- (--, --)
Years from PNH disease start to ravulizumab initiation				
n	6	1	5	0
Mean (SD)	4.0 (7.42)	19.1 (---)	1.0 (0.60)	-- (---)
Median (Q1, Q3)	1.1 (0.5, 1.8)	19.1 (19.1, 19.1)	1.1 (0.5, 1.1)	-- (--, --)
Age at ravulizumab initiation (years)				
n	6	1	5	0
Mean (SD)	48.5 (19.77)	33.0 (---)	51.6 (20.40)	-- (---)
Median (Q1, Q3)	39.5 (33.0, 70.0)	33.0 (33.0, 33.0)	41.0 (38.0, 70.0)	-- (--, --)
Age group at ravulizumab initiation, n (%)				
n	6	1	5	0
<2 years	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
2 to <12 years	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

Notes: Q1 = first quartile; Q3 = third quartile; SD = standard deviation.
(a) PNH disease start is defined as the earliest date among date of PNH diagnosis, date of first PNH symptom, and date of first detected PNH clone.
(b) Patients were classified into the Prior Eculizumab Treatment Unknown group due to unknown prior eculizumab treatment history or because of a missing eculizumab discontinuation date.
(c) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation.
(d) Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.

Source: ADAM.ADSLI
Run Date: 2025-05-13T15:40:34
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ipig/Files/tables/production/programs/t2_demo_i.sas

Table 2
Patient Demographics, by Treatment Status
IPIG PNH Registry Study Population

	All Ravulizumab Patients[b] (N=6)	Prior Eculizumab Treatment[c] (N=1)	Without Prior Eculizumab Treatment[d] (N=5)	Prior Eculizumab Treatment Unknown (N=0)
12 to <18 years	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
18 to <30 years	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
30 to <50 years	4 (66.7)	1 (100.0)	3 (60.0)	0 (0.0)
50 to <65 years	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
65+ years	2 (33.3)	0 (0.0)	2 (40.0)	0 (0.0)

Notes: Q1 = first quartile; Q3 = third quartile; SD = standard deviation.
(a) PNH disease start is defined as the earliest date among date of PNH diagnosis, date of first PNH symptom, and date of first detected PNH clone.
(b) Patients were classified into the Prior Eculizumab Treatment Unknown group due to unknown prior eculizumab treatment history or because of a missing eculizumab discontinuation date.
(c) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation.
(d) Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.

Source: ADAM.ADSLI
Run Date: 2025-05-13T15:40:34
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ipig/Files/tables/production/programs/t2_demo_i.sas

Table 3
Patient Disposition at Last Registry Follow-Up Date, by Treatment Status
Ravulizumab Study Population

	All Ravulizumab Patients[a] (N=62)	Prior Eculizumab Treatment[b] (N=47)	Without Prior Eculizumab Treatment[c] (N=14)	Prior Eculizumab Treatment Unknown (N=1)
Registry discontinuation, n (%)				
N	62	47	14	1
No	61 (98.4)	46 (97.9)	14 (100.0)	1 (100.0)
Yes	1 (1.6)	1 (2.1)	0 (0.0)	0 (0.0)
Reported reason for registry discontinuation, n (%)				
N	1	1	0	0
The patient (or legally authorized representative) requests discontinuation from the PNH registry for any reason	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Lost to follow-up	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Subject withdrawal of consent	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Death of patient	1 (100.0)	1 (100.0)	0 (0.0)	0 (0.0)
Bone marrow transplant	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Other reason	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

Notes:
(a) Patients were classified into the Prior Eculizumab Treatment Unknown group due to unknown prior eculizumab treatment history or because of a missing eculizumab discontinuation date.
(b) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation.
(c) Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.

Source: ADAM.ADSLI
Run Date: 2025-05-13T15:40:36
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ipig/Files/tables/production/programs/t3_disp_i.sas

Table 4
Ultomiris Treatment Discontinuation
Ravulizumab Study Population

	Treated with Ravulizumab (N=62)
Discontinuation of ravulizumab, n (%)	
n	62
No record of discontinuation	61 (98.4)
Discontinuation of ravulizumab	1 (1.6)
Toxicity	0 (0.0)
Patient decision	0 (0.0)
Physician decision	1 (100.0)
Intolerability	0 (0.0)
Cost/Access	0 (0.0)
Switch to another therapy	0 (0.0)
Lack of efficacy	0 (0.0)
Adverse event	0 (0.0)
Compliance issues	0 (0.0)
Death	0 (0.0)
Other	0 (0.0)

Table 5
Ultomiris Treatment Information
IPIG PNH Registry Study Population

	Treated with Ravulizumab (N=6)
Meningococcal vaccination prior to ravulizumab start, n (%)	
n	6
No	0 (0.0)
Yes	6 (100.0)
Weight (kg) at initiation of ravulizumab	
All patients, n	6
Mean (SD)	92.7 (36.71)
Median (Q1, Q3)	84.4 (69.0, 117.9)
< 40kg, n (%)	0 (0.0)
≥ 40kg, n (%)	6 (100.0)
First dose of ravulizumab, n	6
2400mg, n (%)	0 (0.0)
2700mg, n (%)	0 (0.0)
3000mg, n (%)	1 (16.7)
3300mg, n (%)	4 (66.7)
3600mg, n (%)	1 (16.7)
Other, n (%)	0 (0.0)
Subsequent doses of ravulizumab, n	0
All doses <3000mg/8 weeks, n (%)	0 (0.0)

Notes: Q1 = first quartile; Q3 = third quartile; SD = standard deviation.

Source: ADAM.ADSLI
Run Date: 2025-05-13T15:40:38
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ipig/Files/tables/production/programs/t5_ravuinfo_i.sas

Table 5
Ultomiris Treatment Information
IPIG PNH Registry Study Population

	Treated with Ravulizumab (N=6)
All doses ≥3000 to <3300mg/8 weeks, n (%)	0 (0.0)
All doses ≥3300 to <3600mg/8 weeks, n (%)	0 (0.0)
All doses =3600mg/8 weeks, n (%)	0 (0.0)
All doses >3600mg/8 weeks, n (%)	0 (0.0)
Other/Unknown, n (%)	0 (0.0)
Last dose of Ravulizumab, n	0
3000mg, n (%)	0 (0.0)
3300mg, n (%)	0 (0.0)
3600mg, n (%)	0 (0.0)
Other, n (%)	0 (0.0)

Notes: Q1 = first quartile; Q3 = third quartile; SD = standard deviation.

Source: ADAM.ADSLI
Run Date: 2025-05-13T15:40:38
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ipig/Files/tables/production/programs/t5_ravuinfo_i.sas

Table 6
Patient Durations of Follow-up, by Treatment Status
Ravulizumab Study Population

	All Ravulizumab Patients[a] (N=62)	Prior Eculizumab Treatment[b] (N=47)	Without Prior Eculizumab Treatment[c] (N=14)	Prior Eculizumab Treatment Unknown (N=1)
Years from IPIG PNH Registry enrollment to last registry follow-up				
n	62	47	14	1
Mean (SD)	0.4 (0.14)	0.4 (0.14)	0.5 (0.12)	0.3 (---)
Median (Min, Max)	0.4 (0.2, 0.7)	0.4 (0.2, 0.7)	0.4 (0.2, 0.6)	0.3 (0.3, 0.3)
Years of ravulizumab treatment follow-up				
n	62	47	14	1
Mean (SD)	2.8 (0.98)	3.1 (0.61)	1.9 (1.43)	2.7 (---)
Median (Min, Max)	3.2 (0.4, 5.5)	3.3 (0.6, 3.7)	1.9 (0.4, 5.5)	2.7 (2.7, 2.7)

Notes: SD = standard deviation.
(a) Patients were classified into the Prior Eculizumab Treatment Unknown group due to unknown prior eculizumab treatment history or because of a missing eculizumab discontinuation date.
(b) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation.
(c) Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.

Source: ADAM.ADSLI
Run Date: 2025-05-13T15:40:40
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ipig/Files/tables/production/programs/t6_dura_i.sas

Table 7
Vital Status at Last Registry Follow-Up Date, by Treatment Status
Ravulizumab Study Population

	All Ravulizumab Patients[a] (N=62)	Prior Eculizumab Treatment[b] (N=47)	Without Prior Eculizumab Treatment[c] (N=14)	Prior Eculizumab Treatment Unknown (N=1)
Vital status, n (%)				
N	62	47	14	1
Alive	61 (98.4)	46 (97.9)	14 (100.0)	1 (100.0)
Dead	1 (1.6)	1 (2.1)	0 (0.0)	0 (0.0)

Notes: The percentages are the percent of all death reported in the registry.
(a) Patients were classified into the Prior Eculizumab Treatment Unknown group due to unknown prior eculizumab treatment history or because of a missing eculizumab discontinuation date.
(b) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation.
(c) Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation.

Source: ADAM.ADSLI
Run Date: 2025-05-13T15:40:41
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ipig/Files/tables/production/programs/t7_death_i.sas

Table 8.1
Medical History at Ultomiris Initiation, by Treatment Status
IPIG PNH Registry Study Population

Verbatim Term	All Ravulizumab Patients[a] (N=6)	Prior Eculizumab Treatment (N=1)	Without Prior Eculizumab Treatment (N=5)	Prior Eculizumab Treatment Unknown (N=0)
APLASTIC OR HYPOPLASTIC ANEMIA	2 (33.3)	0 (0.0)	2 (40.0)	0 (0.0)
COVID	3 (50.0)	1 (100.0)	2 (40.0)	0 (0.0)

Note: (a) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation. Patients were classified into the Prior Eculizumab Treatment Unknown group due to unknown prior eculizumab treatment history or because of a missing eculizumab discontinuation date.

Source: ADAM.ADSLI, ADAM.ADMEI, ADAM.ADAEI, ADAM.ADCEI
Run Date: 2025-05-13T15:40:42
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ipig/Files/tables/production/programs/t8_1_medhis_i.sas

Table 8.2
Clinical and Adverse Events[a], by Treatment Status
Ravulizumab Study Population

Verbatim Term	All Ravulizumab Patients[b] (N=62)	Prior Eculizumab Treatment (N=50)	Without Prior Eculizumab Treatment (N=12)	Prior Eculizumab Treatment Unknown (N=0)
ACUTE CARDIAC FAILURE	1 (1.6)	1 (2.0)	0 (0.0)	0 (0.0)
PROSTATE CANCER	1 (1.6)	0 (0.0)	1 (8.3)	0 (0.0)
PYREXIA	1 (1.6)	1 (2.0)	0 (0.0)	0 (0.0)
WORSENING OF GALLSTONE DESEASE	1 (1.6)	1 (2.0)	0 (0.0)	0 (0.0)

Notes: (a) Includes clinical and adverse events occurring on or after ravulizumab initiation for participants who initiated ravulizumab in the IPIG PNH registry, as well as for participants who initiated ravulizumab in the Alexion PNH registry and experienced these events during their participation in the IPIG PNH registry.
(b) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation. Patients were classified into the Prior Eculizumab Treatment Unknown group due to unknown prior eculizumab treatment history or because of a missing eculizumab discontinuation date.

Source: ADAM.ADSLI, ADAM.ADMEI, ADAM.ADAEI, ADAM.ADCEI
Run Date: 2025-05-13T15:40:43
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ipig/Files/tables/production/programs/t8_2_ae_i.sas

Table 9
History of Concomitant Medication Use at Ultomiris Initiation, by Treatment Status
IPIG PNH Registry Study Population

Medication Category Medication Class Medication Name	All Ravulizumab Patients[a] (N=6)	Prior Eculizumab Treatment (N=1)	Without Prior Eculizumab Treatment (N=5)	Prior Eculizumab Treatment Unknown (N=0)
ANTI-COMPLEMENT THERAPY	1 (16.7)	1 (100.0)	0 (0.0)	0 (0.0)
UNKNOWN/MISSING MEDICATION CLASS	1 (16.7)	1 (100.0)	0 (0.0)	0 (0.0)
ECULIZUMAB	1 (16.7)	1 (100.0)	0 (0.0)	0 (0.0)
ANTIBIOTIC PROPHYLAXIS	1 (16.7)	1 (100.0)	0 (0.0)	0 (0.0)
UNKNOWN/MISSING MEDICATION CLASS	1 (16.7)	1 (100.0)	0 (0.0)	0 (0.0)
PENICILLIN	1 (16.7)	1 (100.0)	0 (0.0)	0 (0.0)
ANTICOAGULATION THERAPY	4 (66.7)	1 (100.0)	3 (60.0)	0 (0.0)
DIRECT FACTOR XA INHIBITORS	1 (16.7)	0 (0.0)	1 (20.0)	0 (0.0)
APIXABAN	1 (16.7)	0 (0.0)	1 (20.0)	0 (0.0)
HEPARIN GROUP	1 (16.7)	1 (100.0)	0 (0.0)	0 (0.0)
HEPARIN-DERIVATIVE	1 (16.7)	1 (100.0)	0 (0.0)	0 (0.0)
OTHER ANTITHROMBOTIC AGENTS	2 (33.3)	0 (0.0)	2 (40.0)	0 (0.0)
DIRECT ORAL ANTICOAGULANTS	2 (33.3)	0 (0.0)	2 (40.0)	0 (0.0)
PLATELET AGGREGATION INHIBITORS EXCL. HEPARIN	1 (16.7)	1 (100.0)	0 (0.0)	0 (0.0)
ASPIRIN	1 (16.7)	1 (100.0)	0 (0.0)	0 (0.0)
VITAMIN K ANTAGONISTS	1 (16.7)	1 (100.0)	0 (0.0)	0 (0.0)
WARFARIN-DERIVATIVE	1 (16.7)	1 (100.0)	0 (0.0)	0 (0.0)

Note: (a) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation. Patients were classified into the Prior Eculizumab Treatment Unknown group due to unknown prior eculizumab treatment history or because of a missing eculizumab discontinuation date.

Source: ADAM.ADSLI, ADAM.ADCMI
Run Date: 2025-05-13T15:40:45
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ipig/Files/tables/production/programs/t9_cmhis_i.sas

Table 9
History of Concomitant Medication Use at Ultomiris Initiation, by Treatment Status
IPIG PNH Registry Study Population

Medication Category Medication Class Medication Name	All Ravulizumab Patients[a] (N=6)	Prior Eculizumab Treatment (N=1)	Without Prior Eculizumab Treatment (N=5)	Prior Eculizumab Treatment Unknown (N=0)
IMMUNOSUPPRESSION	2 (33.3)	1 (100.0)	1 (20.0)	0 (0.0)
CALCINEURIN INHIBITORS	1 (16.7)	0 (0.0)	1 (20.0)	0 (0.0)
CYCLOSPORIN	1 (16.7)	0 (0.0)	1 (20.0)	0 (0.0)
SELECTIVE IMMUNOSUPPRESSANTS	1 (16.7)	0 (0.0)	1 (20.0)	0 (0.0)
ATG CYCLE 1	1 (16.7)	0 (0.0)	1 (20.0)	0 (0.0)
UNKNOWN/MISSING MEDICATION CLASS	1 (16.7)	1 (100.0)	0 (0.0)	0 (0.0)
CORTICOSTEROIDS	1 (16.7)	1 (100.0)	0 (0.0)	0 (0.0)
IRON CHELATION THERAPY	1 (16.7)	0 (0.0)	1 (20.0)	0 (0.0)
IRON CHELATING AGENTS	1 (16.7)	0 (0.0)	1 (20.0)	0 (0.0)
DEFERASIROX	1 (16.7)	0 (0.0)	1 (20.0)	0 (0.0)
THROMBOPOIETIN RECEPTOR AGONISTS	1 (16.7)	0 (0.0)	1 (20.0)	0 (0.0)
OTHER SYSTEMIC HEMOSTATICS	1 (16.7)	0 (0.0)	1 (20.0)	0 (0.0)
ELTROMBOPAG	1 (16.7)	0 (0.0)	1 (20.0)	0 (0.0)
VACCINATION	3 (50.0)	1 (100.0)	2 (40.0)	0 (0.0)
UNKNOWN/MISSING MEDICATION CLASS	3 (50.0)	1 (100.0)	2 (40.0)	0 (0.0)
COVID	3 (50.0)	1 (100.0)	2 (40.0)	0 (0.0)

Note: (a) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation. Patients were classified into the Prior Eculizumab Treatment Unknown group due to unknown prior eculizumab treatment history or because of a missing eculizumab discontinuation date.

Source: ADAM.ADSLI, ADAM.ADCMI
Run Date: 2025-05-13T15:40:45
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ipig/Files/tables/production/programs/t9_cmhis_i.sas

Table 9
History of Concomitant Medication Use at Ultomiris Initiation, by Treatment Status
IPIG PNH Registry Study Population

Medication Category Medication Class Medication Name	All Ravulizumab Patients[a] (N=6)	Prior Eculizumab Treatment (N=1)	Without Prior Eculizumab Treatment (N=5)	Prior Eculizumab Treatment Unknown (N=0)
MENINGOCOCCAL GROUP ACWY	1 (16.7)	1 (100.0)	0 (0.0)	0 (0.0)
MENINGOCOCCAL GROUP B	1 (16.7)	1 (100.0)	0 (0.0)	0 (0.0)

Note: (a) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation. Patients were classified into the Prior Eculizumab Treatment Unknown group due to unknown prior eculizumab treatment history or because of a missing eculizumab discontinuation date.

Source: ADAM.ADSLI, ADAM.ADCMI
Run Date: 2025-05-13T15:40:45
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ipig/Files/tables/production/programs/t9_cmhis_i.sas

Table 10
Laboratory Values at Ultomiris Initiation, by Treatment Status
IPIG PNH Registry Study Population

	All Ravulizumab Patients[a] (N=6)	Prior Eculizumab Treatment (N=1)	Without Prior Eculizumab Treatment (N=5)	Prior Eculizumab Treatment Unknown (N=0)
Percent GPI-deficient granulocytes				
n	4	1	3	0
Mean (SD)	63.7 (26.27)	76.2 (---)	59.5 (30.52)	-- (---)
Median (Q1, Q3)	68.2 (44.5, 82.9)	76.2 (76.2, 76.2)	60.3 (28.7, 89.7)	-- (--, --)
Percent GPI-deficient granulocytes, n (%)				
n	4	1	3	0
<1%	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
>=1% to <10%	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
>=10% to <50%	1 (25.0)	0 (0.0)	1 (33.3)	0 (0.0)
>=50%	3 (75.0)	1 (100.0)	2 (66.7)	0 (0.0)
LDH (U/L)				
n	6	1	5	0
Mean (SD)	1007.5 (699.72)	230.0 (---)	1163.0 (656.25)	-- (---)
Median (Q1, Q3)	914.0 (450.0, 1352.0)	230.0 (230.0, 230.0)	985.0 (843.0, 1352.0)	-- (--, --)

Notes: eGFR = estimated glomerular filtration rate; GPI = glycophosphatidylinositol; LDH = lactate dehydrogenase; Q1 = first quartile; Q3 = third quartile; SD = standard deviation; ULN = upper limit of normal; WBC = white blood cells.
Data shown are reported in the 6 months prior to the timepoint
(a) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation. Patients were classified into the Prior Eculizumab Treatment Unknown group due to unknown prior eculizumab treatment history or because of a missing eculizumab discontinuation date.

Source: ADAM.ADSLI, ADAM.ADLBI
Run Date: 2025-05-13T15:40:46
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ipig/Files/tables/production/programs/t10_labhis_i.sas

Table 10
Laboratory Values at Ultomiris Initiation, by Treatment Status
IPIG PNH Registry Study Population

	All Ravulizumab Patients[a] (N=6)	Prior Eculizumab Treatment (N=1)	Without Prior Eculizumab Treatment (N=5)	Prior Eculizumab Treatment Unknown (N=0)
LDH ratio (x ULN)				
n	6	1	5	0
Mean (SD)	4.2 (2.80)	1.1 (---)	4.8 (2.62)	-- (---)
Median (Q1, Q3)	3.9 (1.8, 5.5)	1.1 (1.1, 1.1)	4.0 (3.8, 5.5)	-- (--, --)
LDH ratio (x ULN), n (%)				
n	6	1	5	0
<1.5	1 (16.7)	1 (100.0)	0 (0.0)	0 (0.0)
>=1.5	5 (83.3)	0 (0.0)	5 (100.0)	0 (0.0)
Hemoglobin (g/dL)				
n	6	1	5	0
Mean (SD)	9.8 (1.44)	12.2 (---)	9.3 (0.92)	-- (---)
Median (Q1, Q3)	9.7 (9.0, 10.3)	12.2 (12.2, 12.2)	9.6 (9.0, 9.8)	-- (--, --)
Haptoglobin (umol/L)				
n	0	0	0	0
Mean (SD)	-- (---)	-- (---)	-- (---)	-- (---)

Notes: eGFR = estimated glomerular filtration rate; GPI = glycophosphatidylinositol; LDH = lactate dehydrogenase; Q1 = first quartile; Q3 = third quartile; SD = standard deviation; ULN = upper limit of normal; WBC = white blood cells.
Data shown are reported in the 6 months prior to the timepoint
(a) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation. Patients were classified into the Prior Eculizumab Treatment Unknown group due to unknown prior eculizumab treatment history or because of a missing eculizumab discontinuation date.

Source: ADAM.ADSLI, ADAM.ADLBI
Run Date: 2025-05-13T15:40:46
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ipig/Files/tables/production/programs/t10_labhis_i.sas

Table 10
Laboratory Values at Ultomiris Initiation, by Treatment Status
IPIG PNH Registry Study Population

	All Ravulizumab Patients[a] (N=6)	Prior Eculizumab Treatment (N=1)	Without Prior Eculizumab Treatment (N=5)	Prior Eculizumab Treatment Unknown (N=0)
Median (Q1, Q3)	-- (--, --)	-- (--, --)	-- (--, --)	-- (--, --)
Platelets (x10^9/L)				
n	6	1	5	0
Mean (SD)	127.3 (80.17)	227.0 (---)	107.4 (71.09)	-- (---)
Median (Q1, Q3)	105.5 (59.0, 222.0)	227.0 (227.0, 227.0)	85.0 (59.0, 126.0)	-- (--, --)
Serum creatinine (umol/L)				
n	6	1	5	0
Mean (SD)	84.5 (17.05)	85.0 (---)	84.4 (19.06)	-- (---)
Median (Q1, Q3)	84.0 (70.0, 101.0)	85.0 (85.0, 85.0)	83.0 (70.0, 101.0)	-- (--, --)
eGFR (mL/min/1.73 m^2)				
n	6	1	5	0
Mean (SD)	79.3 (11.48)	90.0 (---)	77.2 (11.43)	-- (---)
Median (Q1, Q3)	82.5 (72.0, 89.0)	90.0 (90.0, 90.0)	81.0 (72.0, 84.0)	-- (--, --)
eGFR (mL/min/1.73 m^2), n (%)				
n	6	1	5	0

Notes: eGFR = estimated glomerular filtration rate; GPI = glycophosphatidylinositol; LDH = lactate dehydrogenase; Q1 = first quartile; Q3 = third quartile; SD = standard deviation; ULN = upper limit of normal; WBC = white blood cells.
Data shown are reported in the 6 months prior to the timepoint
(a) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation. Patients were classified into the Prior Eculizumab Treatment Unknown group due to unknown prior eculizumab treatment history or because of a missing eculizumab discontinuation date.

Source: ADAM.ADSLI, ADAM.ADLBI
Run Date: 2025-05-13T15:40:46
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ipig/Files/tables/production/programs/t10_labhis_i.sas

Table 10
Laboratory Values at Ultomiris Initiation, by Treatment Status
IPIG PNH Registry Study Population

	All Ravulizumab Patients[a] (N=6)	Prior Eculizumab Treatment (N=1)	Without Prior Eculizumab Treatment (N=5)	Prior Eculizumab Treatment Unknown (N=0)
<30	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
30 to <60	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
60 to <90	5 (83.3)	0 (0.0)	5 (100.0)	0 (0.0)
>=90	1 (16.7)	1 (100.0)	0 (0.0)	0 (0.0)
Absolute neutrophils (/uL)				
n	6	1	5	0
Mean (SD)	2441.7 (2635.76)	7700.0 (---)	1390.0 (623.70)	-- (---)
Median (Q1, Q3)	1685.0 (1240.0, 1960.0)	7700.0 (7700.0, 7700.0)	1600.0 (1240.0, 1770.0)	-- (--, --)
Absolute reticulocytes (x10^9/L)				
n	6	1	5	0
Mean (SD)	196.3 (135.38)	224.9 (---)	190.6 (150.55)	-- (---)
Median (Q1, Q3)	176.5 (97.0, 229.0)	224.9 (224.9, 224.9)	128.0 (97.0, 229.0)	-- (--, --)
Total WBC (x10^9/L)				
n	6	1	5	0

Notes: eGFR = estimated glomerular filtration rate; GPI = glycophosphatidylinositol; LDH = lactate dehydrogenase; Q1 = first quartile; Q3 = third quartile; SD = standard deviation; ULN = upper limit of normal; WBC = white blood cells.
Data shown are reported in the 6 months prior to the timepoint
(a) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation. Patients were classified into the Prior Eculizumab Treatment Unknown group due to unknown prior eculizumab treatment history or because of a missing eculizumab discontinuation date.

Source: ADAM.ADSLI, ADAM.ADLBI
Run Date: 2025-05-13T15:40:46
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ipig/Files/tables/production/programs/t10_labhis_i.sas

Table 10
Laboratory Values at Ultomiris Initiation, by Treatment Status
IPIG PNH Registry Study Population

	All Ravulizumab Patients[a] (N=6)	Prior Eculizumab Treatment (N=1)	Without Prior Eculizumab Treatment (N=5)	Prior Eculizumab Treatment Unknown (N=0)
Mean (SD)	4.2 (2.72)	9.7 (---)	3.1 (0.50)	-- (---)
Median (Q1, Q3)	3.1 (3.0, 3.9)	9.7 (9.7, 9.7)	3.0 (3.0, 3.1)	-- (--, --)

Notes: eGFR = estimated glomerular filtration rate; GPI = glycophosphatidylinositol; LDH = lactate dehydrogenase; Q1 = first quartile; Q3 = third quartile; SD = standard deviation; ULN = upper limit of normal; WBC = white blood cells.
Data shown are reported in the 6 months prior to the timepoint
(a) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation. Patients were classified into the Prior Eculizumab Treatment Unknown group due to unknown prior eculizumab treatment history or because of a missing eculizumab discontinuation date.

Source: ADAM.ADSLI, ADAM.ADLBI
Run Date: 2025-05-13T15:40:46
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ipig/Files/tables/production/programs/t10_labhis_i.sas

Listing 1
Registry Discontinuation, Cumulative
Ravulizumab Study Population

Patient Number	Population	Gender	Treatment Status[a]	Enrollment Date	Study Discontinuation Date	Primary Reason for Study Discontinuation
5674-0005-440020176	Alexion PNH Registry Study Population	F	Prior Eculizumab Treatment	24SEP2024	01DEC2024	DEATH

Note: (a) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation. Patients were classified into the Prior Eculizumab Treatment Unknown group due to unknown prior eculizumab treatment history or because of a missing eculizumab discontinuation date.

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Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ipig/Files/listings/production/programs/l1_regdis_i.sas

Listing 2
Discontinuation from Ultomiris
Ravulizumab Study Population

Patient Number	Population	Enrollment Date	Treatment Status[a]	Ravulizumab Initiation Date	Last Recorded Date of Ravulizumab Infusion	Primary Reason for Ravulizumab Discontinuation
5674-0005-440020019	Alexion PNH Registry Study Population	28MAY2024	Prior Eculizumab Treatment	30SEP2021	05JUN2024	Physician decision

Note: (a) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation. Patients were classified into the Prior Eculizumab Treatment Unknown group due to unknown prior eculizumab treatment history or because of a missing eculizumab discontinuation date.

Source: ADAM.ADSLI
Run Date: 2025-05-13T15:40:17
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ipig/Files/listings/production/programs/l2_ravudis_i.sas

Listing 3
Deaths
Ravulizumab Study Population

Patient Number	Population	Enrollment Date	Treatment Exposure at Time of Death	Ravulizumab Initiation Date	Ravulizumab Discontinuation Date	Date of Death	Age at Death
5674-0005-440020176	Alexion PNH Registry Study Population	24SEP2024	Ravulizumab	26JAN2022		01DEC2024	70

Note: At the time of the IPIG data download, details regarding the cause of death had not yet been collected and entered into the database.

Source: ADAM.ADSLI
Run Date: 2025-05-13T15:40:19
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ipig/Files/listings/production/programs/l3_death_ii.sas

Listing 4
Major Adverse Vascular Events
Ravulizumab Study Population

Patient Number	Population	Enrollment Date	Status	Treatment Exposure at time of event	Ravulizumab Initiation Date	Date of Event	Event Detail	Body System	Verbatim Term	Outcome	Resolution Date
5674-0005-440020176	Alexion PNH Registry Study Population	24SEP2024	Discontinued	Ravulizumab	26JAN2022	01DEC2024	Cardiac failure acute	Cardiac disorders	ACUTE CARDIAC FAILURE	FATAL	

Source: ADAM.ADSLI, ADAM.ADAEI
Run Date: 2025-05-13T15:40:21
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ipig/Files/listings/production/programs/l4_mave_i.sas

Listing 5
Malignancy
Ravulizumab Study Population

Patient Number	Population	Enrollment Date	Ravulizumab Initiation Date	Status	Treatment Exposure at time of event	Date of Event	Category	Subcategory	Event Detail	Verbatim Term	Outcome	Resolution Date
5674-0005-44002011	Alexion PNH Registry Study Population	26JUL2024	30AUG2022	Active	Ravulizumab	19SEP2024	ADVERSE EVENTS	Neoplasms benign, malignant and unspecified (incl cysts and polyps)	Prostate cancer	PROSTATE CANCER	NOT RECOVERED/NOT RESOLVED	

Listing 6
Infection
Ravulizumab Study Population

THERE IS NO DATA TO MEET THE PROGRAM CRITERIA

Listing 7
Meningococcal Infection
Ravulizumab Study Population

THERE IS NO DATA TO MEET THE PROGRAM CRITERIA

Note: (a) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation. Patients were classified into the Prior Eculizumab Treatment Unknown group due to unknown prior eculizumab treatment history or because of a missing eculizumab discontinuation date.

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Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ipig/Files/listings/production/programs/l7_meningo_i.sas

Listing 8
Impaired Renal Function
Ravulizumab Study Population

THERE IS NO DATA TO MEET THE PROGRAM CRITERIA

Listing 9
Impaired Hepatic Function
Ravulizumab Study Population

THERE IS NO DATA TO MEET THE PROGRAM CRITERIA

Listing 10
Pulmonary Hypertension
Ravulizumab Study Population

THERE IS NO DATA TO MEET THE PROGRAM CRITERIA

Listing 11
Ultomiris Infusion Reactions
Ravulizumab Study Population

THERE IS NO DATA TO MEET THE PROGRAM CRITERIA

Listing 12
Pregnancy Outcome
Ravulizumab Study Population

THERE IS NO DATA TO MEET THE PROGRAM CRITERIA

Note: (a) Sex indicates the gender of the patient. If the subject is male, the Pregnancy Outcome relates to the spouse.

Source: ADAM.ADSLI, ADAM.ADPREGI
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Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ipig/Files/listings/production/programs/l12_pregout_i.sas

Listing 13
Bone Marrow Transplant
Ravulizumab Study Population

THERE IS NO DATA TO MEET THE PROGRAM CRITERIA

Listing 14
All Serious Adverse Events and Special Events
Ravulizumab Study Population

Patient Number	Population	Enrollment Status	Treatment Status[a]	Adverse Event Term	Serious Event (Yes/No)	Serious Event Category	Special Event (Yes/No)	Special Event Type	Start Date	End Date	Outcome
5674-0005-440020111	Alexion PNH Registry Study Population	Active	Without Prior Eculizumab Treatment	PROSTATE CANCER	Y	Life-Threatening; Other	N		19SEP2024		NOT RECOVERED/ NOT RESOLVED
5674-0005-440020140	Alexion PNH Registry Study Population	Active	Prior Eculizumab Treatment	PYREXIA	Y	Hospitalization	N		31OCT2024	02NOV2024	RECOVERED/ RESOLVED
5674-0005-440020176	Alexion PNH Registry Study Population	Discontinued	Prior Eculizumab Treatment	ACUTE CARDIAC FAILURE	Y	Death	N		01DEC2024		FATAL
5674-0005-490030005	Alexion PNH Registry Study Population	Active	Prior Eculizumab Treatment	WORSENING OF GALLSTONE DESEASE	Y	Hospitalization	N		01SEP2024	15NOV2024	RECOVERED/ RESOLVED

Note: (a) Prior eculizumab treatment indicates that the patient discontinued eculizumab within 28 days of ravulizumab initiation. Without prior eculizumab treatment includes patients never treated with eculizumab before ravulizumab initiation, or eculizumab was discontinued at least 28 days prior to ravulizumab initiation. Patients were classified into the Prior Eculizumab Treatment Unknown group due to unknown prior eculizumab treatment history or because of a missing eculizumab discontinuation date.

Source: ADAM.ADSLI, ADAM.ADAEI, ADAM.ADCEI, ADAM.ADMEI
Run Date: 2025-05-13T15:40:32
Program Path: /alxn/pnh-m07001-integ/pnh-m07001-integ-ipig/Files/listings/production/programs/l14_sae_i.sas

Listing 15
Patient Information and Treatment Information
Frequent Treatment Switchers

THERE IS NO DATA TO MEET THE PROGRAM CRITERIA

Listing 16
All Serious Adverse Events and Special Events
Frequent Treatment Switchers

THERE IS NO DATA TO MEET THE PROGRAM CRITERIA

STATISTICAL ANALYSIS PLAN

Version Number: 1.0

Analysis Title:

Characterization of Participants Treated with Ultomiris and Long-Term Safety Outcomes: an IPIG PNH Registry Based Study—Interim Analysis Report

Protocol Number: ALX-PNH-501 and M07-001

Compound: Ultomiris

Project Numbers:

pnh-m07001-integ-ravuema202501(Alexion dataset analysis)

pnh-m07001-integ-ipig (IPIG dataset analysis)

Short Title: 2025 Ultomiris Interim Analysis Report

Sponsor Name: Alexion Pharmaceuticals, Inc.

Legal Registered Address:

121 Seaport Boulevard

Boston, MA 02210

Authors: Ami Patel (Alexion), Alix Augustin-Wright (Alexion), Grace He (Parexel), Jesse Metzger (Parexel)

Version Date: 15 Apr 2025

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VERSION HISTORY

SAP Version	Version Date	Change	Rationale
0.1	13 DEC 2024		Original version
1.0	15 APR 2025	Title Page updated with project number specific to the International PNH Interest group Registry (i.e., IPIG PNH Registry) data and with protocol number M07-001	For this analysis, outputs related to the Alexion PNH registry data analysis are generated under the designated project code *pnh-m07001-integ-ravuema202501*, while outputs specific to the IPIG PNH registry data analysis are generated under the project number *pnh-m07001-integ-ipig*
		Table of tables and tables of figures added	
		Section 1.2– Definition – Addition of protocol number M07-001	This Statistical Analysis Plan (SAP) describes the analytical plan for ALX-PNH-501 inclusive of data from M07-001
		Section 1.2.1– Treatment Status Definition	Prior Soliris treatment is unknown when Soliris treatment end date is missing.
		Introduction Deletion of the following references (Hillmen, 1995; Nishimura, 2004): and survival information corrected based on Socie, 1996.	The two references do not support the survival figure presented in the text. The sentence pertaining to PNH survival is updated as follow based on Socie et al 1996: Prior to the availability of Soliris®(eculizumab), the estimated survival of patients with PNH 15 years after diagnosis was approximately 50%.
		Section 1.2.2 – Exposure Period Definition	Figure 1 updated to reflect brand name Ultomiris and Soliris in place of ravulizumab and eculizumab respectively
		Section 1.2.3 – Time Points of Interest Deletion of "Dates of the time points of interest are actual reported dates, not imputed dates based on assessments (i.e. 6 months after enrollment, 12 months after enrollment, etc.).	Wording not applicable to data imputation strategy in this analysis
		Section 1.2.3 – Time Points of Interest Definition of "last Soliris treated follow-up date updated	Updated text: Last Soliris treated follow-up date: This is only for participants switching treatment from Soliris to Ultomiris only once. The date of last Soliris treated follow-up is subsequently defined as the minimum of 1) 4 weeks after the date of discontinuation of Soliris or 2) 1 day prior to Ultomiris treatment start date or 3) last Alexion PNH Registry follow-up date. For participants missing

SAP Version	Version Date	Change	Rationale
			reported records of Soliris discontinuation, Soliris end date will be set to missing.
		Section 1.3.4 – Additional variable of interest added	Gender, Race and Ethnicity are variables of interest in this analysis and were missing in the SAP.
		Editorial changes throughout body document	• Ravulizumab replaced with brand name "Ultomiris" • Eculizumab replaced with brand name "Soliris" • Cross-referencing adjusted accommodate the addition of Appendix 1 • Date formatting harmonized to Day MONTH Year • IPIG PNH Registry name employed when referring to patients' data originating from the IPIG PNH Registry Alexion Products Silo • Alexion PNH Registry name employed when referring to patients' data originating from the Alexion PNH Registry
		Addition of Appendix 1. IPIG PNH Registry Statistical Analysis Plan	IPIG PNH Registry Statistical Analysis Plan inserted as Appendix 1 to describe the analytical plan for participants enrolled in the IPIG PNH Registry meeting the inclusion/exclusion criteria specified in ALX-PNH-501 study protocol
		Appendix 2. Lab min/max values for analyzable data – Conversion factor updated for Hemoglobin and Absolute Neutrophils	• Hemoglobin conversion factor updated to reflect typical presentation in g/dL • Absolute Neutrophils conversion factor updated to reflect typical presentation in µL
		Appendix 5. List of Abbreviations	List of abbreviation updated to accommodate abbreviated terms included in Appendix 1. IPIG PNH Registry Statistical Analysis Plan

APPROVAL SIGNATURES

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17-Apr-2025

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Min Yee

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17-Apr-2025

Jesse Metzger

Date

Lead Statistician

1. INTRODUCTION

Paroxysmal nocturnal hemoglobinuria (PNH) is an ultra-rare and life-threatening acquired hematologic disorder caused by uncontrolled activation of the terminal complement pathway (Bektas, 2020; DeZern, 2015; Kulasekararaj, 2023). The prevalence is estimated to be between 10 to 38 cases per million (Hansen, 2020; Jalbert, 2019; Richards, 2021). The disease has a roughly equal sex distribution and can occur at any age though is diagnosed most often in the fourth or fifth decade of life (Schrezenmeier, 2020). Patients with PNH are at risk of substantial morbidity and mortality. Thromboembolic events (TEs) are the leading cause of death in patients with PNH and pulmonary hypertension and end-organ damage of vital organs, such as the liver, kidneys, brain, and intestines, are sequelae of TE (Nishimura 2004; Hillmen, 2010). Prior to the availability of Soliris® (eculizumab), the estimated survival of patients with PNH 15 years after diagnosis was approximately 50% (Socié, 1996).

Alexion Pharmaceuticals, Inc. has been the Sponsor of a global PNH Registry (M07-001) since August 2004 and has been enrolling participants with PNH worldwide, including participants treated with Soliris since its first approval in 2007. The primary aim of the Alexion PNH Registry is to record the natural progression of PNH and collect and evaluate safety data specific to the use of Soliris or Ultomiris® (ravulizumab) in patients with PNH. Data from the PNH Registry are intended for health care providers to optimize clinical decision making through enhanced understanding of the natural history of PNH, ultimately aiming to better guide and assess therapeutic interventions. Methods of PNH diagnosis, treatment data, clinical outcomes, and quality of life assessments are also collected. An additional objective is to increase PNH knowledge in the medical community and patient community.

In 2023, the Alexion PNH Registry began transitioning to the International PNH Interest Group (IPIG) PNH Registry with the objective to move from an industry sponsored registry to an academic-led Registry database. The IPIG PNH Registry aims to enroll patients with PNH, regardless of the type of PNH-specific therapy they are receiving, to capture data on clinical outcomes on all enrolled patients, as well as long-term safety data of PNH-specific treatments. In addition, the registry will collect information on disease progression within the PNH population. The IPIG PNH Registry is intended to increase knowledge about PNH in the medical community and patient population.

The IPIG PNH Registry is comprised of the Core PNH disease Registry (Core Registry) and several product-specific silo protocols initiated by IPIG on request by the respective marketing authorisation holders (MAHs). Core variables will be collected in the Core Registry at enrollment and during follow-up, while specific data (e.g., post authorization safety data) for participants treated with PNH-specific therapies will be collected in the silos in order to address specific objectives or requests from regulatory authorities and MAHs.

This analysis leverages data from the Alexion PNH Registry (protocol number M07-001) and the newly established International PNH Interest Group (IPIG) to characterize the long-term safety of Ultomiris as specified in the ALX-PNH-501 post authorization safety study. The Appendix 1: Statistical Analysis Plan for IPIG PNH Registry Data is specific to the analysis of the IPIG PNH Registry dataThe associated report is part of the additional pharmacovigilance activities associated with Ultomiris® (ravulizumab) marketing authorisation application in the European Union (Category 3 study in the EU Risk Management Plan, version 9.0, dated 04SEP24).

1.1. Objectives and Endpoints

Objectives	Endpoints
Primary	
To characterize the safety of Ultomiris in participants with PNH	Incidence of reported SAEs and special events
To characterize the incidence of targeted clinical outcomes among participants with PNH*	Incidence rate of MAVE, TE, malignancy, serious infection, impaired renal function, impaired hepatic function, hemolysis, mortality, and bone marrow transplant. Incidence of pregnancy outcome (both maternal and fetal events)
Secondary	
Describe the demographic and clinical profile at treatment initiation for Ultomiris treated participants with PNH	Frequency and univariate statistics of demographic characteristics, medical history, comedications, and laboratory measures
Assess Ultomiris treatment patterns among participants with PNH	Initiation dose and average dose patterns Number of participants who discontinue Ultomiris and reasons for discontinuation

*Hemolysis is only collected in the IPIG PNH Registry and is thus described in the Appendix 1: Statistical Analysis Plan for IPIG PNH Registry Data
Abbreviations: MAVE= major adverse vascular event; PNH= paroxysmal nocturnal hemoglobinuria; SAE= serious adverse event; TE= thrombotic event

1.2. Definitions

This Statistical Analysis Plan (SAP) describes the analytical plan for ALX-PNH-501 inclusive of data from M07-001.

1.2.1. Treatment Status Definitions

Participants will be classified according to their treatment status as follow:

- **Treated with Ultomiris**: participant has a known date of Ultomiris initiation on or after Alexion PNH Registry enrollment
- **Prior Soliris treatment**: participant treated with Soliris, discontinued Soliris within less than 28 days of Ultomiris initiation, and switched treatment to Ultomiris once on or after Alexion PNH Registry enrollment
- **Without prior Soliris treatment**: participant initiating Ultomiris on or after Alexion PNH Registry enrollment and never treated with Soliris before Ultomiris initiation, or Soliris was discontinued at least 28 days prior to Ultomiris initiation

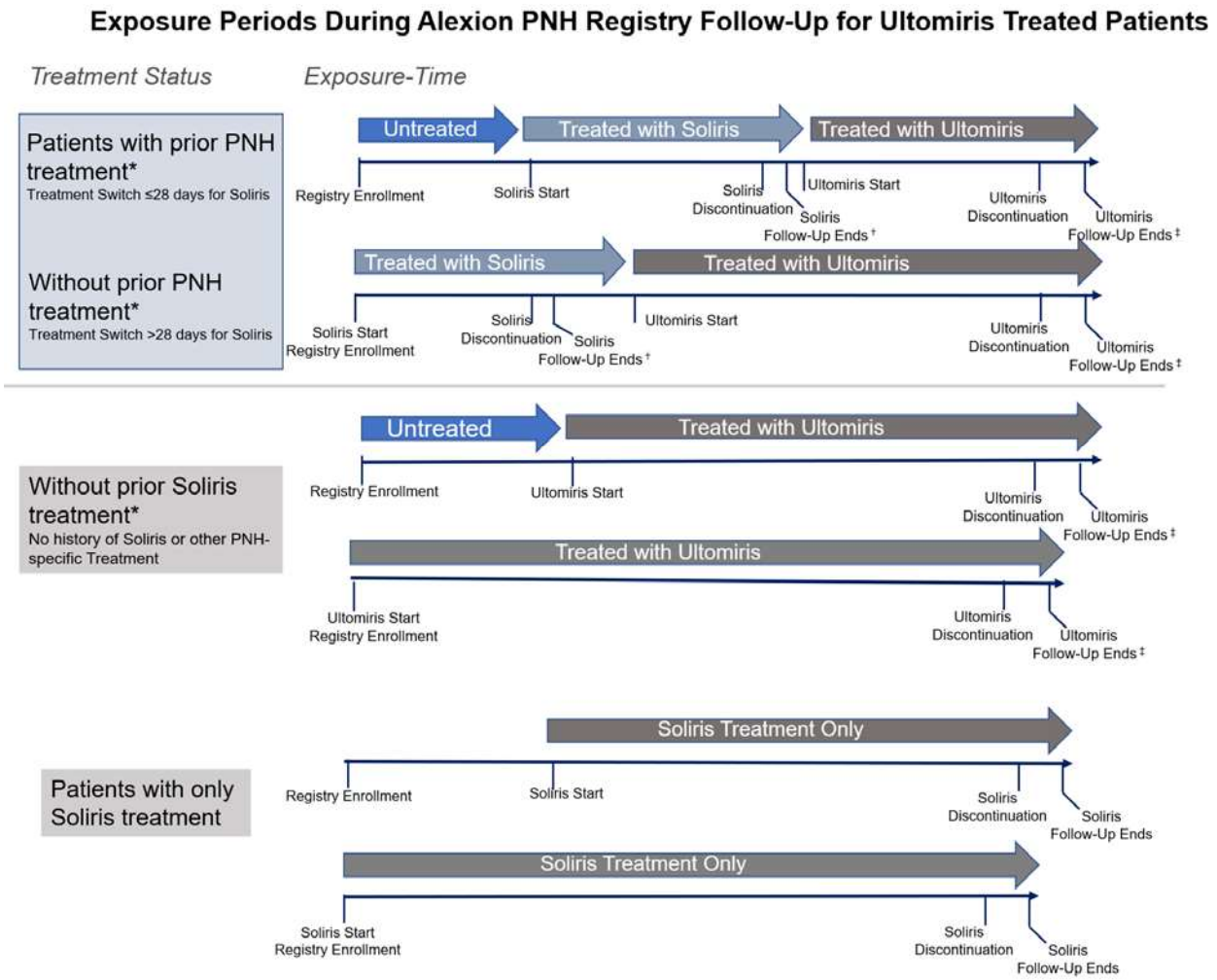
- **Prior Soliris treatment unknown**: participant initiating Ultomiris on or after Alexion PNH Registry enrollment and with Soliris treatment status uncertain based on the data reported in the registry (e.g., missing Soliris treatment end date).

The summary of participant demographics, participant disposition, vital status at last registry follow-up, and the registry follow-up duration will be presented by treatment status. Information collected at Ultomiris initiation, such as medical history, concomitant medication, and laboratory values will be also summarized by treatment status.

1.2.2. Exposure Periods Definitions

The exposure period during Alexion PNH Registry also presented in Figure 1) is defined as follow, where "registry enrollment" refers to enrollment the Alexion PNH Registry:

- **Untreated period** —Participants who are untreated at registry enrollment and initiate any anti-complement treatment (including Soliris, Ultomiris, or other anti-complement treatment) during the registry follow up will contribute untreated person time from enrollment to last untreated follow-up date (as defined in Section 1.2.3).
- **Treated with Soliris** (prior to Ultomiris switch) (Soliris exposure period) —participants switching treatment from Soliris to Ultomiris only once will contribute person time in this category. The Soliris exposure period is from registry enrollment, if Soliris was initiated prior to enrollment, or Soliris initiation date to last Soliris treated follow-up date (as defined in Section 1.2.3).
- **Treated with Ultomiris** (Ultomiris exposure period) — any participants ever-treated with Ultomiris will contribute person time to this exposure period, including participants switching from Soliris to Ultomiris once (e.g. previously treated with Soliris), participants only treated with Ultomiris, and participants treated with Ultomiris and with unknown prior Soliris treatment status. The Ultomiris exposure period covers the period from Ultomiris initiation date to last Ultomiris treated follow-up date (as defined in Section 1.2.3).



*Prior is defined as Soliris or other PNH-specific treatment within at least 28 days of Ultomiris initiation. Patients in Treatment Status 'Without Prior Soliris Treatment' may still contribute Soliris person-time (e.g., if treatment was >4 weeks from Ultomiris initiation).
†Minimum of 4 weeks following Soliris discontinuation and the date prior to Ultomiris start.
‡Last Ultomiris follow-up date is minimum of 16 weeks after Ultomiris discontinuation, date of new non-Ultomiris treatment, or date of data cut-off.

Figure 1. Registry Exposure Periods

1.2.3. Time Points of Interest

- Initiation of Ultomiris, defined as first record of Ultomiris treatment
- Initiation of Soliris, defined as first record of Soliris treatment
- Date of Enrollment, defined as date of enrollment in the Alexion PNH Registry
- Last Registry follow-up date: last follow-up is defined by the first reported date of death, date of bone marrow transplant, or date of discontinuation from the Alexion PNH Registry. In participants not meeting any of these criteria, last follow-up is the date of last contact from the Alexion PNH Registry as reported on the Last Contact at Follow-Up case report form (CRF). For participants without any follow-up, the last registry follow-up date is equivalent to the enrollment date.
- Last Ultomiris treated follow-up date: If an ever-treated participant has a record of discontinuation of Ultomiris, the date of last Ultomiris treated follow-up is the minimum of 16 weeks after the date of discontinuation of Ultomiris, current data download date, or date of new, non-Ultomiris, treatment initiation (if reported Ultomiris discontinuation records are missing). If an ever-treated participant has no record of discontinuation of Ultomiris and no subsequent treatment other than Ultomiris, last Ultomiris treated follow-up is the same as last Alexion PNH registry follow-up date.
- Last Soliris treated follow-up date: This is only for participants switching treatment from Soliris to Ultomiris only once. The date of last Soliris treated follow-up is subsequently defined as the minimum of 1) 4 weeks after the date of discontinuation of Soliris or 2) 1 day prior to Ultomiris treatment start date or 3) last Alexion PNH Registry follow-up date. For participants missing reported records of Soliris discontinuation, Soliris end date will be set to missing.
- Last untreated follow-up date: this is only defined for participants untreated at enrollment; it is missing for all other participants. Defined as one day prior to the date of first initiation of Soliris or Ultomiris for participants who started treatment after enrollment.

1.2.4. Analysis periods

Two different analysis periods will be considered when reporting study outcomes and variables summary. The first analysis will include all events and person-time accrued from Alexion PNH Registry enrollment until last registry follow-up (i.e., cumulative analysis), whereas the second presentation will include only events and person-time accrued during the current analysis period from 06 Jan 2023 until the data download date.

- Cumulative:
    - Includes all events and person-time from Alexion PNH Registry enrollment to last registry follow-up date or date of death.

  - Includes untreated person-time, Soliris treated person-time, and Ultomiris treated person-time.
- During the analysis period:
  - Includes all events and person-time from 06 Jan 2023 to 06 Jan 2025 (i.e., last data download date)
  - Includes untreated person-time, Soliris treated person-time, and Ultomiris treated person-time.

1.3. Outcomes of Interest

1.3.1. Primary Outcomes Definition

1.3.1.1. Reportable Adverse Events (SAEs and special events)

Serious Adverse Events (SAE) are defined as any adverse event (AE) that results in death, or is life-threatening, or requires inpatient hospitalization or prolongation of existing hospitalization, or is an important medical event, or results in persistent or significant disability/incapacity, or is a congenital anomaly/birth defect.

- AEs are reported through the Alexion PNH Registry CRF using the Safety Gateway. Only forms with a "Yes" to the question "Any reportable adverse events" will be included.
- The following data will be listed directly from the "Adverse Events" CRF:
  - Adverse event write-in text
  - Special event regarding the medicinal product (yes/no)
    - If yes, specify: Overdose, Misuse, Medication error, Lack of therapeutic efficacy
  - Serious event: Yes/No
    - If yes, check all that apply (text to be concatenated and displayed in a single listing column): Congenital Anomaly or Birth Defect, Persistent or Significant Disability/Incapacity, Results in Death, Requires or Prolongs Hospitalization, Is Life Threatening, Other Medically Important Serious Event
  - Start date of AE
  - End date of AE
  - Outcome: Not Recovered/Not Resolved, Recovered/Resolved with Sequelae, Recovering/Resolving, Recovered/Resolved, Fatal, Unknown

Special events regarding the use of Ultomiris including any events of misuse, overdose, medication error, occupational exposure of falsified products and lack of therapeutic efficacy will also be analyzed.

1.3.1.2. Clinical events

Clinical events, including death, MAVEs, TE, non-TE MAVE, infection, malignancy, impaired renal function, impaired hepatic function, Ultomiris infusion reactions, pulmonary hypertension

and bone marrow transplant and will be summarized by event rates (as defined in Section 5.3.1) and based on the exposure period defined in Section 1.2.2).

These events are derived from the Alexion PNH Registry Follow-up CRF pages.

- TE
    - Includes thrombophlebitis/deep vein thrombosis; renal vein thrombosis; renal arterial thrombosis; mesenteric/visceral vein thrombosis; mesenteric/visceral arterial thrombosis; hepatic/portal vein thrombosis; dermal thrombosis; acute peripheral vascular disease occlusion; cerebral arterial occlusion/CVA; cerebral venous occlusion, and pulmonary embolus. The "Event Detail" of the TE is the specific CRF item in this list. The "Type" of TE is defined as Venous, Arterial, or Other.
        - Venous TE—thrombophlebitis/deep vein thrombosis; renal vein thrombosis; mesenteric/visceral vein thrombosis; hepatic/portal vein thrombosis; cerebral venous occlusion
        - Arterial TE—renal arterial thrombosis; mesenteric/visceral arterial thrombosis; cerebral arterial occlusion/CVA
        - Other TE—dermal thrombosis; acute peripheral vascular disease occlusion; pulmonary embolus
- Non-TE MAVE
    - Includes amputation (non-traumatic, non-diabetic); myocardial infarction; transient ischemic attack; unstable angina; gangrene (non-traumatic, non-diabetic); and other major adverse vascular event. The "Event Detail" of the Non-TE MAVE is the specific CRF item in this list. The "Type" is always Other.
- MAVE
    - Includes both TE and Non-TE MAVE, as defined above
- Malignancy
    - Malignancy events are collected on the Malignancy at Follow-up CRF pages. In addition, events captured as "Acute Myeloid Leukemia" and "Myelodysplastic Syndromes" Bone Marrow Pathology at Follow-up CRFs will also be included as malignancy events. Duplicates will be removed based on start date of the event
- Infection
    - Infection events are collected on the Infection at Follow-up CRF, or Infection after Initiation of Anti-complement Treatment CRF page for participant initiating Ultomiris treatment prior to enrollment. Duplicates will be removed based on start date of the event.
    - Serious infections, with a particular focus on *Neisseria* infections will be defined as those meeting the SAE definition (reference Section 1.3.1.1 Reportable Adverse Events (SAEs and special events))
- Death

- A participant is defined as having died if 1) primary reason for discontinuation from the Alexion PNH Registry (on Registry Discontinuation form) is "Patient died", or 2) date of death and/or probable cause of death is reported on the Alexion PNH Registry Discontinuation form, or 3) "Is the patient currently alive" is recorded as "No" on any submitted Last Contact form, or 4) "is the patient currently alive" is recorded as "No" or date of death after bone marrow transplant is reported on a Bone Marrow Transplant Outcome Follow-Up form, or 5) "Primary Reason for Ultomiris Discontinuation" is recorded as "Death" on the Discontinuation of Ultomiris form, or 6) "Primary Reason for Soliris Discontinuation" is recorded as "Death" on the Discontinuation of Soliris form. Every participant should have a yes/no value; no participant should be missing this variable.
- Date of death is defined as either the date of death on the Registry Discontinuation form or the Bone Marrow Transplant Outcome Follow-Up form and is only applicable if a participant is indicated to have died as per the definition above. Participants who died may be missing a date of death. If a participant has a date of death reported on the Registry Discontinuation Form different from that in the Bone Marrow Transplant Outcome Follow-Up form, the earlier date of death will be used.
- Cause of death is reported on either the Registry Discontinuation form or the Bone Marrow Transplant Outcome Follow-Up form. If it is reported in both places, the information reported on the Registry Discontinuation form will be used.

Table 1. Cause of Death Category Based on MedDRA Primary System Organ Class

Infections and infestations
Neoplasms benign, malignant and unspecified (includes cysts and polyps)
Blood and lymphatic system disorders Immune system disorders
Psychiatric disorders
Nervous system disorders
Cardiac disorders
Vascular disorders
Respiratory, thoracic and mediastinal disorders
Gastrointestinal disorders
Hepatobiliary disorders
Renal and urinary disorders
General disorders and administration site conditions
Injury, poisoning and procedural complications

- Bone marrow transplant
  - **Yes**—any record before or at the timepoint of interest with a "yes" response and/or a date of the event recorded

- **No**—no record before or at the timepoint of interest has a "yes" response or a date of the event recorded, but there is at least one "no" recorded

- Pregnancy outcomes
  - Pregnancy outcome dates for previous pregnancies should always be considered as individual events, with the event date=the pregnancy outcome date. If the outcome is "maternal complications", this should be ignored.
  - If the participant was "currently pregnant" on any CRF (enrollment or semiannual follow-up), but with no outcome and outcome date reported, the event will not be included in the analysis.
  - The exposure classification for the pregnancy outcomes will be based on the exposure status at the time of the pregnancy outcome and will not reflect the treatment exposure experienced throughout the entire pregnancy.
  - Data issue handling rules:
    - For a participant, if there are 2 pregnancies reported with outcome of "Live birth" and with 3 months or less in between the outcome dates, the pregnancy outcome with the later outcome date will be counted as 1 event and the other event will be excluded.
    - For a participant, if there are 2 pregnancies reported with 1 outcome of "Live birth" and the other outcome missing, with 1 months or less in between the outcome dates, the event with non-missing outcome will be counted as 1 event and the event with missing outcome will be excluded.
    - For a participant, if there are 2 pregnancy outcomes with the same outcome date, but different outcome, the event will be counted by conservative rule (miscarriage/still birth > abortion > live birth).

- Other clinical events of interest
  - Impaired renal function
  - Impaired hepatic function
  - Pulmonary hypertension

  Yes—any record before or at the timepoint of interest with a "yes" response and/or a date of the event recorded
  No—no record before or at the timepoint of interest has a "yes" response or a date of the event recorded, but there is at least one "no" recorded.
  - Ultomiris infusion reaction
    - Specifically, those adverse reactions identified by: anaphylaxis, anaphylactoid reaction, infusion-related reaction, infection site irritation, pruritus, rash, pruritus generalized, rash pruritic, urticaria, hypotension, drug hypersensitivity

1.3.2. Other Variables of Interest and Covariates

The following additional variables of interest will be analyzed.

1.3.2.1. Medical history

History of clinical events include bone marrow disorder (BMD), major adverse vascular event (MAVE), TE, non-TE MAVE, impaired renal function, impaired hepatic function, pulmonary hypertension, malignancy, infection, infusion reactions, pregnancy (female only), and participants' partner pregnancy.

The history of clinical events is derived from the Medical History at enrollment in the Alexion PNH Registry CRF pages.

- History is defined as:
  - Yes—any record before or at the timepoint of interest with a "yes" response and/or a date of the event recorded
  - No—no record before or at the timepoint of interest has a "yes" response or a date of the event recorded, but there is at least one "no" recorded.
- Outcomes of events are the outcome at the time point of interest for participants with any history of the event at the time point of interest. For example, if a participant has a history of aplastic anemia at enrollment, the outcome of aplastic anemia will be either Ongoing, Resolved with sequelae, Resolved, or Missing as of the date of enrollment.
  - Outcomes for grouped events should present the outcomes in the following order of importance: Death, Ongoing, Resolved with sequelae, Resolved, Missing.
  - Example: if a participant has 2 TE subtypes, where one (e.g. renal vein thrombosis) has the outcome "Resolved" and the other (e.g. dermal thrombosis) has the outcome "Ongoing", the outcome for TE for that participant should be "Ongoing"
- History of BMD will include aplastic or hypoplastic anemia; myelodysplastic syndromes; acute myelogenous leukemia; myelofibrosis; and other bone marrow pathology. The "Event Detail" of BMD is the specific CRF item in this list.
- Comedications and treatments at Ultomiris initiation
  - Concomitant medications or treatments reported in the 6 months prior to Ultomiris initiation and include anticoagulation therapy, immunosuppressant therapy, analgesics, oral prophylactics, RBC transfusion.
  - Concomitant medications or treatments will be 1) "Yes" if there is a yes response to the yes/no question at an assessment date within the 6 months prior to and including the timepoint of interest, or if there are any start dates or end dates within the six months prior to and including the timepoint of interest or 2) "No" if neither of the above is true, and there is at least one no response to the yes/no question at an assessment date within the 6 months prior to and including the timepoint of interest.
  - Special case: if the timepoint of interest is initiation of Ultomiris and it is prior to enrollment. In this situation, a "Yes" response is applied just as above, but a "No" response can be provided if the criteria for a "Yes" response are not met, and either 1)

the value reported at enrollment is a "No", or 2) the value reported at enrollment is a "Yes" but the start date is greater than the date of Ultomiris use.

- History of RBC transfusions has a special situation: "History of RBC" can only be presented at enrollment and each semi-annual follow-up. "History of RBC" at initiation of Ultomiris if a participant started Ultomiris prior to enrollment in the Alexion PNH Registry, or any other time points prior to enrollment in the Registry cannot be calculated.
- "Any immunosuppressant therapy" includes cyclosporine and anti-thymocyte globulin; corticosteroids are not included in this category.

1.3.2.2. Laboratory measures

Laboratory values include glycophosphatidylinositol (GPI)-deficient granulocytes, GPI-deficient erythrocytes, lactate dehydrogenase (LDH), LDH ratio, hemoglobin, haptoglobin, platelets, serum creatinine, estimated glomerular filtration rate (eGFR), absolute reticulocytes, total red blood cell (RBC), and total white blood cell (WBC).

- See Appendix 2: Lab min/max values for analyzable data for laboratory outliers
- To be considered at the timepoint of interest (i.e., Ultomiris initiation), the date of the laboratory value must be within 6 months prior to and including the timepoint of interest.
- Except for GPI-Deficient granulocytes and erythrocytes, laboratory values are found on 4 different CRFs ("Lab Tests at Enrollment", "Lab Tests at Initiation of Anti-Complement Treatment", "Lab Tests at Switching of Anti-Complement Treatments", "Lab Tests at Follow-up", which should all be used when looking for laboratory tests at given dates (at enrollment, at follow-up, at initiation of treatment for participants who started Soliris prior to enrollment in the Alexion PNH Registry, and at switching to other anti-complement treatment when participants switched treatment from Soliris prior to enrollment in the Registry).
- Reported GPI-Deficient granulocytes and erythrocyte values are found on the following CRFs: 1) Flow Cytometry at Diagnosis, 2) Flow Cytometry at Enrollment, 3) Flow Cytometry at Initiation of Anti-Complement Treatment, 4) Flow Cytometry at Switching of Anti-complement Treatments, and 5) Flow Cytometry at Follow-up forms.
    - For absolute reticulocytes, if there is no reported value but there is a percent reticulocyte and RBC count on the same day, calculate absolute reticulocytes as:
        - Absolute reticulocyte count (thou/µL) = reticulocyte % (#/100) x RBC count (mill/µL) x 1000
    - eGFR is calculated according to Appendix 3: eGFR Calculations:
        - eGFR is calculated from serum creatinine using the Chronic Kidney Disease Epidemiology Collaboration (CKD-Epi) equation for participants 18 years or older and using the Schwartz equation for participants under 18 years of age

1.3.3. Covariates

The following variables will be used in the multivariable regression models described in Section 5.3.2:

- History of BMD at baseline
  - "Yes" --participant has a record of any of the following on or before baseline: Aplastic or Hypoplastic Anemia, Acute Myelogenous Leukemia; Myelodysplastic Syndrome (MDS); Myelofibrosis; and other bone marrow pathology,
  - "No"— participant does not meet either of the above categories, but has at least one "no" response to any of the following on or before the time point of interest: Aplastic or Hypoplastic Anemia, Acute Myelogenous Leukemia; MDS; Myelofibrosis; and other bone marrow pathology
- History of Aplastic Anemia at baseline
  - "Yes" --participant has a record of Aplastic Anemia before baseline.
  - "No"— participant does not meet the above criteria, but has at least one "no" response to any of the following on or before the time point of interest: Aplastic or Hypoplastic Anemia, Acute Myelogenous Leukemia; MDS; Myelofibrosis; and other bone marrow pathology
- Use of Immunosuppressive concomitant medication at baseline
  - The concomitant medications CRF pages collect information on the use of cyclosporine, corticosteroids and antithymocyte globulin (ATG) separately. For purposes of the assessment of the confounder for the multivariable modelling, use of any of these 3 immunosuppressive medications will count towards Immunosuppressive medication use.
- History of TE at baseline
  - As described in Section 1.3.2.1
- History of MAVEs at baseline
  - As described in Section 1.3.2.1

These variables will be added to the regression model alongside gender, age at baseline (as defined in Section 1.3.4) and LDH at baseline.

1.3.4. Additional Variables of Interest

- PNH Disease start
  - Earliest of: Date of first reported PNH symptom, Date of first detected GPI-Deficient Granulocytes, or PNH diagnosis date.
- Age Group at 1) Enrollment, 2) PNH disease start, 3) Ultomiris initiation
  - <2 years
  - 2 to <12 years
  - ≥12 to <18 years

  - 18 to <30 years
  - 30 to <50 years
  - 50 to <65 years
  - 65+ years
- Gender
- Race
- Ethnicity
- Discontinuation from the Alexion PNH Registry
  - Any participant who reports either 1) a reason for discontinuation from the Registry, or 2) a date of discontinuation from the Registry, or 3) is indicated as having died (defined in Section 1.2.2), is defined as being discontinued from the Registry. Every participant should have a yes/no value; no participant should be missing this variable.
  - For a participant who has died (based on definition in Section 1.3.1.2) the date of death is the date of discontinuation from the Registry. If date of death is missing, the discontinuation date will be used, otherwise the date of discontinuation is missing. For a participant who did not die, the date of discontinuation from the Registry is the date reported on the "Registry Discontinuation" CRF page. Only participants who have a "yes" to having discontinued from the Registry are eligible here.
  - Reason for discontinuation from the Registry is reported on the "Registry Discontinuation" CRF directly. Only participants who have a "yes" to having discontinued from the Registry are eligible here.
- Discontinuation from Ultomiris treatment
  - Only participants ever treated with Ultomiris will have discontinuation from Ultomiris defined. If a participant has the most recently reported dose date with "mark if final dose" checked (regardless if first dose, or a later dose, of Soliris), OR if a participant has a reason for Ultomiris discontinuation reported, then the participant is defined as discontinued from Ultomiris. Otherwise, the participant will be defined as not discontinued from Ultomiris. Every participant ever treated with Ultomiris should have a yes/no value; no participant should be missing this variable.
  - Date of discontinuation is the associated "dose date" if it is the latest dose date and "mark if final dose" is checked. Only participants who are defined as discontinued from Ultomiris will have a date of discontinuation. Some discontinued participants may be missing a date of discontinuation. (Note that if date of discontinuation of Ultomiris is missing, then the date of last Ultomiris treated follow-up is also missing, by definition).
  - Reason for Ultomiris discontinuation is reported on the Discontinuation of Ultomiris CRF form. The reasons will be grouped to the following categories:

death, patient choice, adverse event, lack of efficacy, physician decision, switch to other anti-complement treatment, cost or access consideration, enrollment in the IPIG PNH Registry, or unknown (for participant missing a reason for discontinuation).

- Weight at Initiation of Ultomiris
  - Weight at Ultomiris start if available; if not available, first reported weight after initiation of Ultomiris
  - Continuous variable, and also categorized into:
    <40 kg
    40 to <60 kg
    60 to <100 kg
    >=100 kg Ultomiris Dose
  - First Dose
    - Categorized as 2400 mg, 2700 mg, 3000 mg, or Other
  - Subsequent Doses
    - Categorized as 1) all doses after first dose reported as < 3000 mg/8 weeks, 2) all doses reported as ≥ 3000 to <3300 mg/8 weeks, 3) all doses reported as ≥ 3300 to < 3600 mg/8 weeks, 4) all doses = 3600 mg/8 weeks, 5) all doses > 3600 mg/8 weeks or 6) other/unknown (Note: anything not captured as in the aforementioned categories including missing subsequent doses will be categorized as "other/unknown").
  - Last Dose
    - Categorized as 3000 mg, 3300 mg, 3600 mg, or Other
    - If the treatment log reflects only initial dose amounts, and there are no further records indicating the final dose amount, then it is assumed that last recorded dose amount is continued throughout the participant's entire final treatment period. In this case, the last recorded dose will be carried forward and reported as the last dose.

2. STATISTICAL HYPOTHESES

This is a descriptive analysis with no prespecified hypotheses.

3. SAMPLE SIZE DETERMINATION

N/A

4. ANALYSIS SETS

Analysis will be performed using 06 Jan 2025 data download.

5. STATISTICAL ANALYSES

5.1. Inclusion/Exclusion Criteria

The population for this analysis will include participants who meet the following inclusion criteria:

- Enrolled in the Alexion PNH Registry with valid Patient ID as of 06 Jan 2025 data download
- With known date of birth, sex, enrollment date, and Ultomiris treatment status
- Only participants initiating Ultomiris on or after enrollment will be included in the Ultomiris analysis population
- Only participants initiating Soliris on or after enrollment will be included in the Soliris only analysis population

Note: Frequent treatment switchers, defined as participants who switched their treatment with Soliris or Ultomiris more than once, will not be included in the analysis, e.g. participant switched from Soliris to Ultomiris and then switched back to Soliris will not be included in the descriptive profile of participants at baseline and analyses of disease outcomes. Listings of frequent treatment switchers will be generated *and provide demographics, disposition at last registry follow-up, treatment information characteristics, and SAEs.*

5.2. Statistical Methods

5.2.1. General Considerations

If there is more than 1 assessment with multiple dates within the window of interest, the value closest to the date of interest will be used. If there are pre- and post- equally close values, the pre- value will be used for analysis.

For continuous variables, if there are multiple values on the same date, the mean of the values will be taken.

For categorical variables, if there are multiple conflicting values on the same date, the value on that date will be set to missing.

Participant demographics, medical history, clinical events, laboratory values, concomitant medication, prior treatment with Soliris, and Ultomiris dose will be summarized at initiation of Ultomiris using descriptive analyses.

Treatment and registry discontinuation along with associated reasons, pregnancy and fetal outcomes, and SAEs collected during registry follow-up will also be summarized.

Continuous variables will be characterized with number of non-missing observations, mean and standard deviation, median and interquartile range, minimum and maximum, and number of missing data. Categorical variables will be characterized by the frequency and percent distribution in each category for non-missing data and missing data, as appropriate. The analysis will include 95% confidence intervals of means and percentages, as appropriate

Medical history, clinical events, laboratory values, and concomitant medication will be summarized at initiation of Ultomiris. The following variables will be summarized during the follow-up period:

- Registry discontinuation and the reasons for last Registry follow up
- Ultomiris discontinuation and the reasons for the treatment discontinuation
- Causes of death

Note regarding Output Displays: *Outputs utilize the generic names ravulizumab and eculizumab.*

5.3. Endpoint Analyses

5.3.1. Event Rates

Clinical events, including death, MAVE, TE, non-TE MAVE, infection, malignancy, impaired renal function, impaired hepatic function, Ultomiris infusion reactions, pulmonary hypertension, and bone marrow transplant will be summarized by event rates based on the exposure period defined in Section 1.2.2. Pregnancy outcomes will also be summarized by the exposure period as defined in Section 1.2.2.

Event Rates are calculated by:

- The total number of events and the total person-years during the follow-up period of interest will be determined. The event rate will be the number of events divided by the person-years. Person-years are calculated per the definition of exposure period as defined in Section 1.2.2 for all participants included in the study population, regardless of whether they had an event. The event rate will be calculated using Poisson regression with over-dispersion (See Section 5.3.3) or generalized estimating equations with a log link, as is appropriate.

See Appendix 4 for the example SAS code for event rates and rates difference estimation.

5.3.1.1. Subgroup Analyses

Participants ever treated with Ultomiris in the study population will be stratified by the following subgroups:

- Participants with untreated person time
  - Baseline will be defined as enrollment
- Treated with Ultomiris
  - Baseline will be defined as initiation of Ultomiris
- Treated with Soliris (Prior to Ultomiris Switch)

- Only includes participants with prior Soliris status
- Baseline will be defined as initiation of Soliris

In addition to the above groups, incidence rate analyses will also be performed on participants treated with Soliris only

- Soliris only treated participants
  - Baseline will be defined as initiation of Soliris

Note: All person-time on treatment will be treated as "treated person-time" and person-time not on treatment will be treated as "untreated person time". Therefore, some participants may contribute to both treated and untreated person time. This is a standard epidemiologic approach used in studies to calculate time at risk.

5.3.2. Covariates for Multivariable regression models

The following analysis will employ the indicated covariates, assessed at baseline (as defined in Section 5.3.1.1), in order to control for potential confounding in the rate models:

1. Analysis of infections will use age, gender, history of aplastic anemia at baseline, and use of immunosuppressive concomitant medication at baseline as covariates
2. Analysis of MAVEs/TEs/Non-TE MAVEs will use age at baseline, gender, LDH at baseline, and history of MAVEs at baseline as covariates
3. Analysis of malignancies will use age, gender, history of BMD at baseline as covariates

5.3.3. Statistical Models

Two models will be fitted for the analyses: 1) Unadjusted; 2) Adjusted for all the covariates mentioned above in Section 5.3.2.

SAS procedure PROC GENMOD will be conducted to run the multivariable regression analyses with the MODEL statement as following:

- Unadjusted models:

  model Y = Treatment /dist=Poisson link=log offset = LN;

- Adjusted models:

  model Y = Treatment + Covariates (see section 5.3.2) /dist=Poisson link=log offset = LN;

See Appendix 4 for the example SAS code for event rates.

5.3.4. Conventions

For tables, sample size for each population (as described in Section 1.2.1) will be presented as totals in the column header (N=xxx), where appropriate. Only participants with a known value (i.e., not "missing") will be presented in the subpopulations; therefore, the n's for subpopulation headers may not add up to the total of "All Patients". "All Patients" will include all participants in the study population, regardless of whether they have a known value for the subpopulations

present.

Sample sizes shown with summary statistics (for either categorical or continuous variables) are the number (n) of participants with non-missing values. Therefore, the n for each variable in a table may be smaller than the N in the column header.

Descriptive analyses (means [standard deviation (SD)] or medians [min, max] or [first quartile (Q1), third quartile (Q3)]) for continuous variables; frequencies and percentages for categorical variables.

5.4. Sensitivity Analysis

Having a clone size of at least 1% is an inclusion criterion for enrollment into the Alexion PNH Registry and is an inclusion criterion in ALX-PNH-501. While almost all subjects with available data for clone size meet this criterion, a significant proportion of Ultomiris treated subjects do not have a clone size laboratory value recorded within 6 months of enrollment (roughly 25%). Because of this, a sensitivity analysis will be conducted which will exclude subjects missing clone size at enrollment, and subjects with clone size <1% at enrollment.

The sensitivity analysis will repeat the rate analyses for the cumulative period for the following events: MAVEs, TEs, Malignancies, Infections, Impaired Renal and Hepatic function, Pulmonary Hypertension, Pregnancy, Bone Marrow Transplant, and Deaths. Restricting these analyses to subjects with a known clone size ≥1% at enrollment will be applied to all Ultomiris treated participants, as well as Soliris treated subject, and subjects with untreated person-time.

6. DATA IMPUTATION METHOD

6.1. Data imputation rules

Do not impute a date if year is missing.

If year is not missing, then:

1) if day is missing, then impute with 15;
2) if month is missing then impute with 6;

7. REFERENCES

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8. TABLES, LISTINGS, AND FIGURES (TLF)

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APPENDICES

APPENDIX 1: Statistical Analysis Plan for International PNH Interest Group Registry (IPIG PNH Registry) Data

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1. RATIONALE

The IPIG PNH Registry is comprised of the Core PNH disease Registry (Core Registry) and several product-specific silo protocols initiated by IPIG on request by the respective marketing authorisation holders (MAHs). Core variables will be collected in the Core Registry at enrollment and during follow-up, while specific data (e.g., safety data) for participants treated with PNH-specific therapies will be collected in the silos to address specific objectives or requests from regulatory authorities and MAHs. Participants enrolled in the IPIG PNH Registry, who are treated with Alexion products including Soliris® and Ultomiris® are enrolled in the Alexion Products Silo.

Data within the IPIG PNH Registry consists of data collected at registry enrollment and prospectively through follow-up. Additionally, for IPIG Registry participants who have participated in the Alexion PNH Registry and have consented to sharing their Alexion PNH Registry data with IPIG, retrospective data collected prior to IPIG PNH Registry enrollment will also be assessed.

This Statistical Analysis Plan (SAP) describes the analytical plan for participants enrolled in the IPIG PNH Registry meeting the inclusion/exclusion criteria specified in ALX-PNH-501 study protocol.

2. DEFINITIONS

2.1.1. Inclusion and Exclusion Criteria

The study population for this analysis will include participants enrolled in the IPIG PNH Registry Alexion Products Silo who meet the following inclusion/exclusion criteria.

2.1.1.1. Inclusion Criteria

- Enrolled in the IPIG PNH Registry Alexion Products Silo with valid Patient ID as of 13 Jan 2025 data download date
- With known date of birth, sex, enrollment date, and Ultomiris treatment status
- Only participants initiating Ultomiris on or after enrollment will be included in the Ultomiris analysis population. This condition can be met in two ways and is illustrated in Figure 1:
    - Participants previously enrolled in the Alexion PNH Registry who initiated Ultomiris during their participation in the Alexion PNH Registry and did not have a record of treatment.
    - Participants not previously enrolled in the Alexion PNH Registry, or who did not initiate Ultomiris while enrolled in the Alexion PNH Registry, but who initiate Ultomiris on or after enrollment in the IPIG PNH Registry

2.1.1.2. Exclusion Criteria

- Frequent Treatment Switchers will be excluded

Note: Frequent treatment switchers, defined as participants who switched their treatment with Soliris or Ultomiris more than once, will not be included in the analysis, e.g. participant switched from Soliris to Ultomiris and then switched back to Soliris will not be included in the descriptive profile of participants at baseline and analyses of disease outcomes. Listings of frequent treatment switchers will be generated *and provide demographics, disposition at last registry follow-up, treatment information characteristics, and SAEs.*

2.1.2. IPIG PNH Registry and prior treatment experience in Alexion PNH Registry

Participants meeting the inclusion and exclusion criteria will be classified into two groups based on the time of Ultomiris initiation:

1. Alexion PNH Registry Study Population

   Participants previously enrolled in the Alexion PNH Registry and who initiated Ultomiris during their participation in the Alexion PNH Registry.

2. IPIG PNH Registry Study Population

   Participants who initiated Ultomiris on or after enrollment in the IPIG PNH Registry irrespective of their participation in the Alexion PNH Registry.

Baseline data (i.e., data collected at Ultomiris treatment initiation) for the Alexion PNH Registry Study Population is presented within the Alexion PNH Registry outputs. Therefore, tables and listings tied to this SAP and focusing on baseline data (i.e., history of medical events and

concomitant medications, demographics, laboratory values, Ultomiris treatment information) will be presented only for participants from the IPIG PNH Registry Study Population.

Where appropriate, the tables and listings will present the combined population of Alexion PNH Registry Study Population and the IPIG PNH Registry Study Population. This combined population will be referred to as the Ultomiris Study Population (Figure 2). It is important to note that only prospective data collected within the IPIG PNH Registry will be presented in the tables for the combined Ultomiris Study Population.

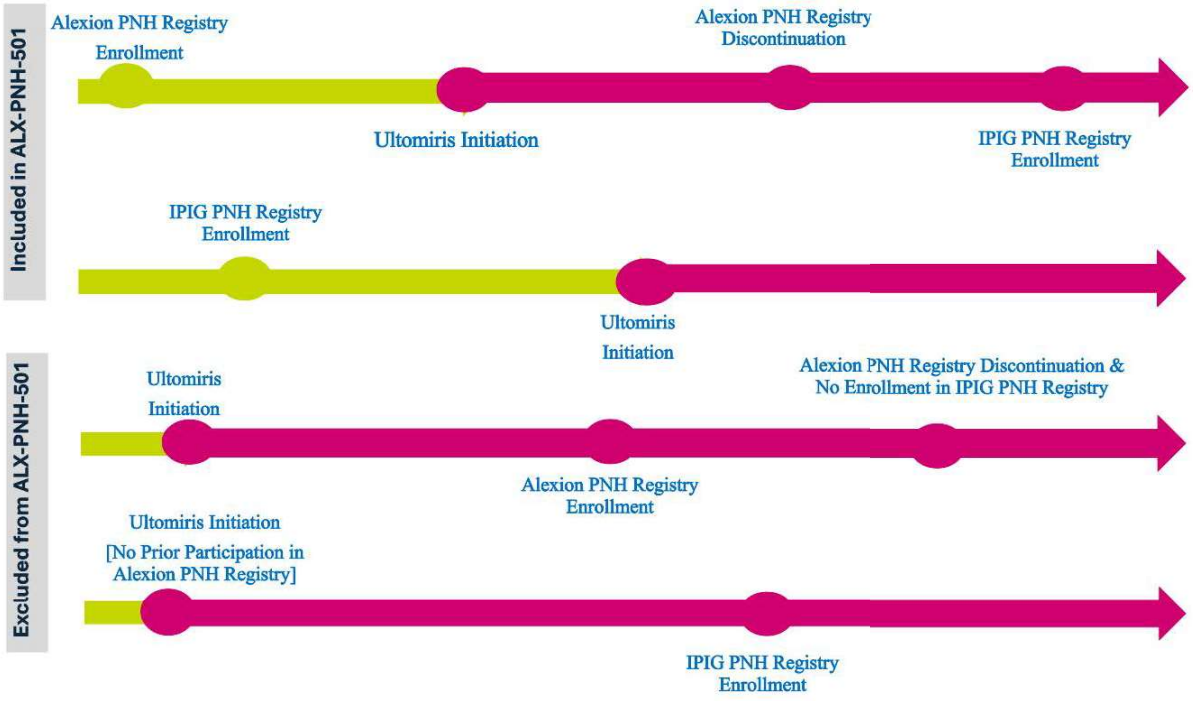

Figure 2. IPIG PNH Registry participants inclusion in ALX-PNH-501 analysis.

2.1.3. Treatment Status Definitions

Participants will be classified according to their treatment status as follow, where "registry enrollment" refers to enrollment in either Alexion or IPIG PNH Registry:

- **Treated with Ultomiris**: participant has a known date of Ultomiris initiation on or after registry enrollment
- **Prior Soliris treatment**: participant treated with Soliris, discontinued Soliris within less than 28 days of Ultomiris initiation, and switched treatment to Ultomiris once on or after registry enrollment

- **Without prior Soliris treatment**: participant initiating Ultomiris on or after registry enrollment and never treated with Soliris before Ultomiris initiation, or Soliris was discontinued at least 28 days prior to Ultomiris initiation
- **Prior Soliris treatment unknown**: participant initiating Ultomiris on or after registry enrollment and with Soliris treatment status uncertain based on the data reported in registry (e.g. missing Soliris treatment end date).

The summary of participant demographics, participant disposition, vital status at last registry follow-up, and the registry follow-up duration will be presented by treatment status. Information collected at Ultomiris initiation, such as medical history, concomitant medication, and laboratory values will be also summarized by treatment status.

2.1.4. Exposure Periods Definitions

The following exposure periods during registry follow-up will be used in the clinical event listings to indicate the treatment status at the time of the event, and are defined as follows:

- **Untreated period** — participants initiating any anti-complement treatment (including Soliris, Ultomiris, or other anti-complement treatment) after enrollment in the IPIG PNH Registry will have an untreated period during which clinical events may be reported in listings. This period will include the time from enrollment to last untreated follow-up date (as defined in Section 2.1.5). Because participants in the study population have initiated treatment with Ultomiris either in the Alexion PNH Registry or on/after enrollment in the IPIG PNH Registry, untreated person-time is expected to be minimal or null.
- **Treated with Soliris** (prior to Ultomiris switch) (Soliris exposure period) —participants switching treatment from Soliris to Ultomiris only once will have time in this category during which events may occur and be reported in the listings. The Soliris exposure period is from Soliris initiation date to last Soliris treated follow-up date (as defined in Section 2.1.5).
- **Treated with Ultomiris** (Ultomiris exposure period) — any participants ever-treated with Ultomiris will have time in this category during which events may occur and be reported in the listings. The Ultomiris exposure period covers the period from Ultomiris initiation date to last Ultomiris treated follow-up date (as defined in Section 2.1.5).

2.1.5. Time Points of Interest

- Initiation of Ultomiris, defined as first record of Ultomiris treatment
- Initiation of Soliris, defined as first record of Soliris treatment
- Date of Enrollment, defined as date of enrollment in the IPIG PNH Registry
- Last Registry follow-up date: last follow-up is defined by the first reported date of death, date of bone marrow transplant, or date of discontinuation from the IPIG PNH Registry.

In participants not meeting any of these criteria, last follow-up date is 13 Jan 2025, the date of the data download from the IPIG PNH Registry.

- Last Ultomiris treated follow-up date: If an ever-treated participant has a record of discontinuation of Ultomiris, the date of last Ultomiris treated follow-up is the minimum of 16 weeks after the date of discontinuation of Ultomiris, or current data download date. If an ever-treated participant has no record of discontinuation of Ultomiris, last Ultomiris treated follow-up is the same as last IPIG PNH Registry follow-up date.
- Last Soliris treated follow-up date: This is only for participants switching treatment from Soliris to Ultomiris only once. The date of last Soliris treated follow-up is defined as the minimum of 1) 4 weeks after the date of discontinuation of Soliris or 2) 1 day prior to Ultomiris treatment start date or 3) Last IPIG PNH Registry Follow-up date.
- Last untreated follow-up date: this is only defined for participants untreated at enrollment in the IPIG PNH registry; it is missing for all other participants. Defined as one day prior to the date of first initiation of Soliris or Ultomiris for participants who started treatment after enrollment in IPIG PNH Registry.

2.1.6. Analysis period

All clinical and adverse events from IPIG PNH Registry enrollment until last registry follow-up will be considered when reporting study outcomes and variables summaries during the exposure periods, as defined in Section 2.1.4. Thus, there is no separate analysis period from the cumulative data.

2.1.7. Outcomes of Interest

2.1.7.1. Clinical and Adverse Events

The reporting of clinical and adverse events will include participants from the full Ultomiris Study Population. For those previously enrolled in the Alexion PNH Registry and who initiated Ultomiris prior to IPIG PNH Registry enrollment, any clinical or adverse event report from IPIG PNH Registry enrollment through data cut off will be included in the tables. For participants included in the IPIG PNH Registry Study Population (who initiated Ultomiris on or after IPIG PNH Registry enrollment), clinical or adverse events occurring on or after Ultomiris initiation will be reported in the tables.

Clinical and Adverse Events are collected in the following CRF forms:

- Clinical Events and outcomes
- Major Adverse Vascular Event
- Bone Marrow Transplant Form
- Infection
- Pregnancy
- Bone Marrow Pathology or Other Hematological Disorder Form
- Malignancies Form

- Adverse Event
- Severe Hepatic Impairment Characterization
- Study completion/termination or subject withdrawal of consent form
- Potential Breakthrough Hemolysis

Descriptive statistics, including counts of subjects with events and percent of total, will be presented for the following clinical events of interest collected in these forms:

1. Deaths

   Information on deaths is collected on the "Study completion/termination or subject withdrawal of consent form", as well as in the details of several other clinical events forms. Cause of death is recorded on the Clinical Events and Outcomes form.

2. Major Adverse Vascular Event (MAVEs)

   The Major Adverse Vascular Event form collects information on the following potential MAVEs:

   - Acute Peripheral Vascular Occlusion
   - Cerebral Arterial Occlusion/CVA
   - Cerebral Venous Occlusion
   - Dermal Thrombosis
   - Hepatic/portal vein thrombosis
   - Mesenteric/visceral arterial thrombosis
   - Mesenteric/visceral vein thrombosis
   - Myocardial Infarction
   - Pulmonary Embolus
   - Renal Arterial Thrombosis
   - Renal Vein Thrombosis
   - Thrombophlebitis/Deep Vein Thrombosis
   - Transient Ischemic Attack
   - Other Major Adverse Vascular Event

   When "Other Major Adverse Vascular Event" is selected, the free-text field indicating the specific type of MAVE will be provided in the tables and listings.

3. Infections

   The Infection form collects information on the following types of infections:

   - Neisseria meningitidis
   - Streptococcus pneumoniae
   - Haemophilus influenzae
   - COVID
   - Other

   When "Other" is selected, the free-text field indicating the specific type of infection will be provided in the tables and listings.

4. Malignancies

   The Malignancies Form collects information on the following types of malignancies:

   - Lung
   - Breast
   - Colorectal
   - Prostate
   - Stomach
   - Liver
   - Ovarian
   - Other

   When "Other" is selected, the free-text field indicating the specific type of malignancy will be provided in the tables and listings.

5. Impaired renal function

   Impaired renal function is reported at enrollment and at each follow-up visit in the Clinical Events and outcomes.

6. Impaired hepatic function

   Impaired hepatic function is reported at enrollment and at each follow-up visit in the Severe Hepatic Impairment Characterization form.

7. Ultomiris infusion reactions

   Infusion reactions are collected in the Adverse Events form. Details of infusion reactions include:

   - Anaphylaxis
   - Anaphylactoid reaction
   - Infusion site irritation
   - Local pruritis
   - Rash (non itchy)
   - Pruritus generalized
   - Rash pruritic
   - Urticaria
   - Hypotension
   - Drug hypersensitivity
   - Other

   When "Other" is selected, the free-text field indicating the specific type of infusion reaction will be provided in the tables and listings.

   These events are reported at enrollment and at each follow-up visit and will be reported in the Medical History table as well as the Clinical and Adverse Events table.

8. Pulmonary hypertension

   Pulmonary hypertension is reported at enrollment and at each follow-up visit in the Clinical Events and Outcomes form.

9. Bone Marrow Disorder

   Bone marrow disorders are reported at enrollment and at each follow-up visit in the Bone Marrow Pathology or Other Hematological Disorder Form, and include the following events

   - Acute Myelogenous Leukemia
   - Aplastic or Hypoplastic Anemia
   - Myelodysplastic Syndrome
   - Myeloproliferative neoplasm
   - Autoimmune hemolytic anemia (AIHA)
   - Idiopathic thrombocytopenic purpura (ITP)
   - Thrombotic thrombocytopenic purpura (TTP)
   - Antiphospholipid syndrome (APS)
   - Other

   When "Other" is selected, the free-text field indicating the specific type of bone marrow disorder will be provided in the tables and listings.

10. Bone marrow transplant.

    Bone marrow transplants are reported at enrollment and at each follow-up visit in the Bone marrow Transplant form.

11. Pregnancy, Exposure During Lactation, and Neonatal Follow-up

    Pregnancies, exposure during lactation, and neonatal follow-up are reported at IPIG PNH Registry enrollment and at each follow-up visit in the Pregnancy form. The exposure classification for the pregnancy outcomes will be based on the exposure status at the time of the pregnancy outcome and will not reflect the treatment exposure experienced throughout the entire pregnancy.

12. Potential Breakthrough Hemolysis

    Potential Breakthrough Hemolysis is reported at enrollment and at each follow-up visit in the Potential Breakthrough Hemolysis CRF page

2.1.7.2. Medical History

Since participants' medical history prior to Ultomiris initiation have already been reported for the Alexion PNH Registry Study Population, the medical history table will only include subjects from the IPIG PNH Registry Study Population. Refer to Section 2.1.2 for a discussion of the Study Populations and further rationale for the exclusion of the Alexion PNH Registry Study Population from the reporting of medical history.

For the IPIG PNH Registry Study Population, medical history will include any medical event occurring prior to Ultomiris initiation, which occurred on or after IPIG enrollment. These events may include bone marrow disorder (BMD), major adverse vascular events (MAVEs), impaired renal function, impaired hepatic function, pulmonary hypertension, malignancy, infection, infusion reactions, pregnancy and potential breakthrough hemolysis.

Similar to Clinical and Adverse Events, descriptive statistics, including counts of subjects with events and percent of total, will be presented for all events occurring prior to enrollment or Ultomiris initiation, whichever is later.

2.1.7.3. Medical Event Listings

The listings of medical events will include events that contribute to the Clinical and Adverse events table.

Details of clinical events such as outcomes and seriousness are not reported on all CRF pages. When available, however, the following details of these events will be reported in the listings:

Seriousness:
When available, an event will be classified as serious in the CRF page with a response of Yes/No. When "Yes" is selected, the event will be further characterized as follow:

- Results in Death of patient.
- Is life-threatening
- Requires or Prolongs Hospitalization
- Is a congenital anomaly/birth defect
- Results in persistent or significant disability/incapacity
- Is a medically important event or reaction

When more than one of the above details is indicated in the CRF page, all details of the seriousness will be concatenated and presented in the listing

Outcomes:
Outcomes of events are not reported on every clinical event CRF page, but when available the outcome of events will be reported with the following possible outcomes:

- Fatal
- Not resolved
- Resolved
- Resolved with sequelae
- Resolving
- Unknown Start date of AE

Additional details of clinical events:

When available, the following details of the clinical events will also be reported:

- Start and end dates (if resolved)

- Treatment status at time of event
- MedDRA reported Body System

2.1.7.4. Comedications and treatments at Ultomiris initiation

Concomitant medications taken within 6-months prior to IPIG PNH Registry enrollment or Ultomiris initiation, whichever is later, will be summarized in table format. All records of concomitant medications prior to Ultomiris initiation have been previously documented for the Alexion PNH Registry study population, hence the comedications and treatment at Ultomiris initiation will only be presented for the IPIG PNH Registry Population.

Categories of medication as collected on the CRF include:

- Anticoagulation therapy
- Antibiotic prophylaxis
- Growth factors
- Immunosuppression
- Thrombopoietin receptor agonists
- Iron chelation therapy
- Vaccinations

In addition to the above categories, counts and percentage of medications used at the participant level will be presented based on the Anatomic Therapeutic Chemical (ATC) class and medication name. Only categories with at least one reported usage will be presented.

2.1.7.5. Laboratory measures

Laboratory values will be summarized with mean values and standard deviation, as well as with the median and inter-quartile range. Similar to other baseline characteristics, laboratory values will be presented only for the IPIG PNH registry study population as described in section 2.

The following laboratory values will be presented, with the units indicated:

- Percent GPI-deficient granulocytes
- LDH (U/L)
- LDH ratio (x ULN)
- Hemoglobin (g/dL)
- Haptoglobin (µmol/L)
- Platelets ($x10^9$/L)
- Serum creatinine (µmol/L)
- eGFR (mL/min/1.73 m^2)
- Absolute neutrophils ($x10^9$/µL)
- Absolute reticulocytes ($x10^9$/L)
- Total WBC ($x10^9$/L)

In addition, counts and percents will be presented for the following categorizations of laboratory values:

- Percent GPI-deficient granulocytes will be categorized into the following groupings: <1%, >=1% to <10%, ≥10% to <50%, and ≥50%.
- LDH will be categorized into less than 1.5 ULN and greater than or equal to 1.5 ULN.
- eGFR will be categorized into the following groupings: <30, 30 to <60, 60 to <90, ≥90 mL/min/1.73 m^2

See Appendix 2: Lab min/max values for analyzable data for laboratory outliers, as well as conversion factors for laboratory values recorded using different units.

To be considered for reporting in the laboratory value table, the date of the laboratory value must be within 6 months prior to IPIG PNH Registry enrollment or Ultomiris initiation, whichever is later.

2.1.7.6. Additional Variables of Interest

- PNH Disease start
  - Earliest of: Date from either the Alexion or IPIG PNH Registry of first reported PNH symptom, first detected GPI-Deficient Granulocytes, or Enrollment date, as well as the PNH diagnosis date from the Alexion PNH Registry.
- Age Group at 1) Enrollment, 2) PNH disease start, 3) Ultomiris initiation
  - <2 years
  - 2 to <12 years
  - ≥12 to <18 years
  - 18 to <30 years
  - 30 to <50 years
  - 50 to <65 years
  - 65+ years
- Gender
- Race
- Ethnicity
- Discontinuation from the Registry
  - Participants will be treated as discontinued from the IPIG PNH Registry when the "Study completion/termination or subject withdrawal of consent" CRF page is completed,
  - Reason for discontinuation from the Registry and discontinuation date are both collected on the "Study completion/termination or subject withdrawal of consent" CRF page. This information will be reported in the tables and listings as appropriate.
- Discontinuation from Ultomiris treatment

- Only participants ever treated with Ultomiris will have discontinuation from Ultomiris defined.
- Date of discontinuation is collected on the Treatment History CRF form for Anti-Complement Therapy.
- Reason for Ultomiris discontinuation is reported on the Treatment History form with the following categories:
  - Patient decision
  - Physician decision
  - Intolerability
  - Cost/Access
  - Switch to another therapy
  - Lack of efficacy
  - Adverse event
  - Compliance issues
  - Death
  - Other

- Weight at Initiation of Ultomiris
  - Weight at Ultomiris start if available; if not available, first reported weight after initiation of Ultomiris
  - Continuous variable, and also categorized into:
    <40 kg
    ≥ 40 kg
  - First Dose
    - Categorized as 2400 mg, 2700 mg, 3000 mg, or Other
  - Subsequent Doses
    - Categorized as 1) all doses after first dose reported as < 3000 mg/8 weeks, 2) all doses reported as ≥ 3000 to <3300 mg/8 weeks, 3) all doses reported as ≥ 3300 to < 3600 mg/8 weeks, 4) all doses = 3600 mg/8 weeks, 5) all doses > 3600 mg/8 weeks or 6) other/unknown (Note: anything not captured as in the aforementioned categories including missing subsequent doses will be categorized as "other/unknown").
  - Last Dose
    - Categorized as 3000 mg, 3300 mg, 3600 mg, or Other
    - If the treatment log reflects only initial dose amounts, and there are no further records indicating the final dose amount, then it is assumed that last recorded dose amount is continued throughout the participant's entire final treatment period. In this case, the last recorded dose will be carried forward and reported as the last dose.

3. ANALYSIS SETS

For this analysis, the SDTM domains will utilize the raw data extract on 13 Jan 2025, as indicated in the ADS datasets.

Analysis will be performed using data collected from 21 May 2024 to 13 Jan 2025 data download.

4. STATISTICAL ANALYSES

4.1. Statistical Methods

4.1.1. General Considerations

If there is more than 1 assessment with multiple dates within the window of interest, the value closest to the date of interest will be used. If there are pre- and post- equally close values, the pre-value will be used for analysis.

For continuous variables, if there are multiple values on the same date, the mean of the values will be taken.

For categorical variables, if there are multiple conflicting values on the same date, the value on that date will be set to missing.

Note that "missing" is a possible response for every variable; Tables, Listings and Figures computed for this analysis.

Participant demographics, medical history, clinical events, laboratory values, concomitant medication, prior treatment with Soliris, and Ultomiris dose will be summarized at initiation of Ultomiris using descriptive analyses.

Treatment and registry discontinuation along with associated reasons, pregnancy and fetal outcomes, and SAEs collected during registry follow-up will also be summarized.

Continuous variables will be characterized with number of non-missing observations, mean and standard deviation, median and interquartile range, minimum and maximum, and number of missing data. Categorical variables will be characterized by the frequency and percent distribution in each category for non-missing data and missing data, as appropriate. The analysis will include 95% confidence intervals of means and percentages, as appropriate.

As the first participant in the Alexion Silo of the IPIG PNH Registry was enrolled 21 May 2024 and based on the total number of participants enrolled in this Silo at the time of data extraction (i.e., 13 Jan 2025 – see Section 3 for details), it is anticipated that less than 100 participants in the IPIG PNH Registry will meet the study eligibility criteria (Section 2.1.1). Further, follow-up data will be minimal as most participants would not have completed their first 6-month follow-up visit.

Note regarding Output Displays: *Outputs utilize the generic names ravulizumab and eculizumab*.

4.2. Endpoint Analysis

It is anticipated that minimal follow-up data are available for participants in the IPIG PNH registry. Therefore, clinical events, including death, MAVEs, infection, malignancy, impaired renal function, impaired hepatic function, Ultomiris infusion reactions, pulmonary hypertension, and bone marrow transplant will be described in frequencies based on the Treatment status defined in

Section 2.1.3, where deemed feasible. Otherwise, event details will be described through listings. Pregnancy outcomes will also be presented in a listing with treatment status as defined in Section 2.1.3.

4.2.1. Subgroup Analyses

A limited amount of person-time and events of interest are anticipated in the IPIG PNH Registry dataset analysis; hence event rates will not be estimated and subgroup analyses are not planned.

4.2.2. Conventions

For tables, sample size for each population will be presented as totals in the column header (N=xxx), where appropriate. Only participants with a known value (i.e., not "missing") will be presented in the subpopulations; therefore, the n's for subpopulation
headers may not add up to the total of "All Patients". "All Patients" will include all participants in the study population, regardless of whether they have a known value for the subpopulations present.

Sample sizes shown with summary statistics (for either categorical or continuous variables) are the number (n) of participants with non-missing values. Therefore, the n for each variable in a table may be smaller than the N in the column header.

Descriptive analyses (means [standard deviation (SD)] or medians [min, max] or [first quartile (Q1), third quartile (Q3)]) for continuous variables; frequencies and percentages for categorical variables.

5. DATA IMPUTATION METHOD

5.1. Data imputation rules

Do not impute a date if year is missing.

If year is not missing then:

1) if day is missing, then impute with 15;
2) if month is missing then impute with 6;

6. TABLES, LISTINGS, AND FIGURES (TLF)

Table 3. Tables, Listings, and Figures IPIG Registry

#	TLF #	TLF Title	Table Naming Convention
1	Table 1	Study Population	t1_pop_i
2	Table 2	Patient Demographics, by Treatment Status	t2_demo_i
3	Table 3	Patient Disposition at Last Registry Follow-Up Date, by Treatment Status	t3_disp_i
4	Table 4	Ultomiris Treatment Discontinuation	t4_ravudisc_i
5	Table 5	Ultomiris Treatment Information	t5_ravuinfo_i
6	Table 6	Patient Durations of Follow-Up, by Treatment Status	t6_dura_i
7	Table 7	Vital Status at Last Registry Follow-Up Date, by Treatment Status	t7_death_i
8	Table 8.1	Medical History at Ultomiris Initiation, by Treatment Status	t8_1_medhis_i
9	Table 8.2	Clinical and Adverse Events, by Treatment Status	t8_2_ae_i
10	Table 9	History of Concomitant Medication Use at Ultomiris Initiation, by Treatment Status	t9_cmhis_i
11	Table 10	Laboratory Values at Ultomiris Initiation, by Treatment Status	t10_labhis_i
12	Listing 1	Registry Discontinuation	l1_regdis_i
13	Listing 2	Discontinuation from Ultomiris	l2_ravudis_i
14	Listing 3	Deaths	l3_death_i
15	Listing 4	Major Adverse Vascular Events	l4_mave_i
16	Listing 5	Malignancy	l5_mal_i
17	Listing 6	Infection	l6_infect_i
18	Listing 7	Meningococcal Infection	l7_meningo_i
19	Listing 8	Impaired Renal Function	l8_irf_i
20	Listing 9	Impaired Hepatic Function	l9_ihf_i
21	Listing 10	Pulmonary Hypertension	l10_ph_i
22	Listing 11	Ultomiris Infusion Reactions	l11_rir_i
23	Listing 12	Pregnancy Outcome	l12_pregout_i
24	Listing 13	Bone Marrow Transplant	l13_bmt_i
25	Listing 14	All Serious Adverse Events and Special Events	l14_sae_i
26	Listing 15	Patient Information and Treatment Information	l15_patinfo_i
27	Listing 16	All Serious Adverse Events and Special Events: Frequent Treatment Switchers	l16_sae_fswitch_i

APPENDIX 2: Lab min/max values for analyzable data

Laboratory Test	Units	Conversion Factor	Lower Limit	Upper Limit
LDH	(U/L) (ukat/L)	None 59.88	100	10,000
LDH Ratio (LDH/Upper Limit Normal)	n/a	n/a	No limit	No limit
GPI-deficient granulocytes	%	n/a	0	100
GPI deficient erythrocytes - type II and III	%	n/a	0	100
Hemoglobin	(g/L) (g/dL) (mmol/L)	0.1 None 1.611	3	20.1
Haptoglobin	(g/L) (mg/dL) (µmol/L)	None 0.01 0.1	0.01	3
Total RBC	(x10^12/L) (10^6/uL)	None 1	2	8
Total WBC	(x10^9/L) (/µL)	None 0.001	0	75
Absolute neutrophils	(x10^9/L) (/µL)	1000 None	0	12000
Platelets	(x10^9/L) (10^3/µL)	None 1	10	800
Absolute reticulocytes	(x10^9/L) (10^3/µL)	None 1	0	1000
Reticulocytes	%	n/a	0	100
Serum creatinine	(µmol/L) (mg/dL)	None 88.402	17.6804	600
eGFR	(mL/min)	None	No limit	No limit

APPENDIX 3: eGFR Calculations

For every serum creatinine lab record available for analysis with a non-missing date, derive a new record for the eGFR parameter based on age at the serum creatinine lab date.

Set the eGFR value to missing for all records with missing involving data regardless of what is missing. The total number of eGFR records would match the number of serum creatinine lab records that are available for analysis.
Age at the serum creatinine lab date is calculated by the lab date - birthdate, in years. Records with missing birthdate a lab date prior to the birthdate will be set to missing for eGFR value.

If the subject is < 18 years at the date of lab test, use the peds formula ("Schwartz method") where height is in cm and sCr (serum creatinine lab) is in mg/dL:

eGFR=0.413[height/sCr]

To find the correct height to use for the equation:

- Impute the date of any non-missing height using the standard date imputation rules (See Section 6.1)
- If there are multiple heights on the same day, take the mean of the heights; check if date within the 6-month window date of the serum creatinine laboratory result, if yes, use this height for eGFR derivation; it not, check the vitals dataset for a height.
  - Convert height to centimeters by dividing inches by 0.3937, if necessary, based on the ST.UNITL variable
  - Ignore the ST.STHTDN ("Height Not Done") variable; if there is a height reported, use it.
- If there is no height (ST.STHT) within 6 months of the serum creatinine laboratory date, then use the height from VS.VSHT where the INSTANCENAME matches the visit of the serum creatinine lab. If there are multiple heights where the INSTANCENAME matches the visit of the serum creatinine lab, take the mean of all of the heights for that INSTANCENAME.

IAVISITN	INSTANCENAME
1	Enroll
2	6 Month FUP
3	12 Month FUP
4	18 Month FUP
Etc.	

  - Convert height to centimeters by dividing inches by 0.3937, if necessary, based on the VS.VSHTU variable
- If there is no VS.VSHT with an INSTANCENAME that matches the serum creatinine laboratory visit, then eGFR is missing

If the subject is ≥ 18 years at the date of the serum creatinine laboratory, calculate the eGFR parameter using the CKD-Epi method, where sCr (serum creatinine) is in mg/dL:

Race and Sex	Serum Creatinine Level, *μmol/L (mg/dL)*	Equation
Black		
Female	≤62 (≤0.7)	$GFR = 166 \times (Scr/0.7)^{-0.329} \times (0.993)^{Age}$
	>62 (>0.7)	$GFR = 166 \times (Scr/0.7)^{-1.209} \times (0.993)^{Age}$
Male	≤80 (≤0.9)	$GFR = 163 \times (Scr/0.9)^{-0.411} \times (0.993)^{Age}$
	>80 (>0.9)	$GFR = 163 \times (Scr/0.9)^{-1.209} \times (0.993)^{Age}$
White or other		
Female	≤62 (≤0.7)	$GFR = 144 \times (Scr/0.7)^{-0.329} \times (0.993)^{Age}$
	>62 (>0.7)	$GFR = 144 \times (Scr/0.7)^{-1.209} \times (0.993)^{Age}$
Male	≤80 (≤0.9)	$GFR = 141 \times (Scr/0.9)^{-0.411} \times (0.993)^{Age}$
	>80 (>0.9)	$GFR = 141 \times (Scr/0.9)^{-1.209} \times (0.993)^{Age}$

Age = serum creatinine laboratory date - birth date, in years
Scr = serum creatinine lab converted to mg/dL. *When converting from umol/L to mg/dL, the factor should be 88.402, i.e. sCr(mg/dL)=sCr (umol/L)/88.402*
Race = ”Black or African Descent” for the Black race in the equation above, and any other non-missing ADSL.RACE is the “White or Other” race in the equation above.
Sex

APPENDIX 4: Additional details on Statistical Methods

Example SAS Code

Event Rates

Use PROC GENMOD to estimate the rate and its corresponding 95% CI. For example, create a relevant temporary dataset e.g. TEMP and let Y=the number of events and LN = log (total person-time of follow-up). Use the sample code below:

Unadjusted:

```
proc genmod data = temp;
model Y = /dist=Poisson link=log offset = LN;
output out=out p=pcount xbeta=xb stdxbeta=std;
run;

data predrates;
   set out;
   lograte=xb-ln;
   prate=exp(lograte);  /* estimated rate */
   lcl=exp(lograte-probit(.975)*std);
   ucl=exp(lograte+probit(.975)*std);
run;
```

Adjusted:

```
ods output ParameterEstimates = ecuosn_means lsmeans=lsm;
proc genmod data = tedata;
    class stratafactor (ref= "Untreated") Any Categorical Covariates (i.e. SEX,
HISTORY OF XXX);
    model numevents = stratafactor Covariate1 Covariate2 Covariate3
Covariate4/link=log dist=poisson offset=ln;
    lsmeans stratafactor / e diff exp cl;
    ods output coef = coeffs;
    store out=insmodel;
run;

data lsm;
  set lsm;
  table_mu = exp(Estimate)*100;
  table_lower = exp(lower) *100;
  table_upper = exp(upper)* 100;
run;
```

Therefore prate and (lcl, ucl) will be the rate and its corresponding 95% CI in the table.

APPENDIX 5: List of Abbreviations

The following abbreviations and acronyms are used in this Statistical Analysis Plan:

Abbreviation or acronym	Explanation
ADS	Analysis Data Sets
AIHA	Autoimmune hemolytic anemia
AE	Adverse Event
APS	Antiphospholipid syndrome
BMD	Bone Marrow Disease
CHMP	Committee for Medicinal Products for Human Use
CI	Confidence Interval
CKD-EPI	Chronic Kidney Disease Epidemiology Collaboration
COVID	Coronavirus Disease
CRF	Case Report Form
CVA	Cerebrovascular Accident
eGFR	Estimated Glomerular Filtration Rate
EMA	European Medicines Agency
EOI	Event of Interest
ESAP	Epidemiology and Statistical Analysis Plan
EU	European Union
GPI	Glycophosphatidylinositol
ITP	Idiopathic thrombocytopenic purpura
IPIG	International PNH Interest Group
LDH	Lactate Dehydrogenase
MAH	Marketing Authorization Holder
MedDRA	Medical Dictionary for Regulatory Activities
MAVE	Major Adverse Vascular Event
PNH	Paroxysmal Nocturnal Hemoglobinuria
Q1	first quartile
Q3	third quartile
RBC	Red Blood Cell
SAE	Serious Adverse Event

Abbreviation or acronym	Explanation
SAS	Statistical Analysis System
SD	Standard Deviation
SDTM	Study Data Tabulation Model
TLF	Table(s), Listing(s) and Figure(s)
TE	Thrombotic Event
TTP	Thrombotic thrombocytopenic purpura
ULN	Upper Limit of Normal
WBC	White Blood Cell

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