An Observational Cohort Study to Assess Long-Term Safety of Danicopan Add-on Therapy in Patients with Paroxysmal Nocturnal Hemoglobinuria: Analysis of IPIG-Registry Data

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Study Planned

Administrative details

EU PAS number

EUPAS1000000876

Study ID

1000000876

DARWIN EU® study

No

Study countries

- [ ] Argentina
- [ ] Australia

- [ ] Austria
- [ ] Belgium
- [ ] Canada
- [ ] China
- [ ] Denmark
- [ ] Finland
- [ ] France
- [ ] Germany
- [ ] Greece
- [ ] Italy
- [ ] Japan
- [ ] Korea, Republic of
- [ ] Netherlands
- [ ] Norway
- [ ] Spain
- [ ] Sweden
- [ ] Switzerland
- [ ] Taiwan
- [ ] Türkiye
- [ ] United Kingdom
- [ ] United States

Study description

This is a non-interventional cohort study that utilizes data from the International PNH Interest Group (IPIG) PNH Registry to assess the long-term safety of danicopan as add-on therapy to ravulizumab or eculizumab for the treatment of adult patients with PNH who have residual hemolytic anemia.

The study utilizes both primary and secondary data from the IPIG PNH Core Registry including the danicopan (Voydeya) Silo registry. The study

population will consist of participants treated with danicopan as add-on therapy compared with participants treated with Soliris/Ultomiris monotherapy.

Study status

Planned

Research institutions and networks

Institutions

Alexion Europe SANS

Contact details

Study institution contact

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Study contact

clinicaltrials@alexion.com

Primary lead investigator

Ami Patel

Primary lead investigator

Study timelines

Date when funding contract was signed

Actual: 22/01/2024

Study start date
Planned: 31/01/2026

Data analysis start date
Planned: 01/02/2026

Date of interim report, if expected
Planned: 31/07/2026

Date of final study report
Planned: 31/07/2030

Sources of funding

- Pharmaceutical company and other private sector

More details on funding

Alexion Pharmaceuticals, Inc.

Study protocol

ALX-PNH-502 PASS Protocol PA 3.0_redacted.pdf (1.89 MB)

Regulatory

Was the study required by a regulatory body?

Yes

Is the study required by a Risk Management Plan (RMP)?

EU RMP category 3 (required)

Methodological aspects

Study topic:

Disease /health condition

Human medicinal product

Study type:

Non-interventional study

Scope of the study:

Safety study (incl. comparative)

Data collection methods:

Combined primary data collection and secondary use of data

Study design:

This PASS uses primary and secondary data from the IPIG PNH Registry, collected retrospectively and prospectively. Primary data will assess Voydeya’s safety; retrospective data, including Alexion International PNH Registry, will describe medical history, participant characteristics, and clinical pro

Main study objective:

This study aims to characterize the long-term safety of danicopan as add-on therapy to ravulizumab or eculizumab for the treatment of adult patients with PNH who have residual hemolytic anemia.

Study Design

Non-interventional study design

Cohort

Study drug and medical condition

Medicinal product name

VOYDEYA

Study drug International non-proprietary name (INN) or common name

DANICOPAN

Anatomical Therapeutic Chemical (ATC) code

(L04AJ09) danicopan

danicopan

Medical condition to be studied

Paroxysmal nocturnal haemoglobinuria

Population studied

Age groups

- **Adult and elderly population (≥18 years)**
  - Adults (18 to < 65 years)
    - Adults (18 to < 46 years)
    - Adults (46 to < 65 years)
  - Elderly (≥ 65 years)
    - Adults (65 to < 75 years)
    - Adults (75 to < 85 years)
    - Adults (85 years and over)

Special population of interest

Hepatic impaired

Nursing women

Pregnant women

Estimated number of subjects

50

Study design details

Setting

Persons: Adult participants with PNH with a detected proportion of PNH cells, who have provided written informed consent, are not participating in an interventional clinical study specific to PNH are eligible for participation in the IPIG PNH Registry. Those meeting the study inclusion/exclusion criteria will be selected.

Place: Participants enrolled in the global IPIG PNH Registry

Inclusion Criteria: (1) Adult participants aged ≥ 18 years at treatment initiation. (2) Initiated treatment with Ultomiris, Soliris, and/or danicopan on or after IPIG or Alexion International PNH Registry enrollment

Exclusion Criteria: Participants without known year of birth, sex, informed consent date, or treatment status of danicopan and Ultomiris and/or Soliris.

Treatment Groups: (1) Participants ever-treated with danicopan as add-on therapy to ravulizumab/eculizumab on or after IPIG PNH Registry enrollment. (2) Participants initiating treatment with Ultomiris or Soliris on or after IPIG or Alexion
International PNH Registry enrollment and without any danicopan treatment experience during follow-up.

Subpopulation of interest: Include participants ever-treated with danicopan as add-on therapy to ravulizumab/eculizumab and distinguish: (1) Participants with severe hepatic impairment; (2) Pregnant participants, pregnant partners of participants, or participants who are breastfeeding.

Comparators

The study population will consist of 2 treatment cohorts: (1) Participants ever-treated with danicopan as add-on therapy to ravulizumab/eculizumab on or after IPIG PNH Registry enrollment. (2) Participants initiating treatment with Ultomiris or Soliris on or after IPIG or Alexion International PNH Registry enrollment and without any danicopan treatment experience during follow-up.

Outcomes

Primary Outcomes:

AEs (serious and nonserious) including for a subpopulation of patients with severe hepatic impairment

Special situations and causes of death

Rate of meningococcal infection

Rate of serious infections

Rate of malignancies and hematologic abnormalities

Secondary Outcomes:

Pregnancy-related outcomes and infant health abnormalities up to 12 months of age in pregnant participants, pregnant partners of participants, or participants who are breastfeeding only.

Demographic characteristics, medical history, PNH-specific treatment history, concomitant medications, and laboratory values.

Number of participants who discontinue danicopan and reasons for discontinuation.

Data analysis plan

Descriptive analyses: Continuous variables will be characterized with number of nonmissing 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 nonmissing data and missing data, as appropriate. The analysis will include 95% confidence intervals of means and percentages, as appropriate.

Outcome measure analysis:
Event rates will be measured for participants in 1) the danicopan as add-on therapy to ravulizumab/eculizumab cohort, 2) IPIG Registry Ultomiris/Soliris monotherapy cohorts (treated exposure period only),
and 3) Ultomiris/Soliris monotherapy cohorts (treated exposure period only). The event rate for the Ultomiris/Soliris monotherapy cohort inclusive of events recorded in the Alexion PNH registry will be presented in the final PASS report.

Incidence of meningococcal infections, serious infections, and malignancies and hematological abnormalities will also be assessed in danicopan-treated participants by exposure period pending feasibility. Specific to the characterization of clinical events with bone marrow pathology or other hematological disorders, an ever-exposed analysis will also be performed in the danicopan as add-on therapy to ravulizumab/eculizumab cohort and the IPIG Registry Ultomiris/Soliris
monotherapy cohort.

Data management

ENCePP Seal

The use of the ENCePP Seal has been discontinued since February 2025. The ENCePP Seal fields are retained in the display mode for transparency but are no longer maintained.

Data sources

Data source(s), other

IPIG PNH Registry (including retrospective data from the International Alexion PNH Registry)

Data sources (types)

Disease registry

Use of a Common Data Model (CDM)

CDM mapping

Yes

CDM Mappings

CDM name

CDISC SDTM

CDM website

https://www.cdisc.org/standards/foundational/sdtm

Data quality specifications

Check conformance

Yes

Check completeness

Yes

Check stability

Yes

Check logical consistency

Yes

Data characterisation

Data characterisation conducted

Yes