Natural History Study of Acute Hepatic Porphyria (AHP) Patients with Recurrent Attacks.

Published: 03-03-2015
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To characterize the natural history and clinical management of AHP patients with porphyria attacks.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Metabolism disorders NEC
Study type	Observational invasive

Summary

ID

NL-OMON47799

Source
ToetsingOnline

Brief title
AHP study

Condition

- Metabolism disorders NEC

Synonym
acute hepatic porphyria

Research involving
Human

Sponsors and support

Primary sponsor: Alnylam Pharmaceuticals Inc
Source(s) of monetary or material Support: Alnylam;pharmaceutisch bedrijf

Intervention

Keyword: acute hepatic porphyria, observational

Outcome measures

Primary outcome

To characterize the natural history and clinical management of AHP patients with porphyria attacks.

Secondary outcome

In Part A, to characterize the following in AHP patients with porphyria attacks:

* Plasma and urine ALA and PBG levels between and during attacks;

* Porphyria signs and symptoms between and during attacks;

* Medical history and familial history;

* QoL and healthcare utilization;

* Chemistry, hematology, and urinalysis laboratory parameters;

* Exploratory biomarker sample collection. Genetic testing will not be conducted on biomarker samples.

In Part B, to perform long-term assessment of the following in AHP patients with porphyria attacks:

* Pain intensity and impact as measured by Brief Pain Inventory form

* Changes in disease activity as measured by survey instruments (questionnaires)

Study description

Background summary

There is a significant unmet need for more efficacious and tolerable therapies for patients with AHP with porphyria attacks. Alnylam Pharmaceuticals is developing ALN-AS1, a synthetic RNA interference (RNAi) therapeutic designed to decrease liver ALAS1 expression and thus reduce the hepatic production of neurotoxic intermediates, especially ALA, resulting in a decrease in the number of attacks in patients who experience them on a recurrent basis.
While there are some data characterizing AHP patients and their management from both single country and multi-country studies, there is a lack of prospectively collected longitudinal data as well as information regarding comorbid conditions, healthcare utilization, and quality of life in these patients.
While it is estimated that up to 1,000 patients experience porphyria attacks (more than 3 per year) in the US and EU combined, these numbers have not been determined from data collected from multiple countries, over the same time interval.
Thus, an observational, natural history study would also help to clarify the current number of AHP patients that are experiencing porphyria attacks. Data from this study may further the understanding of the AHPs, and aid in the design of future interventional clinical trials.

Study objective

To characterize the natural history and clinical management of AHP patients with porphyria attacks.

Study design

A prospective, multi-center, multi-national, observational natural history study.

This study will consist of two periods: Part A, which will include a combination of telephone and clinic visits for up to 1 year, and Part B, which will be an optional long-term evaluation via survey instrument assessments which may be conducted by mail and confirmed by telephone for up to an additional 3 years. There will not be any required clinic visits in Part B.

In Part A, consented eligible patients with a history of porphyria attacks will be enrolled for the study and return to the study sites for a visit approximately 6 months later. A detailed medical history and a medication use history (including herbal or vitamin supplements) will be collected for the period since the patient*s porphyria diagnosis or onset of symptoms, but in general at least 24 months prior to the Baseline Visit. In addition to undergoing physical examinations at each site visit, patients will also have blood and urine testing (to measure delta-aminolevulinic acid (ALA) and porphobilinogen (PBG)) and complete quality of life (QoL), pain, and healthcare

utilization assessments. Additional blood and urine samples will be collected for biomarker exploratory analyses. Site staff will call the patient approximately every 2 months after the Baseline Visit to collect general health information, complete a porphyria phone assessment, and to remind patients to send a urine sample to the central laboratory. If a patient experiences a porphyria attack during the study period and is treated at the site, urine and plasma samples, porphyria attack questionnaires, and an attack treatment form will be collected. Site staff will also call the patient approximately 1 week and 2 weeks after treatment for the attack is completed to collect information for a porphyria assessment.

The optional Part B is open to all patients who meet the eligibility criteria and provide consent; participation in Part A is not a prerequisite of participation in Part B. Consent to participate in Part B may be performed remotely where permitted by local regulations.

Study burden and risks

The burden and risk when the patient participates in this observational study is minimal: 1 extra blood sample and completion of 4 questionnaires. Blood sampling is only for Part A.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)

Inclusion criteria

1. Male or female patient aged > 12 years;
2. Diagnosis of one of the AHPs (AIP, HCP, VP and ADP made by a porphyria specialist including a history of clinical features of porphyria (such as acute attacks of abdominal, back, or limb pain; biochemical evidence during an attack [at least 1 documented instance of urine or plasma ALA or PBG level >4 times the upper limit prior to the Baseline Visit]); and molecular confirmation of at least one of the following has been documented previously:
a. Acute Intermittent Porphyria (AIP): disease-causing mutation in the HMBS (also called PBGD) gene
b. Hereditary Coproporphyria (HCP): disease-causing mutation in the CPOX gene
c. Variegate Porphyria (VP): disease-causing mutation in the PPOX gene
d. Aminolevulinic acid dehydratase deficient porphyria (ADP): disease-causing mutation in the aminolevulinic acid dehydratase (ALAD) homozygous or compound heterozygous genes
e. If no mutation can be identified, the patient is eligible as long as one of the following signs is present: decreased HMBS activity, increased fecal coproporphyrins with a ratio of coproporphyrin III/coproporphyrin I >4 with or without elevation of fecal protoporphyrin, and the patient has been determined to have AHPs (AIP, HCP, VP, or ADP) by a porphyria specialist;
3. Patients in part A experience attacks of porphyria as defined by meeting one of the following:
a. patient experienced at least 3 porphyric attacks (requiring increased pain medication or carbohydrate intake, hemin administration or hospitalization for symptoms and signs of acute porphyria including but not limited to, severe abdominal pain, vomiting, tachycardia, constipation, hypertension, or hyponatremia) within 12 months of the Baseline Visit with at least 1 prior attack requiring hemin or treatment at a hospital or clinic;
b. patients who have experienced only 1 attack within 12 months of the Baseline Visit in Part B of the study.
c. patient is receiving hemin on an average (average of the 12 months prior to Baseline Visit) of one or more times per month;
d. patient is receiving gonadotropin-releasing hormone (GnRH) analogues to prevent porphyric attacks.
4. Patient is willing to provide detailed medical history, including porphyria history, family history, and prior medication usage, for at least 24 months prior to the Baseline Visit.
5. Patient is willing and able to comply with the protocol-required visit schedule and visit requirements and provide written informed consent. ;In Part B, patients experience recent porphyria attack activity or is on treatment to prevent attacks as defined by meeting one of the following:
a. patients who have experienced only 1 attack within 12 months of the Baseline Visit.

;Patients in Part B of the study are subject to the same eligibility criteria, except that for new patients who did not participate Part A, the timing of the requirements described in #3 above (<= inclusion criteria) are relative to Part B study entry.

Exclusion criteria

1. Current participation in a clinical trial with an investigational product;
2. Per Investigator judgement, patient is not a good candidate for study participation.

Patients in Part B of the study are subject to the same eligibility criteria.

Study design

Design

Study type: Observational invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Other

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	23-03-2015
Enrollment:	11
Type:	Actual

Ethics review

Approved WMO Date:	03-03-2015
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	10-06-2015

Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	11-08-2015
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	16-12-2016
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	07-08-2017
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	01-07-2019
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
ClinicalTrials.gov	NCT02240784
CCMO	NL50347.078.14