An international, non-drug interventional, real-world cohort of PAH patients newly initiating PAH therapy with guideline-directed assessments of disease severity

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Research QuestionThis study is designed to describe PAH patients in terms of their clinical characteristics, therapies used, disease progression, and outcomes (eg, death, hospitalization, risk category for predicted mortality risk [Boucly 2017;...

Ethical review	Approved WMO
Status	Completed
Health condition type	Heart failures
Study type	Observational invasive

Summary

ID

NL-OMON52230

Source
ToetsingOnline

Brief title
CARE PAH

Condition

- Heart failures
- Respiratory disorders NEC

Synonym
Increased bloodpressure in the arteries of the lung, Pulmonary arterial hypertension

Research involving
Human

Sponsors and support

Primary sponsor: Actelion Pharmaceuticals
Source(s) of monetary or material Support: Actelion Pharmaceuticals Ltd Actelion Pharmaceuticals Ltd (a Janssen Pharmaceutical Company of Johnson & Johnson)

Intervention

Keyword: Interventional, Non-drug, PAH, real-world

Outcome measures

Primary outcome

The primary objectives of this study are:

• To describe the time to all-cause death in the overall study population and

within each cohort (see the Cohort Definitions section).

• To describe the time to death due to PAH or first hospitalization due to PAH

in the overall study population and within each cohort.

Secondary outcome

The secondary objectives of this study are:

Death and Hospitalization Objectives

• To describe the time to death due to PAH in the overall study population and

within each cohort.

• To describe the time to first all-cause hospitalization and time to first

hospitalization due to PAH in the overall study population and within each

cohort.

• To describe the time to first morbidity/mortality event (see Section 3.6.3)

in the overall study population and within each cohort.

• To describe the time to clinical worsening (see Section 3.6.2) in the overall

study population and within each cohort.

• To describe medical resource utilization in the overall study population and within each cohort.

Clinical Characteristics Objectives

• To describe demographics including socio-economic status, other participant characteristics, and clinical characteristics at baseline, at first follow-up at 3 to 6 months after baseline, and every 6 months after baseline in the overall study population and within each cohort.

• To describe the change in 6-minute walking distance (6MWD), World Health Organization (WHO) functional class (FC), and N-terminal-pro-hormone brain natriuretic peptide (NT-proBNP) from baseline to first follow-up at 3 to 6 months after baseline, and every 6 months after baseline in the overall study population and within each cohort.

• To describe the time to worsening in WHO FC from baseline to every 6 months after baseline in the overall study population and within each cohort.

Risk Category Objectives

• To describe the change in the number of low-risk noninvasive criteria based on WHO FC, 6MWD, and NT-proBNP (see Table 4) from baseline to first follow-up at 3 to 6 months after baseline, and every 6 months after baseline in the overall study population and within each cohort.

• To describe the time to all-cause death based on the number of low-risk noninvasive criteria based on WHO FC, 6MWD, and NT-proBNP in the overall study

population and within each cohort.

• To describe the change in the number of participants within each overall risk category (low, intermediate, or high) according to the noninvasive criteria, REVEAL Lite 1 or REVEAL Lite 2 variables from baseline, to first follow-up at 3 to 6 months after baseline, and every 6 months after baseline in the overall study population and within each cohort.

• To describe the time to all-cause death based on the risk category determined by the noninvasive criteria, REVEAL Lite 1 or REVEAL Lite 2 in the overall study population and within each cohort.

• To describe the risk assessment strategy(ies) used at baseline in the overall study population by geographical region.

Patient-reported Outcome Objectives

• To describe the change in health-related quality of life of participants from baseline to first follow-up at 3 to 6 months after baseline, and every 6 months after baseline in the overall study population and within each cohort, as assessed by the emPHasis-10, 5-Level EuroQoL 5 Dimension Questionnaire (EQ-5D-5L©), Work Productivity and Activity Impairment Questionnaire: General Health (WPAI:GH), and Patient Health Questionnaire-8 (PHQ-8) questionnaires.

• For the PAH-SYMPACTTM substudy only: To describe the change in PAH-SYMPACT from baseline to first follow-up at 3 to 6 months after baseline, and every 6 months after baseline in the overall study population and within each cohort, as assessed by the PAH SYMPACT questionnaire.

Other Objectives

• To describe treatment patterns of PAH therapies 6 months prior to baseline,

at baseline, at first follow-up at 3 to 6 months after baseline, and every 6

months after baseline in the overall study population and within each cohort.

• To describe the safety profile of PAH therapies in the overall study

population and within each cohort.

Study description

Background summary

Pulmonary arterial hypertension (PAH) is a serious chronic disorder of the cardiopulmonary circulation, of diverse etiology and pathogenesis, characterized by a progressive increase in pulmonary arterial pressure and pulmonary vascular resistance affecting right heart function and potentially leading to right heart failure and death (Benza 2010; Kylhammar 2014; Oudiz 2013). Estimated 1-, 3- and 5 year survival rates are 85% to 86%, 68% to 73%, and 57% to 65%, respectively (Benza 2012a; Korsholm 2015; Radegran 2016). The available therapies have positive effects on PAH, but the disease will progress in many patients. Thus, PAH remains a serious life-threatening condition, and research continues for better therapies.
Following results of the AMBITION trial (Galiè 2015) and various registry analyses (REVEAL [Benza 2019a], SPAHR [Kylhammar 2018], COMPERA [Hoeper 2017], FPHN [Boucly 2017]), based on the risk category for 1-year mortality defined in the 2015 European Society of Cardiology (ESC) and the European Respiratory Society (ERS) guidelines, current PAH treatment recommendations (Galiè 2019) advocate the use of combined PAH therapies for an improved outcome for the majority of patients.

Study objective

Research Question
This study is designed to describe PAH patients in terms of their clinical characteristics, therapies used, disease progression, and outcomes (eg, death, hospitalization, risk category for predicted mortality risk [Boucly 2017; Benza 2019a; Benza 2020], and patient-reported outcomes [PROs]) in real-world clinical practice. This study will collect high-quality real-world data that may be used as a stand-alone dataset or in combination with other data sources to address relevant research questions (eg, serve as an external control

dataset to another study) to support development and access to PAH therapies, as well as to contribute to the knowledge base of PAH through publications.

Study design

This is a prospective, non-drug interventional, international, multicenter study to collect real-world data from participants in a routine clinical setting who newly initiate any PAH therapy(ies) in a real-world clinical setting, either as first therapies, as replacement therapies, or as additional therapies, or have already been receiving macitentan 10 mg for at least 3 months prior to index date. The index date is defined as the date when participants starts the first new PAH therapy after baseline assessments have been completed. Certain clinical visits and noninvasive assessments recommended in the 2015 ESC/ERS guidelines are mandated in this study to ensure availability of data to address the study objectives (Galiè 2016).
The decision of patients to participate in this study must not, in any way, impact upon the standard of care that they are receiving or any benefits to which they are otherwise entitled. The treatment decision must have been taken prior to and independently of the participant's inclusion in the study. All aspects of treatment and clinical management of participants will be in accordance with local clinical practice and applicable local regulations, and at the discretion of the participating physician (or treating physician where different).
The study population will consist of consenting participants who have newly initiated a PAH therapy since the beginning of the enrollment period in participating centers, clinics, or healthcare facilities. All participants qualifying to the enrollment plan (designed based on PAH therapy initiated at index date, geographic location, site type, background PAH therapy, etc) and fulfilling all the inclusion criteria and none of the exclusion criteria will be enrolled in the study and be observed in the study until end of study, withdrawal of informed consent, loss to follow-up, or death.
All participants must sign an informed consent form (ICF) on the same day or before any data collection and source data verification in accordance with local requirements and/or sponsor policy.
To ensure data quality, certain follow-up visits and noninvasive assessments recommended in the 2015 ESC/ERS guidelines (Galiè 2016) will be mandated in this study. In addition, participants will be followed by their physician according to routine clinical practice and as permitted by local regulation. Furthermore, study sites will have quarterly telephone contacts with participants to capture data related to occurrence of clinical events, safety events, and changes in PAH and/or concomitant medications. Aside from the mandated visits, participants will be followed by their physician as needed.
The end of the study will be the last data point collection for the last participant. The overall duration of the study may be up to 6 years; however, this non-drug interventional study may be discontinued at any time by the sponsor at the sponsor's discretion.

Study burden and risks

The burden and risks of only the study assessments (blood sampling and completing questionnaires) are low. Completing the questionnaires takes approximately 15 to 20 minutes in total. 2.5 ml of blood is taken per blood sample (8 times in total)
The study assessments are carried out during the visits that are already taking place as part of the standard treatment.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

1. Signed ICF.

2. Male or female participants age >=18 years.
3. Symptomatic PAH in any PAH subtype.
4. PAH diagnosis confirmed by hemodynamic evaluation at rest at any time prior to or at the index date fulfilling all of the criteria below:
a) Mean pulmonary artery pressure >20 mmHg, AND
b) Pulmonary artery wedge pressure or left ventricular end diastolic pressure <=15 mmHg, AND
c) Pulmonary vascular resistance >= 3 Wood Units (ie, >=240 dyn*sec/cm5).
5. Newly initiating 1 or more PAH therapy(ies) (as monotherapy or add-on therapy) at index date.
6. All mandated assessments must be performed and recorded at the baseline visit before the initiation of the new PAH therapy.
7. Participants must agree to follow study protocol, including all mandated visits and mandated assessments.
8. For the PAH-SYMPACT substudy only: Participants initiating any endothelin receptor antagonist (ERA) or phosphodiesterase-5 inhibitor therapies at index date must provide consent to enroll in the optional PAH-SYMPACT substudy. Refusal to give consent for the optional PAH-SYMPACT substudy will not exclude a participant from participation in the main study.

Exclusion criteria

1. Participants enrolled in any interventional clinical trial with an investigational therapy in the 3-month period prior to index date.
2. Any PAH therapy initiated at index date was used by the participant (including different route of administration of the same compound) within 3 months prior to index date for any reason. (Administration for vasoreactivity testing is permitted.)
3. presence or known presence of moderate or severe obstructive lung disease
4. presence or known presence of moderate or severe restrictive lung disease

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	13-01-2022
Enrollment:	115
Type:	Actual

Ethics review

Approved WMO Date:	20-10-2021
Application type:	First submission
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	22-11-2021
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	05-04-2022
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	22-08-2022
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)

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	NCT04955990
CCMO	NL77818.028.21

Study results

Date completed:	12-12-2022
Results posted:	03-01-2024
Actual enrolment:	12

Summary results
Trial ended prematurely

First publication
06-10-2023

URL result
URL
Type
int
Naam
M2.2 Samenvatting voor de leek
URL

Internal documents
File