The power and the flow: raising the bars in the treatment of pulmonary arterial hypertension

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Heart failures
Study type	Interventional

Summary

ID

NL-OMON40011

Source
ToetsingOnline

Brief title
GOSPEL: Goal Oriented Strategy to Preserve Ejection Fraction trial

Condition

- Heart failures
- Pulmonary vascular disorders

Synonym
pulmonary arterial hypertension; increased pressure in the pulmonary blood vessels

Research involving
Human

Sponsors and support

Primary sponsor: Vrije Universiteit Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W,Bedrijven,United

Therapeutics Corporation

Intervention

Keyword: magnetic resonance imaging, medical treatment, pulmonary arterial hypertension, right ventricular function

Outcome measures

Primary outcome

The primary endpoint will be preservation/improvement of RVEF after 1 year of follow-up.

RVEF will be measured at baseline and after 4, 8, 12 and 24 months of follow-up. In case of decrease in RVEF >3% compared to the previous measurement, additional medical treatment will be applied. Our hypothesis will be proven to be correct when the additional medical treatment result in improved RVEF during the subsequent follow-up measurement.

Secondary outcome

Secondary endpoints will be the change in pulmonary vascular resistance, mean pulmonary artery pressure, cardiac output, exercise capacity and NYHA functional class after 1 year of follow-up.

Study description

Background summary

Rationale: The current goal oriented strategy in patients with pulmonary arterial hypertension (PAH) is to improve exercise capacity which can be achieved by decreasing pulmonary vascular resistance (PVR) and subsequently increasing cardiac output (CO). Despite this load reduction, a substantial proportion of patients show progressive right ventricular (RV) dysfunction

leading to clinical worsening and death. A possible explanation is that current therapies show a relatively modest reduction in PVR, leaving mean pulmonary artery pressure (mPAP) unchanged. As a consequence, RV work, defined as the product of CO and mPAP increases, contributing to progressive RV dysfunction.

Hypothesis: A goal oriented therapeutic strategy in patients with PAH that is able to preserve RV function will result in improved clinical outcome. RV function can only be preserved when early and aggressive combination therapy not only reduces PVR but also mPAP.

Study objective

The primary goal of the study is to assess whether a goal oriented strategy to preserve/improve right ventricular function by application of upfront combination therapy will improve clinical outcome.

Study questions:
1. Will a goal oriented strategy to preserve/improve RV function, measured by right ventricular ejection fraction (RVEF) be effective?

2. Does early and aggressive combination therapy result in improved RV function and survival during long term follow-up?

3. Does a strategy to preserve RVEF also translate into improvements of other clinically meaningful parameters?

4. Can RVEF be replaced by more simple measures?

5. Will a goal oriented strategy to improve RVEF also lead to improvement of myocardial performances and coupling of the RV to its load?

Study design

This is a prospective longitudinal, clinical study. Thirty newly diagnosed idiopathic or heritable PAH patients with NYHA functional class II or III will be included.
Maintenance/improvement of RVEF will be our primary outcome parameter and therefore cardiac magnetic resonance imaging (CMR) will be performed at baseline and after 4, 8, 12 and 24 months of follow-up. Six-minute walk testing (6MWT), quality of life questionnaires and blood sampling (NT-proBNP) will be performed during similar follow-up intervals. In addition, right heart catheterization (RHC) will be performed at baseline and after 4, 12 and 24 months of follow-up.
Patients with NYHA functional class II at baseline, will start with a single agent endothelin receptor antagonist (ERA) or phosphodiesterase-5 inhibitor

(PDE 5I). Patients with baseline NYHA functional class III will initially start on combination therapy consisting of an ERA and a PDE 5I. All therapeutic decisions will be based on measurements of RVEF by CMR. In case of a stable/improved RVEF (defined as no decrease in RVEF of more than 3%), treatment remains unchanged. In case of a deteriorating RVEF, additional medical treatment will be added. In case of a deteriorating RVEF in a patient already using triple therapy (ERA, PDE 5 I and prostacyclin (P GI2)), lung transplantation listing will be discussed. Our hypothesis will be proven to be correct when the additional medical treatment result in improved RVEF during the subsequent follow-up measurement.

Intervention

Not applicable.

Study burden and risks

Because RHC and MRI are part of our routine clinical assessment protocol at baseline and during regular one-year follow-up assessment, the present study requires two MRI measurements (at 4 and 8 months follow-up) and one additional RHC measurement (at 4 months follow-up) per patient. In addition, blood sampling and 6MWT are already performed on a regular basis for clinical purposes.
RHC performed in experienced centres has low morbidity (1.1%) and mortality rates (0.055%) (Hoeper, JACC, 2006). We consider that the additional measurements are justified by an expected improvement of patients clinical symptoms, quality of life and survival by our goal oriented therapeutic approach in order to preserve/improve RV function during long term follow-up. Furthermore, the results of the present study will provide essential insights in the mechanism of RV failure and its depence on pulmonary hemodynamics and could be of great value in order to improve the treatment strategy for PAH patients world wide.

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

-Idiopathic or heritable pulmonary arterial hypertension
-NYHA functional class II and III
-Age 18-80 years

Exclusion criteria

-Other causes of pulmonary arterial hypertension (PAH) (i.e. collagen vascular disease, congenital heart disease, chrono-thromboembolic pulmonary hypertension, pulmonary venous hypertension, left heart failure, hypoxemic lung disease)
-PAH targeted therapies before study inclusion

Study design

Design

Study type: Interventional

Masking:	Open (masking not used)
Control:	Uncontrolled

Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	17-05-2013
Enrollment:	30
Type:	Actual

Ethics review

Approved WMO

Date:	24-04-2013
Application type:	First submission
Review commission:	METC Amsterdam UMC

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
CCMO	NL41878.029.13