A Randomized, Double-blind, Placebo-controlled, Multinational, Phase 3 Study of the Efficacy and Safety of Inhaled Treprostinil in Subjects with Idiopathic Pulmonary Fibrosis (TETON-2) // A Multinational, Uncontrolled, Usability Evaluation Study of the TD-300/A Tyvaso Inhalation Device Used in RIN-PF-303

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This study has been transitioned to CTIS with ID 2024-514761-19-00 check the CTIS register for the current data. The primary objective of RIN-PF-303 is to evaluate superiority of inhaled treprostinil against placebo for the annual rate of change in…

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Lower respiratory tract disorders (excl obstruction and infection)
Study type	Interventional

Summary

ID

NL-OMON56203

Source
ToetsingOnline

Brief title
RIN-PF-303 // RIN-PF304

Condition

- Lower respiratory tract disorders (excl obstruction and infection)

Synonym
Interstitial Lung Disease (ILD), Lungfibrosis

Research involving
Human

Sponsors and support

Primary sponsor: United Therapeutics Corp.
Source(s) of monetary or material Support: Industry (United Therapeutics Corp)

Intervention

Keyword: IPF, RIN-PF-303 // RIN-PF304, Treprostinil, Tyvaso Inhalation Device

Outcome measures

Primary outcome

The primary endpoint of the study is the change in absolute FVC in subjects

with IPF from baseline to Week 52.

Safety will be assessed by reviewing the following parameters:

• Adverse events (AEs) and serious adverse events (SAEs)

• Clinical laboratory parameters

• Vital signs, including saturation of peripheral capillary oxygenation (SpO2)

• 12-lead electrocardiograms (ECGs)

Secondary outcome

Secondary efficacy endpoints of the study are:

• Time to clinical worsening (including time to death, respiratory

hospitalization, or >=10% relative decline in % predicted FVC)

• Time to first acute exacerbation of IPF

• Overall survival at Week 52

• Change from baseline in % predicted FVC at Week 52

• Change from baseline in King*s Brief Interstitial Lung Disease Questionnaire

score at Week 52

• Change from baseline in diffusion capacity of lungs for carbon monoxide

(DLCO) at Week 52

Exploratory efficacy endpoints of the study are:

• Change from baseline in absolute FVC at Weeks 16, 28, and 40

• Change from baseline in N-terminal pro-brain natriuretic peptide (NT-proBNP)

at Week 52

• Change from baseline in resting supplemental oxygen use at Week 52

Study description

Background summary

Idiopathic Pulmonary Fibrosis (IPF) is a serious, chronic, progressive, fibrosing interstitial pneumonia with no known cause typically occurring in patients above 50 years of age. It is characterized by progressive fibrosis, lung scarring, and a typical radiological pattern. IPF is associated with increasing cough and dyspnea, greatly impacts patient quality of life, and eventually leads to death from respiratory failure or complicating comorbidities. Currently there is no cure for IPF, and only 2 drugs are approved to treat the condition (nintedanib and pirfenidone). (protocol 1.1)
Treprostinil belongs to the group of prostacyclins and has a well-characterized pharmacology. treprostinil is approved for the treatment of pulmonary arterial hypertension (PAH) following the subcutaneous, intravenous, inhaled (as treprostinil sodium), or oral (as treprostinil diolamine) routes of administration. (protocol 1.2.1)
The improvements in FVC and reduced exacerbations of underlying lung disease from the INCREASE study (RCT), combined with the preclinical evidence of antifibrotic activity of treprostinil, suggest that inhaled treprostinil may offer a treatment option for patients with IPF. (protocol 1.3)
This study hypothesizes that inhaled treprostinil will have a positive effect

on absolute FVC after 52 weeks of therapy as compared with placebo when administered to subjects with IPF. (protocol 1.4)

Study objective

This study has been transitioned to CTIS with ID 2024-514761-19-00 check the CTIS register for the current data.

The primary objective of RIN-PF-303 is to evaluate superiority of inhaled treprostinil against placebo for the annual rate of change in absolute forced vital capacity (FVC) from baseline to Week 52.

Study design

This is a Phase 3, randomized, double-blind, placebo-controlled, multinational, efficacy and safety study of subjects with IPF treated with inhaled treprostinil over a 52-week period.

Intervention

Daily treatment duirng 52 weeks with inhaled treprostinil or placebo using the TD-300 ultrasonic nebulizer.

Study burden and risks

Treprostinil has a long history of safety and efficacy in WHO Group 1 PAH and is currently marketed as 3 formulations (parenteral solution, inhalation solution, and oral tablet) in various regions. Additionally, the recently completed INCREASE study (RIN-PH-201) demonstrated
that inhaled treprostinil is safe and efficacious for the treatment of PH-ILD. The pulmonary function test safety results from INCREASE suggest that inhaled treprostinil may provide substantial benefit with minimal risks for the treatment of IPF.
The TD-300/A has been in use since 01 May 2018. Use of the TD-300/A has resulted in no occasional, probable, or frequent severe ADEs. A further analysis of the anticipated ADEs resulting from the risk mitigation processes, which incorporate the TD-300/A post-market use,
can be found in the TD-300/A IB. The potential benefits of the nebulised treprostinil solution administered with the TD-300/A in IPF subjects discussed previously, and the minimal observed risk of the TD-300/A after more than 4 million exposure days, suggest the TD-300/A provides substantial benefit with minimal risks for the treatment of IPF.

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

Eligible subjects must be >=40 years of age at the time of signing informed consent; have a diagnosis of IPF based on the 2018 ATS/ERS/JRS/ALAT Clinical Practice Guideline (Raghu 2018) and
confirmed by central review of high-resolution computed tomography imaging and if available, surgical lung biopsy; and have a FVC >=45% predicted. Subjects on pirfenidone or nintedanib must be on a stable and optimized dose for >=30 days prior to Baseline.

Exclusion criteria

Subjects with forced expiratory volume in 1 second (FEV1)/FVC <0.70, those on

>10 L/min of
supplemental oxygen at rest at Baseline, and women who are pregnant or lactating will not be eligible to participate in the study.

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	16-06-2023
Enrollment:	16
Type:	Actual

Medical products/devices used

Generic name:	TD-300 Tyvaso inhalation system
Registration:	No
Product type:	Medicine
Brand name:	Tyvaso inhalation solution
Generic name:	treprostinil for inhalation

Ethics review

Approved WMO

Date:	11-10-2022

Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	13-02-2023
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	26-05-2023
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	06-06-2023
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	06-09-2023
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	20-11-2023
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	12-12-2023
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	14-02-2024
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

Approved WMO Date:	12-03-2024
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

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
EU-CTR	CTIS2024-514761-19-00
EudraCT	EUCTR2021-005881-17-NL
ClinicalTrials.gov	NCT05255991
CCMO	NL82375.100.22