Published: 13-10-2023
Last updated: 07-04-2024

To evaluate the long-term safety and tolerability of inhaled treprostinil in subjects with IPF.

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

Summary

Source

ToetsingOnline

Brief title

RIN-PF-302

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 :	United Therapeutics Corp

Intervention

Keyword :	IPF, Treprostinil, Tyvaso Inhalation Device

Outcome measures

Primary outcome

Efficacy will be assessed by evaluating the effect of continued long-term therapy with inhaled treprostinil on the following parameters:

• Change in absolute forced vital capacity (FVC)

• Time to clinical worsening (including time to death, respiratory hospitalization, or >=10% relative decline in % predicted FVC)

• Time to acute exacerbation of IPF

• Overall survival

• Change in % predicted FVC

• Change in King*s Brief Interstitial Lung Disease (K-BILD) Questionnaire score

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

• Change in diffusion capacity of lungs for carbon monoxide (DLCO)

• Change in resting supplemental oxygen use

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

• 12-lead electrocardiograms

Secondary outcome

N/A

Study description

Background summary

Interstitial lung disease (ILD) encompasses a heterogeneous group of parenchymal lung diseases that are characterized by significant scarring or fibrosis of the bronchioles and alveolar sacs within the lungs (Travis 2013, Seeger 2013). Increased fibrotic tissue in ILD prevents oxygenation and free gas exchange between the pulmonary capillaries and alveolar sacs. The symptomatology of ILD is non-specific and covers a wide range of symptoms, and severity of symptoms can vary substantially among patients. Only 2 therapies are currently approved by the Food and Drug Administration (FDA) and European Medicines Agency for ILD indications, nintedanib (Ofev®) and pirfenidone (Esbriet®). Nintedanib is a kinase inhibitor approved for the treatment of idiopathic pulmonary fibrosis (IPF), chronic fibrosing ILDs with a progressive phenotype, and systemic sclerosis-associated ILD (Ofev Prescribing information 2020, Ofev Summary of Product Characteristics 2021). Pirfenidone belongs to the pyridone class and is approved for the treatment of IPF (Esbriet Prescribing information 2019, Esbriet Summary of Product Characteristics 2021).

While results from randomized studies show that nintedanib and pirfenidone slow the rate of decline in forced vital capacity (FVC), additional treatment options for IPF are needed as pulmonary fibrosis continues to confer high morbidity and mortality despite currently available treatments (Montesi 2020, King 2014). The results of RIN-PH-201 (INCREASE) (Section 1.2.3) in patients with pulmonary hypertension (PH) associated with ILD (PH-ILD) provide evidence that inhaled treprostinil may offer a treatment option for patients with IPF.

Study objective

To evaluate the long-term safety and tolerability of inhaled treprostinil in subjects with IPF.

Study design

This is a Phase 3, multicenter, multinational, open-label extension (OLE) study for eligible subjects who completed RIN-PF-301 or RIN-PF-303.

Intervention

Daily treatment with inhaled treprostinil using the TD-300 inhalation system.

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

Public

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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. Subject gives voluntary informed consent to participate in the study.
2. The subject participated in RIN-PF-301 or RIN-PF-303 and had 1 of the following
applied:
a. Remained on study drug and completed all scheduled study visits
b. Was enrolled in RIN-PF-301 or RIN-PF-303 at the time that the study or study subject was discontinued by the Sponsor.
3. Women of childbearing potential must be non-pregnant (as confirmed by a urine
pregnancy test at OLE Entry Visit and Baseline) and non-lactating, and will do 1 of the
following:
a. Abstain from intercourse (when it is in line with their preferred and usual lifestyle)

b. Use 2 medically acceptable, highly effective forms of contraception for the duration
of the study, and at least 30 days after discontinuing study drug. Medically acceptable, highly effective forms of contraception can include approved hormonal
contraceptives (oral, injectable, and implantable) and barrier methods (such as a
condom or diaphragm) when used with a spermicide.
Women who are successfully sterilized or postmenopausal are not considered to be of
reproductive potential.
4. Males with a partner of childbearing potential must use a condom for the duration of
treatment and for at least 48 hours after discontinuing study drug.
5. In the opinion of the Investigator, the subject is able to communicate effectively with
study personnel, and is considered reliable, willing, and likely to be cooperative with
protocol requirements, including attending all study visits.

Exclusion criteria

1. Subject is pregnant or lactating.
2. In the opinion of the Investigator, enrollment in RIN-PF-302 would represent a risk to the
subject*s overall health.

Study design

Design

Study phase :	3
Study type :	Interventional
Masking :	Open (masking not used)
Control :	Uncontrolled
Primary purpose :	Treatment

Recruitment

NL

Recruitment status :	Pending
Start date (anticipated) :	01-07-2024
Enrollment :	16
Type :	Anticipated

Medical products/devices used

Generic name :	TD-300 Tyvaso inhalation system
Registration :	No

Ethics review

Approved WMO Date :	13-10-2023
Application type :	First submission
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
Other	CTIS: 2023-504471-25-00
CCMO	NL85188.100.23