A randomised, double-blind, placebo-controlled parallel group study in IPF patients over 12 weeks evaluating efficacy, safety and tolerability of BI 1015550 taken orally.

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Respiratory disorders NEC
Study type	Interventional

Summary

ID

NL-OMON49255

Source
ToetsingOnline

Brief title
A study to test BI 1015550 affects lung function in people with IPF

Condition

- Respiratory disorders NEC

Synonym
IPF, lung fibrosis

Research involving
Human

Sponsors and support

Primary sponsor: Boehringer Ingelheim
Source(s) of monetary or material Support: De opdrachtgever Boehringer Ingelheim

Intervention

Keyword: BI 1015550, IPF, Lung function

Outcome measures

Primary outcome

The primary endpoint is the change from baseline in FVC at 12 weeks (in mL).

Secondary outcome

The secondary endpoint is the Percentage of patients (%) N with Treatment

Emergent Adverse Events (TEAE).

Study description

Background summary

IPF is a progressive, fibrosing interstitial lung disease (ILD) characterized by decline in lung function and worsening dyspnea. IPF carries a poor prognosis, with a median post-diagnosis survival in untreated patients of approximately 3 years.
IPF occurs worldwide. The prevalence of the disease appears to be increasing, although it is unclear whether this reflects increased recognition or a true increase in incidence. The incidence of IPF appears to be higher in North America and Europe (3 to 9 cases per 100,000 person-years) than in South America and East Asia (fewer than 4 cases per 100,000 person-years). In the United States, the prevalence of IPF has been reported to range from 10 to 60 cases per 100,000. Increasing rates of hospital admissions and deaths due to IPF also suggest an increasing burden of disease.
Nintedanib and pirfenidone are the only drugs registered for the treatment of IPF and recommended in the recent ATS/ERS/JRS/ALAT Clinical Practice Guideline for the Treatment of Idiopathic Pulmonary Fibrosis. Despite the availability of these drugs, the medical need remains high in this devastating disease.

Study objective

The purpose of this trial is to demonstrate proof of concept of clinical activity of BI 1015550 on the change of Forced Vital Capacity (FVC) between baseline and 12 weeks. New treatments are needed that further reduce the decline in FVC, positively affect symptoms and improve quality of life in patients with Idiopathic Pulmonary Fibrosis. This trial will investigate BI 1015550 to be used in this patient population either as stand-alone treatment or in addition to local standard of care (SoC), which may or may not include currently approved antifibrotic treatments (nintedanib or pirfenidone). FVC change from baseline will be used to generate sufficient evidence of efficacy in the subpopulation on no background antifibrotic treatment, to inform the phase III program.

Study design

This phase II trial is a double-blind, placebo-controlled comparison of BI 1015550 18 mg b.i.d over 12 weeks in patients treated with antifibrotic treatment or not treated with antifibrotic treatment at baseline.
See protocol section 3.1

Intervention

BI 1015550 18mg b.i.d. will be given for 12 weeks. Please see section 4 - investigational treatments

Study burden and risks

Preclinical experiments have shown that BI 1015550 affects the fibrotic pathway and the effects may be complementary and/or synergistic to those of nintedanib. Based on this, it is postulated that BI 1015550 may provide therapeutic benefit to patients with IPF or other progressive fibrosing ILDs but this has not yet been determined clinically.

Due to the limited short treatment duration in this study, only patients on no background antifibrotic treatment may have an improvement of FVC versus baseline. Nevertheless, patients* participation in this 12 weeks trial in IPF patients with or without background antifibrotic therapy treated with BI 1015550, 18 mg b.i.d. is of utmost importance to investigate the safety, tolerability, efficacy and PK profile of BI 1015550 when administered alone or on background antifibrotic treatment prior to progressing to longer term treatment Phase III to show an effect on FVC decline in the overall IPF population.

Two PDE4 inhibitors are marketed with indications of psoriasis and chronic obstructive pulmonary disease (COPD). Studies conducted in non-human primates with both marketed compounds suggest that primates are less sensitive than rats to PDE4i-associated toxicity. No adverse vascular changes in humans have been

reported.
Overall, BI 1015550 is expected to be safe and well tolerated with an improved tolerability compared to other marketed PDE4 inhibitors due to lower affinity for PDE4 D.

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

Patients aged *40 years when signing the informed consent.

Diagnosis:
a. IPF based on 2018 ATS/ERS/JRS/ALAT Guideline [R18-2794] as confirmed by the investigator based on chest HRCT scan taken within 12 months of Visit 1 and if available surgical lung biopsy.

b. UIP or probable UIP HRCT pattern consistent with the clinical diagnosis of IPF

Stable for at least 8 weeks prior to Visit 1. Patients have to be either :
- not on therapy with nintedanib or pirfenidone for at least 8 weeks prior to Visit 1 (combination of nintedanib plus pirfenidone not allowed), or
- on stable* therapy with nintedanib or pirfenidone for at least 8 weeks prior to Visit 1 and planning to stay stable on this background therapy after randomisation.
- Forced Vital Capacity (FVC) *45% of predicted normal at Visit 1
- DLCO (corrected for haemoglobin [Hb] [Visit 1]) > 25% to < 80% of predicted normal at Visit 1.
- Signed and dated written informed consent in accordance with ICH-GCP and local legislation prior to admission to the trial.

Exclusion criteria

- Relevant airways obstruction (pre-bronchodilator FEV1/FVC < 0.7) at Visit 1.
- In the opinion of the Investigator, other clinically significant pulmonary abnormalities.
- Acute IPF exacerbation within 4 months prior to screening and/or during the screening period (investigator-determined).
- Lower respiratory tract infection requiring antibiotics within 4 weeks prior to Visit 1 and/or during the screening period.
- Major surgery (major according to the investigator*s assessment) performed within 3 months prior to Visit 1 or planned during the course of the trial. (Being on a transplant list is allowed).
- Any documented active or suspected malignancy or history of malignancy within 5 years prior to Visit 1, except appropriately treated basal cell carcinoma of the skin, *under surveillance* prostate cancer or in situ carcinoma of uterine cervix.
- Evidence of active infection (chronic or acute) based on clinical exam or laboratory findings (see table 5.2.3 :1) at Visit 1 or at Visit 2.
- Any suicidal behaviour in the past 2 years (i.e. actual attempt, interrupted attempt, aborted attempt, or preparatory acts or behavior).
- The patient has a confirmed infection with SARS-CoV-2 within the 4 weeks prior to Visit 1
and/or during the screening period.
- Further criteria apply.

Study design

Design

Study phase:	2
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	04-02-2021
Enrollment:	4
Type:	Actual

Ethics review

Approved WMO Date:	12-05-2020
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	09-07-2020
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	11-08-2020
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	08-09-2020

Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	19-10-2020
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	17-11-2020
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	31-03-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

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
EudraCT	EUCTR2019-004167-45-NL
CCMO	NL73653.056.20