A double blind, randomized, placebo-controlled trial evaluating the efficacy and safety of BI 1015550 over at least 52 weeks in patients with Idiopathic Pulmonary Fibrosis (IPF)

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

Summary

ID

NL-OMON55951

Source
ToetsingOnline

Brief title
PDE4 Phase III trial in IPF (Fibroneer- IPF)

Condition

- Respiratory disorders NEC

Synonym
idiopathic pulmonary fibrosis, IPF

Research involving
Human

Sponsors and support

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

Intervention

Keyword: BI 1015550, FIBRONEER, IPF

Outcome measures

Primary outcome

The primary objective is to demonstrate a reduction in lung function decline as measured by the change from baseline in FVC for BI 1015550 when compared to placebo in patients with IPF.

The primary endpoint of the trial is the absolute change from baseline in Forced Vital Capacity (FVC) [mL] at Week 52.

Secondary outcome

The main secondary objective of the trial is to demonstrate BI 1015550*s ability in reducing the occurrence of clinically meaningful events such as acute IPF exacerbation, hospitalization for respiratory cause or death over the duration of the trial when compared to placebo in patients with IPF. An additional secondary objective of the trial is to show an effect of BI 1015550 on symptoms and lung function. The key secondary endpoint in this trial is time to the first occurrence of any of the components of the composite endpoint: time to first acute IPF exacerbation, first hospitalization for respiratory cause, or death (whichever occurs first) over the duration of the trial. The secondary endpoints of the trial are: - Time to first acute IPF exacerbation or

death over the duration of the trial - Time to hospitalization for respiratory cause or death over the duration of the trial - Time to absolute decline in FVC % predicted of >10% from baseline or death over the duration of the trial - Time to absolute decline in (DLCO) % predicted of >15% from baseline or death over the duration of the trial - Time to death over the duration of the trial - Absolute change from baseline in Living with Pulmonary Fibrosis (L-PF) Symptoms Dyspnea domain score at Week 52 - Absolute change from baseline in Living with Pulmonary Fibrosis (L-PF) Symptoms Cough domain score at Week 52 - Absolute change from baseline in Living with Pulmonary Fibrosis (L-PF) Symptoms Fatigue domain score at Week 52 - Absolute change from baseline in FVC % predicted at Week 52 - Absolute change from baseline in DLCO % predicted at Week 52

Study description

Background summary

IPF and other progressive fibrosing interstitial lung diseases (PF-ILDs) share common pathophysiological features; alveolar epithelial cell damage and subsequent dysregulated repair, characterized by excessive deposition of extracellular matrix and loss of normal parenchymal architecture and lung function. In IPF, fibroblasts exhibit unregulated proliferation and differentiate into myofibroblasts. The latter is considered to be the hallmark cell in the development and establishment of pulmonary fibrosis. Several growth factors are involved in the proliferation, migration and transdifferentiation of the fibroblast and myofibroblast pool in pulmonary fibrosis.

Currently, nintedanib and pirfenidone are the only drugs authorized for the treatment of IPF and are recommended in the recent clinical practice guideline ATS/ERS/JRS/ALT for the treatment of idiopathic pulmonary fibrosis. Nintedanib is also approved in the US, European Union and many other countries for the treatment of other fibrosing ILDs with progressive phenotype. Despite the availability of these drugs, medical need remains high in these devastating diseases.

Study objective

The aim of this study is to evaluate the efficacy, safety and tolerability of BI 1015550 9 mg BID and 18 mg BID compared to placebo in patients with IPF, in addition to the patient's standard of care. The primary objective of this study is to demonstrate the ability of BI 1015550 to reduce lung function decline based on forced vital capacity (FVC) between baseline and week 52 compared to placebo.

Study design

Patients who will participate in the study will be screened for eligibility after signing the consent form. After signing the consent form, the first visit (Visit 1) will be conducted to determine the patient's eligibility. Eligible patients attend the randomization visit (Visit 2) to collect all clinical and safety information and to review all inclusion and exclusion criteria.

Patients are randomized in a 1:1:1 ratio to CI 1015550 9 mg BID, CI 1015550 18 mg BID or placebo and then enter the treatment phase for at least 52 weeks.

The randomization of patients will be stratified based on the presence of background antifibrotic therapy (AF group vs. non-AF group).
- Non-AF group: patients not being treated with an approved antifibrotic medication (nintedanib or pirfenidone) in the last 8 weeks at study entry (e.g., previously treated with antifibrotics but discontinued that treatment or patients never previously treated with antifibrotics treated with antifibrotics).
- AF group: Patients on stable treatment with an approved antifibrotic drug (e.g. nintedanib or pirfenidone) for at least 12 weeks at study entry and are expected to continue on this background treatment after randomization.

The research will be conducted in 2 parts. Treatment Period A of the study will consist of visits 2 through 10, up to one year after randomization. Treatment Period B begins upon completion of the visit at week 52 (visit 10); patients will continue treatment with blinded trial drug in treatment period B and have trial visits every 12 weeks. Assuming a respective recruitment period (approximately 11 months), the first randomized patients can receive trial treatment for up to 130 weeks.

Within the last 2 months before the last randomized patient reaches 52 weeks of treatment, all patients still on blinded study treatment will have an end of treatment visit and an end of study visit (if applicable). The study ends when all patients have completed these visits.

See protocol section 3.1

This trial will include an option for participants and participant caregivers to complete anonymized questionnaires to provide feedback on their clinical trial experience. Providing this feedback is not required for trial participation, and information collected from these questionnaires will not be analyzed as part of the clinical data for the trial (see Section 10.7).

Intervention

One group will receive a 9 mg tablet of BI 1015550 twice daily, a second group will receive an 18 mg tablet of BI 1015550 twice daily, and the third group will receive a placebo tablet twice daily.

Study burden and risks

Patients with IPF who receive treatment with BI 1015550 have the potential benefit of slowing lung function decline, improving symptoms, and improving quality of life over a long-term period.

The toxicology data support administration of BI 1015550 to women and men in the planned Phase III clinical trials in patients with IPF and other forms of progressive pulmonary fibrosis irrespective of background antifibrotic treatment, except for women who are pregnant or breastfeeding.

Data from the Phase II trial 1305-0013 in patients with IPF indicated a beneficial treatment effect of 18 mg BI 1015550 bid, with the preservation of Forced Vital Capacity (FVC) over 12 weeks together with an acceptable safety and tolerability profile supporting further investigation in Phase III clinical trials as a treatment for IPF and other forms of progressive pulmonary fibrosis.

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. Patients >=40 years old at the time of signed informed consent. 2. IPF diagnosis based on 2022 ATS / ERS / JRS / ALAT Guidelines 3. Forced Vital Capacity (FVC) >=45% of predicted normal 4. DLCO >=25% of predicted normal corrected for hemoglobin (Hb) 5. On stable treatment with nintedanib or pirfenidone for at least 12 weeks or not on treatment with either nintedanib or pirfenidone for at least 8 weeks 6. Signed and dated written informed consent in accordance with ICH-GCP and local legislation prior to admission to the trial

Exclusion criteria

1.Prebronchodilator FEV1/FVC <0.7) 2. Acute IPF exacerbation within 3 months and / or during the screening period 3. Treated with immunomodulatory medications (other than oral corticosteroids) or prednisone >15 mg/day or equivalent for respiratory or pulmonary reasons 4. Active, unstable or uncontrolled vasculitis within 8 weeks 5. Any suicidal behavior in the past 2 years 6. Any suicidal ideation of type 4 or 5 on the C-SSRS in the past 3 months 7. In the opinion of the Investigator, other clinically significant pulmonary abnormalities

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:	Completed
Start date (anticipated):	06-03-2023
Enrollment:	24
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	BI 1015550
Generic name:	Not applicable

Ethics review

Approved WMO Date:	13-10-2022
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	05-12-2022
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	29-12-2022

Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	11-01-2023
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	21-02-2023
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	28-02-2023
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	30-03-2023
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	04-04-2023
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	03-07-2023
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	26-07-2023
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

Approved WMO Date:	08-09-2023
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	02-10-2023
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	02-11-2023
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	02-01-2024
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	21-01-2024
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	02-02-2024
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	28-03-2024
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	23-05-2024
Application type:	Amendment

Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	28-05-2024
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	31-05-2024
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
EudraCT	EUCTR2022-001091-34-NL
CCMO	NL81397.100.22