A double blind, randomized, placebo-controlled trial evaluating the efficacy and safety of BI 1015550 over at least 52 weeks in patients with Progressive Fibrosing Interstitial Lung Diseases (PF-ILDs)

Published: 13-10-2022
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This study has been transitioned to CTIS with ID 2024-512803-37-00 check the CTIS register for the current data. 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...

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

Summary

ID

NL-OMON53889

Source
ToetsingOnline

Brief title
PDE4 Phase III trial in PF-ILD (Fibroneer- ILD)

Condition

- Respiratory disorders NEC

Synonym
PF-ILD, progressive fibrosing interstitial lung diseases

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, PF-ILD

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 compared to placebo in patients with progressive fibrosing ILDs.

The primary endpoint of the study is the absolute change from baseline in forced vital capacity (FVC) [ml] at week 52.

Secondary outcome

The main secondary aim of the study is to demonstrate the ability of BI 1015550 to reduce the occurrence of clinically meaningful events such as acute ILD exacerbation, respiratory hospitalization or death over the duration of the study compared to placebo in patients with progressive fibrosing ILD. An additional secondary aim of the study is to demonstrate an effect of BI 1015550 on symptoms and lung function. The primary secondary endpoint in this study is time to first occurrence of any component of the composite endpoint: time to first acute ILD exacerbation, first respiratory hospitalization, or death (whichever occurs first) over the duration of the research. The secondary

endpoints of the study are: - Time to first acute ILD exacerbation or death over the duration of the study - Time to hospitalization for respiratory cause or death over the duration of the study - Time to absolute decrease in FVC % predicted of >10% from baseline or death over the duration of the study - Time to Absolute Reduction in (DLCO) % Predicted of >15% from Baseline or Death Over Study Duration - Time to death during the duration of the trial - Absolute Change from Baseline in Life with Pulmonary Fibrosis (L-PF) Symptoms Dyspnea Domain Score at Week 52 - Absolute Change from Baseline in Life with Pulmonary Fibrosis (L-PF) Symptoms Cough Domain Score at Week 52 - Absolute Change from Baseline in Life 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 Percentage Predicted at Week 52

Study description

Background summary

Progressive fibrosing interstitial lung diseases (PF-ILDs) and idiopathic pulmonary fibrosis (IPF) share common pathophysiological features; alveolar epithelial cell damage and consequences, subsequent dysregulated repair of extracellular matrix and loss of normal parenchymal architecture and lung. 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 care remains high with these devastating

diseases.

Study objective

This study has been transitioned to CTIS with ID 2024-512803-37-00 check the CTIS register for the current data.

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 PF-ILD, 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.

Around the time 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 10.6)

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 PF-ILD treated with BI 1015550 have the potential benefit of slowing decline in lung function, improving symptoms, and improving long-term quality of life.

The toxicology data support the administration of BI 1015550 to women and men in planned phase III clinical studies in patients with IPF and other forms of progressive pulmonary fibrosis, regardless of background antifibrotic therapy, except for pregnant or breast-feeding women.

Data from the phase II study 1305-0013 in patients with IPF indicated a beneficial treatment effect of 18 mg BI 1015550 twice daily, with forced vital capacity (FVC) maintenance for 12 weeks, along with an acceptable safety and tolerability profile to support of further investigation in Phase III clinical trials as a treatment for PF-ILD 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 >=18 years old at the time of signed informed consent 2. Progressive fibrosing ILD other than IPF based on predefined criteria 3. Forced Vital Capacity (FVC) >=45% of predicted normal 4. DLCO >=25% of predicted normal corrected for Haemoglobin (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 prednisone >15mg/day or equivalent within 4 weeks; cyclophosphamide, tocilizumab, mycophenolate, pirfenidone within 8 weeks; rituximab within 6 months 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:	Recruiting
Start date (anticipated):	06-03-2023
Enrollment:	29
Type:	Actual

Medical products/devices used

Registration:	No
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:	27-12-2022
Application type:	Amendment
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:	10-01-2023
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:	01-03-2023
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:	24-04-2023
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	15-05-2023
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:	02-08-2023
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:	29-09-2023
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	03-11-2023
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:	06-02-2024
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:	27-05-2024
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
EU-CTR	CTIS2024-512803-37-00
EudraCT	EUCTR2022-001134-11-NL
CCMO	NL81398.100.22