Health Technology Briefing
March 2024

BI 1015550 for treating idiopathic pulmonary fibrosis or progressive pulmonary fibrosis

Company/Developer	Boehringer Ingelheim Ltd

☒ New Active Substance ☐ Significant Licence Extension (SLE)

NIHRIO ID: 30099	NICE ID: N/A	UKPS ID: 665537

Licensing and Market Availability Plans

Currently in phase III clinical development.

Summary

BI 1015550 is in clinical development for the treatment of idiopathic pulmonary fibrosis (IPF) and progressive pulmonary fibrosis (PPF) in people aged 18 years and over. IPF is a long-term disease of the lungs characterised by the progressive deposition of collagen and fibrous tissue in the lungs. This causes the lung tissue to become inflamed and thick and form scars. As a result, the lungs become unable to work normally, reducing the transfer of oxygen from the air into the blood. It is associated with a gradual decline in lung function, progressive respiratory failure, and a high death rate. Symptoms include persistent cough, frequent lung infections, tiredness, severe shortness of breath, and loss of appetite/weight loss. The disease course of PFF is similar to that of IPF, with worsening respiratory symptoms, decline in lung function and early mortality. Several treatments can help reduce the rate at which IPF progresses, but there's currently no treatment that can stop or reverse the scarring of the lungs.

BI 1015550 is an oral inhibitor of the enzyme phosphodiesterase 4B (PDE4B), with combined antifibrotic and anti-inflammatory effects. BI 101550 offers an alternative therapeutic strategy by inhibiting the enzyme PDE4B preferentially, potentially leading to anti-inflammatory and antifibrotic effects whilst circumventing many of the adverse events associated with more general PDE4 inhibitors. If licenced, BI 1015550 will offer an additional treatment option for treatment of adult patients with IPF or PPF.

Proposed Indication

Treatment of adult patients with idiopathic pulmonary fibrosis (IPF) or progressive pulmonary fibrosis (PPF).[1]

Technology

Description

BI 1015550 (nerandomilast) is a phosphodiesterase 4 (PDE4) inhibitor that has antifibrotic properties. PDE4 is widely expressed in immune system cells, and inhibition of PDE4 reduces the release of pro-inflammatory mediators and the recruitment of inflammatory cells. PDE4 inhibitors are associated with anti-inflammatory and antifibrotic effects and have the potential to reduce pulmonary inflammation and fibrotic remodelling in lung diseases. The use of oral PDE4 inhibitors is currently limited due to their association with adverse events. BI 101550 offers an alternative therapeutic strategy by inhibiting the enzyme PDE4B preferentially, potentially leading to anti-inflammatory and antifibrotic effects whilst circumventing many of the adverse events associated with more general PDE4 inhibitors.[2]

BI 101550 is in clinical development for the treatment of IPF or PPF in people aged 18 years and over.[3] In the phase III trial (FIBRONEER-ON, NCT06238622), BI 1015550 is administered as a 9mg or 18mg tablet twice a day for up to one year and ten months.[1]

Key Innovation

IPF is a debilitating and fatal disease with a median survival time of 3 years upon diagnosis.[4] It is a progressive disease that may have a steady decline or worsen rapidly.[5,6] There is currently no cure for IPF, but there are treatments that can help relieve the symptoms and slow down its progression.[7] Current treatment recommendations can slow, but not stop or reverse, disease progression and are associated with side effects that can delay treatment initiation or lead to discontinuation. This means there is currently an unmet need for new treatments for IPF that can be used alone or with standard of care.[2] Treatments for non-IPF interstitial lung disease (ILD) fail in a large subset of patients that manifests the progressive fibrotic phenotype. Therefore, once the fibrotic progression has started, these treatments are ineffective to avoid further clinical decline.[8]

If licenced, BI 1015550 will offer an additional treatment option for treatment of adult patients with IPF or PPF who have few well-tolerated effective therapies available.

Regulatory & Development Status

BI 1015550 does not currently have marketing authorisation in the EU/UK for any indication.

BI 1015550 is in phase II development for the treatment of interstitial lung disease secondary to systemic sclerosis.[9]

BI 1015550 has the following regulatory designations/awards:[10,11]

- an Orphan Drug by the US FDA for IPF in October 2022.
- a Breakthrough Therapy by the US FDA for IPF in February 2022.

Patient Group

Disease Area and Clinical Need

IPF is a specific form of chronic, progressive fibrosing interstitial pneumonia of unknown cause.[12] It affects the tissue surrounding the air sacs, or alveoli, in the lungs. IPF develops when the lung tissue becomes thick and stiff. Over time, these changes can cause permanent scarring in the lungs, called fibrosis, that makes it progressively more difficult to breathe.[12,13] It usually affects people who are around 70 to 75 years old, and is rare in people under 50 years.[14] Symptoms include; breathlessness, persistent cough, fatigue, clubbing of the fingertips or toenails.[15] The exact cause of IPF is unclear, however, it has been linked to a number of risk factors, including: exposure to certain types of dust, viral infections, family history of IPF, acid reflux, and smoking.[14] A significant proportion of patients with fibrosing ILDs other than IPF will develop a progressive phenotype comparable to untreated IPF that can occur despite conventional treatment. PPF is characterised by a disease course similar to that of IPF, with worsening respiratory symptoms, decline in lung function and early mortality.[16]

In the UK around 32,500 people are living with IPF, and it is more common in males than females. In 2012, approximately 50 people in every 100,000 had been diagnosed at some time in their life with IPF.[17] In England 2022-23, there were 15,611 finished consultant episodes (FCEs) and 7,904 admissions for interstitial pulmonary diseases with fibrosis (ICD-10 code J84.1), which resulted in 56,801 FCE bed days and 1,874 day cases.[18]

Recommended Treatment Options

The National Institute for Health and Care Excellence (NICE) currently recommend pirfenidone for the treatment of IPF in adults and nintedanib for the treatment of IPF or progressive fibrosing interstitial lung diseases (PF-ILD) in adults.[19,20]

Clinical Trial Information

Trial	NCT06238622; An Open-label Extension Trial of the Long-term Safety and Efficacy of BI 1015550 Taken Orally in Patients With Idiopathic Pulmonary Fibrosis (IPF) and Progressive Pulmonary Fibrosis (PPF) (FIBRONEER™-ON) **Phase III –** Starting July 2024 **Location(s):** Not available **Primary completion date:** April 2027
Trial Design	Open-label, single group assignment, extension
Population	N=1,700 (planned); subjects with IPF or PPF who have completed treatment in a previous study with BI 1015550 (study 1305-0014 or 1305-0023); aged 18 years and over
Intervention(s)	BI 1015550 tablets
Comparator(s)	-
Outcome(s)	Primary outcome: occurrence of any adverse event over the course of the extension trial (yes/no) See trial record for full list of other outcomes

Results (efficacy)	-
Results (safety)	-

Clinical Trial Information	
Trial	NCT05321082, **EudraCT** 2022-001134-11; 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) **Phase III** – Ongoing **Locations:** 24 EU countries, UK, USA, Canada, and others **Primary completion date:** December 2024
Trial Design	Double blind, randomized, placebo-controlled
Population	N=1,178 (actual); subjects with a form of PF-ILD other than IPF; aged 18 years and over
Intervention(s)	BI 1015550 tablets
Comparator(s)	Placebo
Outcome(s)	Primary outcome: absolute change from baseline in Forced Vital Capacity (FVC) (mL) at Week 52 See trial record for full list of other outcomes
Results (efficacy)	-
Results (safety)	-

Clinical Trial Information	
Trial	NCT05321069, **EudraCT** 2022-001091-34; 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) **Phase III** – Ongoing **Locations:** 19 EU countries, UK, USA, Canada, and others **Primary completion date:** August 2024
Trial Design	Double blind, randomized, placebo-controlled
Population	N=1,177 (actual); subjects with IPF; aged ≥ 40 years old
Intervention(s)	BI 1015550 oral tablets
Comparator(s)	Matched placebo
Outcome(s)	Primary outcome: absolute change from baseline in FVC (mL) at week 52 [Time frame: at baseline, at week 52] See trial record for full list of other outcomes

Results (efficacy)	-
Results (safety)	-

Clinical Trial Information

Trial	NCT04419506, **EudraCT** 2019-004167-45; 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 **Phase II** – Completed **Locations:** 11 EU countries, UK, USA, Canada, and others **Actual study completion date:** October 2021
Trial Design	Randomised, double-blind, placebo-controlled parallel group study
Population	N=147 (actual); subjects with IPF and usual interstitial pneumonia (UIP); aged ≥ 40 years old
Intervention(s)	BI 1015550 oral tablets (1x 6mg tablet, 1x 12 mg tablet) twice daily (36 mg daily), in the morning and evening for 12 weeks.
Comparator(s)	Matched placebo
Outcome(s)	Primary outcome: change from baseline in forced vital capacity (FVC) at 12 weeks [Time frame: baseline (day 1) and week 12.] See trial record for full list of other outcomes
Results (efficacy)	Treatment with BI 1015550, either alone or with background use of an antifibrotic agent, prevented a decrease in lung function in patients with IPF.[21]
Results (safety)	The most frequent adverse event was diarrhoea. A total of 13 patients discontinued BI 1015550 treatment owing to adverse events. The percentages of patients with serious adverse events or severe adverse events were similar in the two trial groups.[21]

Estimated Cost

The cost of BI 1015550 is not yet known.

Relevant Guidance

NICE Guidance

- NICE technology appraisal. Nintedanib for treating idiopathic pulmonary fibrosis when forced vital capacity is above 80% predicted [TA864]. February 2023.
- NICE technology appraisal. Nintedanib for treating progressive fibrosing interstitial lung diseases [TA747]. November 2021.
- NICE technology appraisal. Pirfenidone for treating idiopathic pulmonary fibrosis [TA504]. February 2018.
- NICE technology appraisal. Nintedanib for treating idiopathic pulmonary fibrosis [TA379]. January 2016.

- NICE clinical guideline. Idiopathic pulmonary fibrosis in adults: diagnosis and management [CG163]. June 2013.
- NICE quality standard. Idiopathic pulmonary fibrosis in adults [QS79]. January 2015.

NHS England (Policy/Commissioning) Guidance

- NHS England. Interstitial Lung Disease Service Adult. Service Specifications. 17009/S. June 2017.

Other Guidance

- American Thoracic Society/European Respiratory Society/Japanese Respiratory Society/ Asociación Latinoamericana de Tórax. Idiopathic Pulmonary Fibrosis (an Update) and Progressive Pulmonary Fibrosis in Adults: An Official ATS/ERS/JRS/ALAT Clinical Practice Guideline. 2022.[12]

Additional Information

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