A randomised, double-blind, placebo-controlled, parallel group, dose-finding study evaluating efficacy, safety and tolerability of BI 1291583 qd over at least 24 weeks in patients with bronchiectasis (Airleaf*)

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Bronchial disorders (excl neoplasms)
Study type	Interventional

Summary

ID

NL-OMON53709

Source
ToetsingOnline

Brief title
CatC inhibitor Phase II in bronchiectasis (1397-0012) / (Airleaf*)

Condition

- Bronchial disorders (excl neoplasms)

Synonym
bronchiectasis, dilatation and inflammation of the bronchi

Research involving

Human

Sponsors and support

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

Intervention

Keyword: BI 1291583, bronchiectasis, CatC inhibitor

Outcome measures

Primary outcome

The primary endpoint is the time to first pulmonary exacerbation up to 48 weeks

after first drug adminstration.

Secondary outcome

The key secondary endpoint is the rate of pulmonary exacerbations (number of

events per person-time) up to week 48 after first drug administration.

secondary endpoints:

1) Absolute change from baseline in Quality of Life Questionnaire -

Bronchiectasis (QOL-B) respiratory symptoms domain score at week 24 after first

drug administration

2) Relative change from baseline in neutrophil elastase (NE) activity in sputum

at week 12 after first drug administration

3) Absolute change from baseline in St. George's Respiratory Questionnaire

(SGRQ) Symptoms score at week 24 after first drug administration

4) Absolute change from baseline in percent predicted postbronchodilator forced

expiratory volume in one second (FEV1%pred) at week 24 after first drug

administration

5) Occurrence of an exacerbation by week 24

Study description

Background summary

Bronchiectasis is a heterogenous respiratory syndrome characterised by abnormal and irreversible dilated bronchioles. Patients with bronchiectasis can have a variety of symptoms which include persistent cough, production of large volumes of sputum, dyspnea, chronic fatigue and hemoptysis. These symptoms are burdensome and are often associated with social stigmatism, urine incontinence, anxiety, depression and a reduced quality of life.
Bronchiectasis is characterised by neutrophilic bronchial inflammation. Serine proteases released by neutrophils, such as neutrophil elastase, cause structural damage to the airways, mucus gland hyperplasia, impaired mucus clearance, and result in a vicious cycle of recurrent severe infections and further airway damage.
There is a high unmet medical need for efficacious anti-inflammatory treatments to ameliorate neutrophilic bronchial inflammation. This dose finding trial will investigate BI 1291583 in patients with bronchiectasis to evaluate efficacy, safety and tolerability over at least 24 weeks and up to 48 weeks.

Also refer to protocol sections 1.1 (medical background) and 1.3 (rationale for performing the trial).

Study objective

The primary objective of the trial is to assess a non-flat dose-response curve and to evaluate the dose-response relationship for 3 oral dose regimens of BI 1291583 versus placebo, on the primary endpoint, time to first pulmonary exacerbation up to 48 weeks.

Study design

This is a multi-center, randomised, placebo-controlled, double-blind, parallel group clinical trial to investigate the efficacy, safety and tolerability of three different doses of BI 1291583 (orally, qd).
Approximately 240 eligible patients will be randomised in a 2:1:1:2 ratio to one of the treatment groups.

Also refer to protocol section 3.1.

Intervention

24 to 48 weeks of treatment with BI 1291538 (orally, qd).
- Placebo qd (n = 80)
- BI 1291583 1 mg qd (n = 40)
- BI 1291583 2.5 mg qd (n = 40)
- BI 1291583 5 mg qd (n = 80)

Also refer to protocol section 4.1.

Study burden and risks

Burden:
Study subjects will visit the hospital more often compared to regular care. Additionally, the visits are likely to take more time. Study visits can be experienced as intensive and time-consuming. During the visits, additional tests are performed, including Pulmonary Function Tests, and blood is drawn. All assessments are summarized in the protocol flowchart (p. 5-7).

Risks:
The risks relating to specific study procedures are summarized in protocol table 1.4.2.

The clinical data of BI 1291583 showed an acceptable safety profile in healthy volunteers. No clinical data of BI 1291583 in patients are available to date. A Phase II trial with another CatC inhibitor, brensocatib, showed that 24 weeks treatment resulted in a slightly increased occurrence of periodontal disease and skin exfoliation. No elevated risk of infection was reported in previous clinical studies with other inhibitors of CatC or with inhibitors of NE.

Also refer to protocol section 1.4.

Contacts

Public
Boehringer Ingelheim

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

- Male or female patients
- Age of patients when signing the informed consent >=18 and <=85 years.
- Clinical history consistent with bronchiectasis (cough, chronic sputum production and/or recurrent respiratory infections) and investigator confirmed diagnosis of bronchiectasis by computed tomography (CT) scan.
- History of pulmonary exacerbations requiring antibiotic treatment. In the 12 months before Visit 1, patients must have had either:
-- at least 2 exacerbations, or
-- at least 1 exacerbation and a SGRQ Symptoms score of >40 at screening visit 1.
For patients on stable oral or inhaled antibiotics as chronic treatment for bronchiectasis, at least one exacerbation must have occurred since initiation of stable antibiotics.
- Current sputum producers with a history of chronic expectoration

Exclusion criteria

- AST and / or ALT >3.0 x ULN at Visit 1, or moderate or severe liver disease (defined by Child-Pugh score B or C hepatic impairment).
- Estimated glomerular filtration rate (eGFR) according to CKD-EPI formula <30 mL/min at Visit 1.
- An absolute blood neutrophil count <1,000/mm3 at Visit 1.
- Any findings in the medical examination and/or laboratory value assessed at Screening Visit 1 or during screening period, that in the opinion of the

investigator may put the patient at risk by participating in the trial.
- Positive serological tests for hepatitis B, hepatitis C, or human immunodeficiency virus (HIV) infection, or known infection status.
- A current diagnosis of
-- Cystic Fibrosis
-- Hypogammaglobulinemia
-- Common variable immunodeficiency
-- α1-antitrypsin deficiency treated with augmentation therapy
-- Allergic bronchopulmonary aspergillosis being treated or requiring treatment
-- Tuberculosis or non tuberculous mycobacterial infection being treated or requiring treatment according to local guidelines [Laboratory tests (e.g. Quantiferon Gold test) may be performed at the discretion of the investigator]
-- Palmoplantar keratosis; or keratoderma climactericum
-- Hypothyroidism, myxedema, chronic lymphedema with associated hyperkeratosis of the skin, acrocyanosis. If a subject has hypothyroidism but is treated and compensated, the subject is allowed into the trial
-- Psoriasis affecting palms and soles; or body surface area for psoriasis >= 10%
-- Reactive arthritis (Reiter*s syndrome); keratoderma blennorrhagicum
-- Pityriasis rubra pilaris
-- Atopic dermatitis affecting palms and soles; or body surface area for atopic dermatitis >= 10%.
-- Active extensive verruca vulgaris, as per investigator*s discretion
-- Active fungal infection of hand and/or feet not adequately treated and responsive to antifungal therapy, as per investigator*s discretion
- Any clinically relevant (at the discretion of the investigator) acute respiratory infection within 4 weeks prior Visit 2, or any other acute infection requiring systemic or inhaled anti-infective therapy within 4 weeks prior Visit 2.
- Any evidence of a concomitant disease, such as Papillon-Lefevre Syndrome, relevant pulmonary, gastrointestinal, hepatic, renal, cardiovascular, metabolic, immunological, or hormonal disorders or
patients who are immunocompromised with a higher risk of invasive pneumococcal disease or other invasive opportunistic infections (such as histoplasmosis, listeriosis, coccidioidomycosis, pneumocystosis), that in the opinion of the investigator, may put the patient at risk by participating in the study.
- Received any live attenuated vaccine within 4 weeks prior to Visit 2.
- Medical conditions associated with periodontal disease (to be evaluated by a periodontist or dentist).
- Patients who must or wish to continue the intake of restricted medications or any drug considered likely to interfere with the safe conduct of the trial.

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):	01-09-2022
Enrollment:	7
Type:	Actual

Medical products/devices used

Registration:	No
Product type:	Medicine
Brand name:	Niet van toepassing
Generic name:	Niet van toepassing

Ethics review

Approved WMO Date:	20-12-2021
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	12-04-2022
Application type:	First submission

Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	28-06-2022
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	07-07-2022
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	28-12-2022
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:	02-06-2023
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	14-06-2023
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	02-07-2023
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

Approved WMO

Date:	09-08-2023
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	01-07-2024
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	EUCTR2021-003304-41-NL
ClinicalTrials.gov	NCT05238675
CCMO	NL79730.100.21