Evaluation of safety and tolerability of pirfenidone in asbestosis, a multicenter study

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to investigate the safety and tolerability of pirfenidone in asbestosis patients

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Lower respiratory tract disorders (excl obstruction and infection)
Study type	Interventional

Summary

ID

NL-OMON47764

Source
ToetsingOnline

Brief title
PIRF-asbestosis

Condition

- Lower respiratory tract disorders (excl obstruction and infection)

Synonym
black lung disease, pneumoconiosis

Research involving
Human

Sponsors and support

Primary sponsor: Nederlandse vereniging voor artsen voor longziekten en tuberculose NVALT
Source(s) of monetary or material Support: Roche BV

Intervention

Keyword: asbestosis, fibrosis, pirfenidone, safety

Outcome measures

Primary outcome

The primary objective is to investigate the safety and tolerability of pirfenidone in asbestosis patients as measured by weekly digital symptom and AE score

Secondary outcome

Secondary objective is describing the effect of pirfenidone, as measured by daily home spirometry, in-hospital pulmonary function (spirometry and diffusion capacity), 6-minute walking test and patient reported outcomes as measured by King*s Brief Interstitial Lung disease Questionnaire (K-BILD) and Leicester Cough Questionnaire (LCQ).

Study description

Background summary

Recently, antifibrotic therapy has been approved for the treatment of idiopathic pulmonary fibrosis (IPF), a progressive fibrotic lung disease. Pirfenidone is an antifibrotic agent with anti-inflammatory properties that has been shown to reduce disease progression significantly, as measured by changes in forced vital capacity (FVC). The tolerability and effect of pirfenidone on other fibrosing lung diseases like asbestosis is not clear yet. Asbestosis is a rare and progressive pneumoconiosis, caused by inhalation of asbestos fibers. The disease course is variable but characterized by progressive fibrosis. Sometimes, disease appearance and disease course are hard to distinguish from idiopathic lung fibrosis (IPF). There is currently no specific treatment for asbestosis, except preventive and supportive measures like smoking cessation and supplemental oxygen when needed.

Study objective

to investigate the safety and tolerability of pirfenidone in asbestosis patients

Study design

This is a prospective, multicenter descriptive safety study

Intervention

the patients receive treatment with pirfenidone 3 times daily 801mg during 24 weeks

Study burden and risks

The patients are asked to perform a home monitoring program with real-time wireless home spirometry and weekly symptom and AE score to assess safety and tolerability. A recent pilot study in IPF showed that the majority of patients considered daily spirometry easy (80%) and not burdensome at all (90%), the other patients were neutral. All patients considered real-time spirometry useful and would recommend it to others, 90% wished to continue home monitoring after the pilot.
amount and number of blood samples: 7x (at inclusion, and 6x monthly during treatment)
number of site visits & physical examinations 4X (at inclusion, week 0, 12 and 24 of treatment)
number of pulmonary function test: 4X (at inclusion, week 0, 12 and 24 of treatment)
number of 6 minute walking tests: 4x (at inclusion, week 0, 12 and 24 of treatment)
number of questionnaire: 4X (at inclusion, week 0, 12 and 24 of treatment) King*s Brief Interstitial Lung disease Questionnaire (K-BILD) and Leicester Cough Questionnaire (LCQ).
risks associated with the investigational treatment: summary of the safety profile of Pirfenidone from CPC text.

The most frequently reported adverse reactions during clinical study experience with pirfenidone at a dose of 2,403 mg/day compared to placebo, respectively, were nausea (32.4% versus 12.2%), rash (26.2% versus 7.7%), diarrhoea (18.8% versus 14.4%), fatigue (18.5% versus 10.4%), dyspepsia (16.1% versus 5.0%), anorexia (11.4% versus 3.5%), headache (10.1% versus 7.7%), and photosensitivity reaction (9.3% versus 1.1%).
Tabulated list of adverse reactions
The safety of pirfenidone has been evaluated in clinical studies including 1,650 volunteers and patients. Pirfenidone has been investigated in open studies for more than five years and some for up to 10 years.

Contacts

Public
Nederlandse vereniging voor artsen voor longziekten en tuberculose NVALT

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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 (40-85 years) with confirmed asbestosis by Dutch NVALT IPF expertise-panel (History of asbestos exposition with 15-30 years latency ;AND pleural plaques OR asbestos fibers in pulmonary lavage OR asbestos fibers confirmed in lung biopsy), AND criteria 1-6 ;1. written informed consent
2. FVC * 50% predicted, DLCO * 25%
3. Minimal 6 minute walk test distance 150 meter
4. FEV1/FVC > 0.70
5. Documented disease progression in 3-6 months (absolute of relative FVC decrease 5% in 3-6 months or absolute or relative DLCOc decrease > 10% in 3-6 months, or decrease * 25 meter on 6 minute walk test in 3-6 months)

Exclusion criteria

1. current smoker
2. > 15% emphysema on HRCT thorax
3. >10mg prednisone daily or other immunosuppressant (MTX, azathioprine, cyclophosphamide)
4. malignancy
5. Hepatic impairment (History of hepatic impairment, elevation of transaminase enzymes, or the confirmation of any of the following liver function test criteria above the specified limits: Total bilirubin above the upper limit of normal (ULN), Aspartate aminotransferase (AST) or alanine aminotransferase (ALT) >1.5 × ULN, Alkaline phosphatase > 2.0 × ULN)
6. Renal impairment (GFR < 30 ml/min or dialysis)
7.Pregnancy
8.Concomitant use of a strong and selective inhibitor of CYP1A2 (Fluvoxamin, enoxacin)

Study design

Design

Study phase:	2
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	26-04-2019
Enrollment:	10
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Esbriet
Generic name:	pirfenidone

Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	01-11-2018
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	07-03-2019
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	19-06-2019
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	04-05-2020
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

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	EUCTR2018-001781-41-NL
CCMO	NL61183.078.18