Randomized, Double-blind, Placebo-controlled, Three-Period Crossover Study to Assess the Safety and Tolerability of Inhaled PA101 in Idiopathic Pulmonary Fibrosis (IPF) Patients with Chronic Cough

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* To assess the safety and tolerability of inhaled PA101 delivered via eFlow in patients with IPF with refractory chronic cough.* To assess the efficacy potential of inhaled PA101 by measuring the changes in cough severity and the urge-to-cough as...

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

Summary

ID

NL-OMON41901

Source
ToetsingOnline

Brief title
PA101-CC-01

Condition

- Bronchial disorders (excl neoplasms)

Synonym
Idiopathic Pulmonary fibrosis, Scarring of lung tissue with unknown cause

Research involving

Human

Sponsors and support

Primary sponsor: Patara Pharma, LLC
Source(s) of monetary or material Support: Patara Pharma;LLC

Intervention

Keyword: Chronic Cough, Idiopathic Pulmonary Fibrosis, Inhalation, PA101

Outcome measures

Primary outcome

The efficacy variables for this study will be:

* Change from pre-dose Day 1 to pre-dose Day 4 in 24-hour cough severity measured by VAS scale

* Change from pre-dose Day 1 to pre-dose Day 4 in urge-to-cough measured by VAS scale

* Change in total cough count measured by LCM from the first 24 hours of monitoring to the last 24 hours of monitoring

Safety outcome variables for this study will include AEs and changes from baseline in the following parameters:

* Change from pre- to post-dose in vital signs (i.e., systolic/diastolic blood pressure, heart rate) on Days 1 and 4

* Change from pre- to post-dose in 12-lead ECG parameters (including QTc) on Days 1 and 4

* Change in PFTs (i.e., FEV1, FVC and FEV1/FVC ratio) from pre-dose on Day 1 to post-dose on Day 4

Secondary outcome

Not applicable

Study description

Background summary

Patara Pharma, LLC is developing a new inhalation formulation of cromolyn sodium (PA101) delivered via the eFlow® high efficiency nebulizer system (PARI GmbH, Germany). PA101 is a novel inhalation solution formulation of cromolyn sodium having osmolality and pH adjusted to a physiologically well tolerable range. PA101 is preservative free, room temperature-stable formulation optimized for improved tolerability via oral inhalation and long-term chemical stability. The eFlow nebulizer is a portable, handheld, silent, high-efficiency nebulizer with rapid delivery that can deliver a dose in less than 3 minutes. A recently completed study in healthy subjects, patients with allergic asthma and patients with systemic mastocytosis demonstrated that PA101 is safe and well tolerated, and delivering PA101 with the eFlow nebulizer system (*Cromoflow*) achieves higher lung deposition and systemic levels of cromolyn sodium relative to currently marketed inhalation and oral formulations of cromolyn sodium (Clinical Study Report PA101-01).

Study objective

* To assess the safety and tolerability of inhaled PA101 delivered via eFlow in patients with IPF with refractory chronic cough.
* To assess the efficacy potential of inhaled PA101 by measuring the changes in cough severity and the urge-to-cough as measured by Visual Analog Scale (VAS) and the change in 24-hour cough count measured by Leicester Cough Monitor (LCM).

Study design

This is a Phase 1b, randomized, double-blind, single-center, 3-period crossover study conducted in 6 patients of 40-79 years of age with idiopathic pulmonary fibrosis (IPF) with refractory chronic cough. In each Treatment Period, patients will receive one of three treatments: PA101, Placebo A or Placebo B.

Intervention

During the Screening Visit, the patients will first receive an explanation of the purpose and nature of the study and sign the consent form. The following

procedures will then be performed:
* Determine eligibility according to the inclusion/exclusion criteria
* Obtain patient*s medical history
* Perform physical examination including height, weight and BMI
* Perform urine pregnancy test (females of child-bearing potential only)
* Record vital signs (i.e., systolic and diastolic blood pressure, heart rate) and 12-lead ECG
* Perform alcohol breath or urine test
* Perform urine testing for drugs of abuse
* Review and record concomitant medications taken within the last 14 days.
In each treatment period, the patients will visit the clinic in the morning to receive the first dose on Day 1 (Visit 1) and the last dose on Day 4 (Visit 2); the other doses will be self-administered by the patients. A self-recorded daily diary will be used to record dosing information in each treatment period. The safety assessments (AEs, vital signs and 12-lead ECG), pulmonary function testing (FEV1, FVC, and FEV1/FVC ratio), and the cough severity and the urge-to-cough assessments using VAS scale will be performed in the morning during clinic visits on Day 1 and Day 4 in each Treatment Period. In addition, a cough count device (LCM) will be dispensed in the morning on Day 1 for continuous measurement of cough count for the duration of each Treatment Period. A safety follow-up call will be placed within 5 days (± 2 days) following the last study treatment.

Study burden and risks

This study may produce the following most commonly reported side effects (at least 2 patients/subjects): cough, shortness of breath, tickle in the throat, dizziness, headache, change in taste.
Less common reported side effects (one patient/subject) include nasal congestion, nausea, sneezing, wheezing, diarrhoea, itching, muscle pain, abdominal pain, rash, irritability, fatigue

In very rare cases a generalised allergic reaction may occur, the first time the study medication is inhaled. In some cases, inhaled PA101 may create a narrowing of the airways.
The knowledge about potential side effects increases with every study.

Patients may not benefit directly from participating, but this study might deliver data that helps development of medication for IPF patients

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. Male or female patients age 40 through 79 years, inclusive;2. Diagnosis of Idiopathic Pulmonary Fibrosis with the consensus of the multidisciplinary team based on the presence of definitive or possible usual interstitial pneumonia (UIP) pattern on high-resolution computed tomography (HRCT) and after excluding alternative diagnoses, including lung diseases associated with environmental and occupational exposure, with connective tissue diseases and with drugs ;3. Chronic cough present for at least 8 weeks and not responsive to current therapies ;4. Daytime cough severity score on visual analogue scale >40 mm at the Screening Visit;5. Transfer capacity for carbon monoxide corrected for hemoglobin (TLCOc) >25% predicted value within 3 months and Forced Vital Capacity (FVC) >50% predicted value within 1 month of the Screening Visit

Exclusion criteria

1. Current or recent history of clinically significant medical condition, laboratory abnormality, or illness that could put the patient at risk or compromise the quality of the study data as determined by the investigator;2. Significant cardiac disease (i.e., myocardial infarction within 6 months or unstable angina within 1 month of the Screening Visit);3. An upper or

lower respiratory tract infection within 4 weeks of the Screening Visit;4. Acute exacerbation of IPF within 3 months of the Screening Visit;5. Long-term daily oxygen therapy (>10 hours/day) ;6. Presence of pulmonary arterial hypertension with limitation of activity;11. Use of the following drugs within 2 weeks prior to the Screening Visit: Prednisone, narcotic antitussives, baclofen, gabapentin, and inhaled corticosteroids

Study design

Design

Study type:	Interventional
Intervention model:	Crossover
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	07-01-2015
Enrollment:	6
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	NA
Generic name:	Cromolyn sodium

Ethics review

Approved WMO

Date:	09-12-2014
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek

	(Assen)
Approved WMO Date:	18-12-2014
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

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	EUCTR2014-005180-32-NL
CCMO	NL51634.056.14

Study results

Results posted: 21-09-2016

First publication
01-01-1900