Evaluation of Pharmacokinetics, Relative Bioavailability, and Tolerability of Three Different Formulations of PA101 in Healthy Subjects, Patients with Systemic Mastocytosis, and Patients with Chronic Cough due to Idiopathic Pulmonary Fibrosis

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON42687

Source
ToetsingOnline

Brief title
PATARA PA101-PK-02

Condition

- Other condition
- Allergic conditions

Synonym

Systemic Mastocytosis and inflammatory

Health condition

aandoeningen gerelateerd aan de mast cellen (mastocyten)

Research involving
Human

Sponsors and support

Primary sponsor: PATARA PHARMA, LLC
Source(s) of monetary or material Support: PATARA PHARMA

Intervention

Keyword: Bioavailability, Pulmonary Fibrosis, Systemic Mastocytosis, Tolerability

Outcome measures

Primary outcome

Pharmacokinetic measurements: The PK parameters to be evaluated for plasma DSCG are maximum concentration (Cmax), time to maximum concentration (Tmax), terminal elimination half-life (T1/2), area under the plasma concentration-time curve from time = 0 to time of last measurable drug concentration (AUC0-t), and area under the plasma concentration-time curve from time = 0 to infinity (AUC0-inf). Urine DSCG levels will be measured for total DSCG excretion in the urine.

Safety measurements: Adverse events, changes in vital signs and 12-lead ECG.

Secondary outcome

Biomarker sample will be analyzed for potential predictive biomarkers as an exploratory analysis. The biomarkers tested will include the following:

• Cytokines (IL-1β, IL-2, IL-3, IL-4, IL-5, IL-6, IL-8, among others)

• Chemokines (CCL22, CCL3, CCL5, CXCL7, among others)

• Eicosanoids (PGD2, PGE1, PGE2, LTB4, LTC4, LTD4, LTE2, among others)

• Other mediators (tryptase, chymase, serotonin, among others)

• MicroRNA profile

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 preservative-free, room temperature-stable formulation with optimized pH and osmolality 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. Delivering PA101 with the eFlow nebulizer system (*Cromoflow*) achieves higher lung deposition and systemic levels of cromolyn sodium relative to currently marketed formulations of cromolyn sodium.

PA101 is being investigated as a first-line maintenance therapy for the treatment of clinical symptoms related to systemic mastocytosis, chronic cough related to idiopathic pulmonary fibrosis, and other mast cell associated disorders. Currently, PA101 is being tested in Phase 2 clinical trials in Europe in patients with ISM and in patients with refractory chronic cough in IPF and chronic idiopathic cough.

Study objective

The objectives of the study are as follows:

Primary:
• Part 1: To assess the pharmacokinetics and relative bioavailability of three different formulations of PA101 (4% cromolyn sodium with and without mannitol, and 6% cromolyn sodium without mannitol) in healthy adult volunteers.
• Parts 2 and 3: To assess the pharmacokinetics and relative bioavailability of two different formulations of PA101 (4% cromolyn sodium with and without mannitol) in patients with indolent systemic mastocytosis and patients with chronic cough due to idiopathic pulmonary fibrosis.

Secondary:
• To assess the safety and tolerability of three different formulations of PA101 using AEs, vital signs and ECGs.

• To assess biomarkers prior to and following PA101 administration.

Study design

This is a Phase 1, randomized, double-blind, crossover study conducted in three parts: Part 1 will be a 4-period crossover study conducted in 12 healthy adult subjects; Part 2 will be a 3-period crossover study in 6 patients with indolent systemic mastocytosis (ISM); and Part 3 will be a 3-period crossover study in 6 patients with chronic cough due to idiopathic pulmonary fibrosis (IPF). Part 1 will be completed first followed by Parts 2 and 3 after the analysis of data from Part 1.

Intervention

The study will start with a screening visit. During the screening visit standard medical assessments including safety laboratory tests (blood draw, urine collection), an alcohol breath test, urine drug screen, a physical examination, ECG and a vital signs measurement will be performed.

After the subject passes all above mentioned tests, the subject will be enrolled in the medication phase. During study the subjects will enter the clinic, will receive 2 or 3 medication formulations and placebo during 3 or 4 periods. They will be asked on a regular basis for possible side effects, blood will be drawn for safety and PK measurements and the vital signs will be checked regularly during the confinement periods. .

Finally a follow-up phone call will be performed. During this call the subjects will be asked for possible side effects.

Study burden and risks

There were no serious AEs, and most AEs were mild in intensity. The most common AEs were cough, dyspnea, throat irritation, dizziness, headache, and dysgeusia.

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

Part 1: Healthy Subjects
1. Male or female subjects 18-45 years of age, inclusive
2. Body weight > 50 kg and Body Mass Index of 18-25 kg/m2, inclusive
3. Normal 12-lead ECG recording at the Screening Visit
4. Normal or clinically insignificant changes in 12-lead ECG recording at the Screening Visit
Part 2:
1. Male or female subjects 18-65 years of age, inclusive
2. Diagnosed with indolent systemic mastocytosis (ISM) according to the WHO criteria
3. History of gastrointestinal symptoms related to systemic mastocytosis
4. Clinically stable systemic mastocytosis
5. Normal lung function (FEV1 >= 90% of predicted normal value) at the Screening Visit;Part 3:
1. Male or female patients age 40 through 75 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 and Forced Vital Capacity (FVC) > 50% predicted value within 3 months of the Screening Visit

Exclusion criteria

Part 1:
1. Current or recent history of clinically significant cardiovascular, respiratory, hematological, renal, neurologic, hepatic, endocrine, psychiatric, malignant or other illnesses that could put the subject at risk or compromise the quality of the study data as determined by the investigator
2. An upper or lower respiratory tract infection within 4 weeks
Part 2:
1. Aggressive systemic mastocytosis, mast cell leukemia, or systemic mastocytosis with an associated clonal hematologic non-mast cell disorder
2. Current or recent history of clinically significant cardiovascular, respiratory, hematological, renal, neurologic, hepatic, endocrine, psychiatric, malignant or other illnesses that could put the subject at risk or compromise the quality of the study data as determined by the investigator
3. History of systemic corticosteroid use within 6 weeks or immunosuppressive therapy within 6 months of the Screening Visit
Part 3:
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)

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):	20-10-2015
Enrollment:	24
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	PA101
Generic name:	PA101
Product type:	Medicine
Brand name:	PA101-B
Generic name:	PA101-B

Ethics review

Approved WMO Date:	15-09-2015
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	25-09-2015
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	EUCTR2015-003375-30-NL
CCMO	NL54835.056.15