An open label, randomized, single inhaled dose, three-way cross over pilot study to compare the pharmacokinetic profiles of different dry powder inhalers with tiotropium bromide in healthy volunteers.

Published: 01-08-2017
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Primary objective:* To compare the bioavailability of different dry powder formulations of tiotropium bromide in healthy volunteersSecondary objectives:* To compare the safety and tolerability of different dry powder formulations of tiotropium...

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

Summary

ID

NL-OMON44319

Source
ToetsingOnline

Brief title
PGTB001

Condition

- Bronchial disorders (excl neoplasms)

Synonym
COPD

Research involving

Human

Sponsors and support

Primary sponsor: Phargentis SA
Source(s) of monetary or material Support: Phargentis SA

Intervention

Keyword: Dry powder, Inhalation, Tiotropium bromide

Outcome measures

Primary outcome

* The area under the plasma concentration-time curve from time zero to time t

of the last measured concentration above the limit of quantification (AUC0-t).

* The area under the plasma concentration-time curve from zero to infinity

(AUC0-*).

* The maximum plasma concentration (Cmax).

* The time to reach maximum plasma concentration (tmax).

* The terminal elimination rate constant (*z) with the respective half-life

(t*).

Secondary outcome

* (Treatment emergent) adverse events

* Physical examination

* Vital signs

* ECG

* Spirometry

* Clinical safety laboratory

Study description

Background summary

Phargentis is developing a tiotropium bromide DPI product to aim for a generic by taking into consideration intellectual property issues for all aspects related to the drug substance, formulation, capsule selection, and inhaler device. Phargentis has developed two DPI formulations, which are expected to be comparable to the reference product Spiriva HandiHaler marketed by Boehringer Ingelheim. The two formulations differ with respect to the original product for the polymorphic form of the API and for the composition of the capsule shells (Hydroxypropylmethylcellulose capsule shells instead of PEG/gelatin capsule shells used by the originator). The formulations are supposed to be inhaled by means of an inhaler that is comparable to the Reference Device HandiHaler. Taking into account the features of the active ingredient and the used excipients, the sponsor concluded that there was no need to perform additional pre-clinical safety studies with their new tiotropium bromide inhalation powders.
The aim of the present study is to obtain preliminary pharmacokinetic data on the two Phargentis test formulations and the reference product which will allow for the selection of the final Phargentis formulation and the design and sample size calculation of the pivotal bioequivalence study.

Study objective

Primary objective:
* To compare the bioavailability of different dry powder formulations of tiotropium bromide in healthy volunteers
Secondary objectives:
* To compare the safety and tolerability of different dry powder formulations of tiotropium bromide in healthy volunteers

Study design

This is an open label, randomized, single inhaled dose, three -way cross over pilot study with a wash-out of at least two weeks between successive dosing occasions.

Intervention

After assessing eligibility during a screening period of up to 4 weeks, 18 subjects will be enrolled in this study. The study will consist of 3 periods, each separated by a wash-out period of at least 2 weeks between successive dosing occasions. During each period, subjects will come to the study center on the day before administration (Day -1) of the study drug, for baseline

assessments, inhalation instructions/training on the correct use of the inhalers and to re*confirm eligibility. On Day 1, all subjects will receive one single dose of tiotropium (consisting of two capsules) under fasted conditions. Blood samples for determination of tiotropium will be collected pre*dose and at specified time points up to Day 7 post*dose. Safety evaluations including adverse events recording and spirometry will be obtained at regular time points throughout the study. Subjects will be discharged from the clinic in the morning of Day 2. Subjects will return to the clinic for at least 4 more ambulant visits up to Day 7. After the blood sample on Day 7 of the last study period, subjects will undergo an End*of*study examination.
The overall study duration per subject will be approximately 10 weeks.

Study burden and risks

This study is being conducted in healthy volunteers. There are no anticipated benefits of the IMPs. Please see the IMP information (IB and SmPC) for further information.

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. Subjects must be healthy male or female subjects 18-50 years of age, inclusive.
2. Subjects must have normal lung function at Screening and prior to first dosing according to the investigator, e.g. FEV1 * 80% of the predicted normal value (inclusive).
3. Subject must be able to adequately follow the inhalation instructions and inhale correctly through both devices.

Exclusion criteria

1. A history of a clinically significant endocrine, gastrointestinal, cardiovascular, hematological, hepatic, immunological, renal, respiratory, genitourinary or major neurological (including stroke and chronic seizures) or any other clinically significant abnormality or disease.
2. An upper and/or lower respiratory tract infection within 3 weeks of Screening.
3. Any chronic and/or symptomatic upper or lower airway disease such as asthma, COPD, bronchiectasis, sarcoidosis, lung cancer, allergic airway disease (e.g. pollen allergy inside the relevant season or symptomatic to pets while daily exposed to them).
4. Current smokers (smoked in the previous 12 months or stopped smoking less than 12 months prior to Screening) or ex-smokers with more than 10 pack-year smoking history (e.g., at least 1 pack/day for 10 years, or 2 packs/day for 5 year).

Study design

Design

Study type:	Interventional
Intervention model:	Crossover
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	21-08-2017
Enrollment:	18
Type:	Actual

Medical products/devices used

Generic name:	MRX003-T10 DPI Inhalation device
Registration:	No
Product type:	Medicine
Brand name:	Phargentis test capsule 1
Generic name:	n.a.
Product type:	Medicine
Brand name:	Phargentis test capsule 2
Generic name:	n.a.
Product type:	Medicine
Brand name:	Spiriva capsule
Generic name:	n.a.
Registration:	Yes - NL intended use

Ethics review

Approved WMO

Date:	01-08-2017
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

Approved WMO

Date:	09-08-2017
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	EUCTR2017-002705-35-NL
CCMO	NL62461.056.17