A randomised, double-blind, double-dummy, multi-site, phase III, single dose, 4-way cross-over pharmacodynamic study evaluating the efficacy of Bricanyl Turbuhaler M3 compared to Bricanyl Turbuhaler M2 by studying the protective effect on methacholine induced bronchoconstriction in patients with stable, mild to moderate asthma

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Primairy Objective: To demonstrate therapeutic equivalence between Bricanyl Turbuhaler M3 and Bricanyl Turbuhaler M2 using bronchoprotective effect as outcome measure. Secondary Objective: To compare safety of Bricanyl Turbuhaler M2 and Bricanyl...

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

Summary

ID

NL-OMON42299

Source
ToetsingOnline

Brief title
BATMAN

Condition

- Bronchial disorders (excl neoplasms)

Synonym
Asthma

Research involving
Human

Sponsors and support

Primary sponsor: Astra Zeneca
Source(s) of monetary or material Support: AstraZeneca BV.

Intervention

Keyword: Asthma, Bricanyl Turbuhaler, Methacholine challenge test, Therapeutic equivalence

Outcome measures

Primary outcome

PC20 (Methacholine provocative concentration causing a 20% drop in FEV1)

Secondary outcome

Adverse events and Serious adverse events.

Study description

Background summary

Turbuhaler M3 was developed in late 1990*s and is considered a technical improvement over Turbuhaler M2. The basic functions and mechanisms were retained, while user-friendliness and robustness have been enhanced. A more accurate dose indicator was provided and the exterior design of the mouthpiece has been modified to become more comfortable and to clearly indicate a suitable position in the mouth. Moreover, the M3 product contains improved powder formulations, including lactose monohydrate, resulting in good filling and dosing properties.
Bricanyl Turbuhaler M3 has no marketing authorisation anywhere in the world. However, it has been developed for blinding purposes in clinical studies. It

has been used in clinical studies, as an investigational product (IP) in 2 studies and as blinded reliever medication (10 studies).

This study is designed to demonstrate that Bricanyl Turbuhaler M3 is therapeutically equivalent to Bricanyl Turbuhaler M2 to allow for a switch from Bricanyl Turbuhaler M2 to Bricanyl Turbuhaler M3.
The study design (a single-dose, randomised, double-blind, double dummy, multi-site 4 way cross-over study), the selection of the primary variable, the provocative concentration of methacholine which produces a 20% (PC20) fall in forced expiratory volume in one second (FEV1) and the selection of patients are in line with the Orally Inhaled Products (OIP) regulatory guideline (CHMP 2009) for demonstration of therapeutic equivalence between two products containing a short-acting β2-agonist. The study will evaluate the bronchoprotective effect of 0.5 and 1.5 mg Bricanyl Turbuhaler M2 compared with the corresponding doses of Bricanyl Turbuhaler M3 on methacholine induced bronchoconstriction, by means of the PC20 in patients with stable asthma. Moreover, the study will evaluate assay sensitivity, i.e. to show dose response, by analyzing the two dose levels of each device.
The 0.5 mg dose was chosen because 0.5 mg/dose is the lowest strength available in all European countries. The 1.5 mg dose (3 x 0.5 mg) was chosen because this is the highest recommended dose to be taken at a single occasion.

Study objective

Primairy Objective: To demonstrate therapeutic equivalence between Bricanyl Turbuhaler M3 and Bricanyl Turbuhaler M2 using bronchoprotective effect as outcome measure.

Secondary Objective: To compare safety of Bricanyl Turbuhaler M2 and Bricanyl Turbuhaler M3

Study design

A randomised, double-blind, double-dummy, multi-site, phase III, single dose, 4-way cross-over pharmacodynamic study evaluating the efficacy of Bricanyl Turbuhaler M3 compared to Bricanyl Turbuhaler M2 by studying the protective effect on methacholine induced bronchoconstriction in patients with stable asthma.

Intervention

- Spirometry
- Methacholine Challenge test.

Each patient will receive four different single-dose treatments in a randomised 4-way cross-over design:
•0.5 mg terbutaline sulphate administered via Turbuhaler M2

•1.5 mg terbutaline sulphate administered via Turbuhaler M2
•0.5 mg terbutaline sulphate administered via Turbuhaler M3
•1.5 mg terbutaline sulphate administered via Turbuhaler M3
The study will consist of 6-7 visits to the study site and one follow-up phone contact. The visits to the study site include 2/3 enrolment visits (visits 1a, 1b and 2) and 4 randomised terbutalin dosing visits (visits 3-6). Methacholine challenge test will be performed at 6 visits.

Study burden and risks

The subject is asked to visit the site at least 6 times. The visit time will last maximally two hours.
The subject will be contacted by telephone 1 time. The telephone contact will last maximally 10 minutes.

1 Blood sample will be taken in this study.
The subject will undergo 1 physical examination
Methacoline challange test will be performed at 6 visits.
1 ECG will be done.

Contacts

Public
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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

- Female and male aged 18 and 65 years.
- At least 6 months of documented clinical diagnosis of asthma as defined by GINA 2012 or American Thoracic Society (Expert Panel Report 3 2007) prior to visit 1
- Stable asthmatics on SABA alone, on low dose ICS (200-400 µg budesonide corresponding) or on fixed combination of low ICS/LABA
- At the enrolment visit 1a, the visit baseline FEV1 must be >=80 % of that predicted normal (NHANES III). For LABA patients the visit baseline FEV1 must be >=80 % of that predicted normal (NHANES III) at both visit 1a and visit 1b. If not, the patient will be withdrawn from the study
- At the enrolment visits 1a or 1b (LABA patients only) and at the end of run-in period, visit 2, eligible patients should demonstrate an airway responsiveness to methacholine PC20 <8 mg/mL. If not, the patient will be withdrawn from the study
- Capable of using Turbuhaler inhalation device as judged by investigator.

Exclusion criteria

- Diagnosed with COPD or history of cystic fibrosis, bronchiectasis or other respiratory diseases
- Pregnancy, breast-feeding, lactation, or planned pregnancy during the study. Fertile women not using acceptable contraceptive measures
- Conditions which could alter airway reactivity to methacholine (e.g. pneumonia, upper respiratory tract infection, viral bronchitis and/or sinobronchitis) within past six weeks
- Exacerbation due to asthma or change in asthma medication during the last 3 months prior to enrolment
- Night time awakenings due to asthma symptoms on 2 consecutive nights during the last 4 weeks prior to enrolment
- Smokers 6 months prior to the study start or with a history of smoking of more than 10 pack years (e.g. 20 cigarettes/day for at least 10 years, or 10 cigarettes/day for at least 20 years, or equal).

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Crossover
Masking:	Double blinded (masking used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	07-04-2015
Enrollment:	10
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Bricanyl
Generic name:	Terbutaline
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	12-02-2015
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	07-04-2015
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

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	EUCTR2014-001457-16-NL
CCMO	NL52187.042.15
Other	volgt