A 4-week Dose-Ranging, Dose-Interval, Efficacy, Safety and Tolerability Study of GSK961081 in Subjects with COPD.

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Respiratory disorders NEC
Study type	Interventional

Summary

ID

NL-OMON36391

Source
ToetsingOnline

Brief title
MAB115032

Condition

- Respiratory disorders NEC

Synonym
COPD

Research involving
Human

Sponsors and support

Primary sponsor: GlaxoSmithKline
Source(s) of monetary or material Support: GlaxoSmithKline BV

Intervention

Keyword: beta2 agonist, COPD, GSK961081, muscarinic antagonist

Outcome measures

Primary outcome

Change from baseline in trough FEV1 on Day 29.

Secondary outcome

Weighted mean for 0 to 24 H serial FEV1, other pulmonary function parameters,

adverse events, exacerbations, PK, PK-PD.

Study description

Background summary

COPD is a disorder characterized by airflow obstruction and reduced maximum expiratory flow from the lungs that is not fully reversible. Previous clinical research has indicated that combining an inhaled muscarinic antagonist with a beta2-agonist is more effective than the individual components in managing stable COPD to improve lung function. Therefore, the development of a novel chemical entity which combines both pharmacological approaches in a single bifunctional molecule (i.e. a dual pharmacophore) affords clear advantages. GSK961081 is a bifunctional molecule that demonstrates both anti-muscarinic receptor activity and beta-adrenergic agonist activity in both pre-clinical and clinical studies. In previous studies, inhaled GSK961081 has been administered as a dry powder either as the edisylate or succinate salt. GSK961081 has been safe and well tolerated and demonstrated bronchodilatory activity in these studies. In this and future studies, GSK961081 dry powder formulations will contain the succinate salt. This study is primarily designed to assess the dose response, dose interval, efficacy and safety of 3 once daily and 3 twice daily doses for 28 days in subjects with moderate/severe COPD versus placebo. Salmeterol 50mcg BID is included in the study as an active comparator.

Study objective

The primary objective of this study is to evaluate the dose response, dose interval, efficacy, and safety of GSK961081 by studying three QD doses and three BID doses in subjects with COPD.
The study will also evaluate the population PK, systemic PK-PD, dose-response

and dose-time-response FEV1 profile of GSK961081, and collect blood samples for a pharmacogenetic study.

Study design

Multicenter randomized double blind phase IIb parallel group study en active and placebo control.
Randomisation (1:1) to treatment with:
1. GSK961081 100 mcg QD
2. GSK961081 400 mcg QD
3. GSK961081 800 mcg QD
4. GSK961081 100 mcg BID
5. GSK961081 200 mcg BID
6. GSK961081 400 mcg BID
7. Salmeterol 50 mcg BID
8. Placebo.

Administration as inhaled dry powder formulation.
Startification according to reversibility (salbutamol) and steroid use.
Treatmnent duration 4 weeks.
Approx 425 patients, 35 in NL.

Intervention

Treatment with GSK961081, salmeterol or placebo.

Study burden and risks

Risk: Adverse effects of study medication.
Burden: 6 visits in 6 weeks. Duration 4-14 h (2 long measurement days of approx. 14 h). Fasting required for 2 visits.
Pulmonary function tests: 1x incl. reversibility. During 5 visits serial measurements (3 visits: 2 tests in 2 h, 2 visits: 10 tests in 13 h).
Blood tests during 4 visits (thereof on 2 occasions 4 draws), 100 ml in total , pregnancy test (if relevant) 3x, ECGs during 4 vistis (thereof on 2 occasions 4 recordings).
Daily completion of diary.
Chest X-ray only if not performed in the past 6 months.
Optional blood sample for pharmacogentic research (10 ml).

Contacts

Public
GlaxoSmithKline

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

• COPD patients >=40 years of age.
• (Ex) smokers, at least 10 pack years.
• Post salbutamol FEV1/FVC ratio <70%.
• Post salbutamol FEV1 30-70% of predicted.
• Safe contraception for women of childbearing potential.

Exclusion criteria

• Pregnancy.
• Bronchial asthma.
• Oral steroids in the past 6 weeks.
• Hospitalization in the past 12 weeks for COPD or pneumonia.
• Antibiotics for lower respiratory tract infection in the past 6 weeks.
• BMI >35 kg/m2.
• Pacemaker.
• Significant ECG abnormalities (see protocol for details).
• Contraindications for the use of anticholinergics.

• Treatment with specified (mainly COPD) therapies within a specified time frame (see protocol for details).

Study design

Design

Study phase:	2
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	01-02-2011
Enrollment:	35
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	GSK961081
Generic name:	GSK961081
Product type:	Medicine
Brand name:	Serevent
Generic name:	salmeterol
Registration:	Yes - NL intended use

Ethics review

Approved WMO

Date:	22-10-2010
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	04-11-2010
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	11-01-2011
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	26-01-2011
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	28-01-2011
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	04-02-2011
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	24-02-2011
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

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
Other	clinicaltrials.gov, registratienummer n.n.b.
EudraCT	EUCTR2010-022796-62-NL
CCMO	NL34210.060.10