Randomised, Double-Blind(Sponsor Open), Placebo-Controlled, Multicentre, Dose Ranging Study to Evaluate the Efficacy and Safety of Danirixin Tablets Administered Twice Daily Compared With Placebo for 24Weeks in Adult Participants With Chronic Obstructive Pulmonary Disease (COPD) (study 205724)

Published: 18-04-2017
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Primary:To characterize the dose response of danirixin compared with placebo on the incidence and severity of respiratory symptoms in subjects with COPD and to compare the safety of danirixin with placebo.Secondary:To assess the annual rate of...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Lower respiratory tract disorders (excl obstruction and infection)
Study type	Interventional

Summary

ID

NL-OMON45435

Source
ToetsingOnline

Brief title
205724

Condition

- Lower respiratory tract disorders (excl obstruction and infection)

Synonym
chronic obstructive airways disease (COPD)

Research involving
Human

Sponsors and support

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

Intervention

Keyword: COPD, Danirixin, dose ranging, placebo

Outcome measures

Primary outcome

Change from baseline in respiratory symptoms measured by the E-RS:COPD daily diary. Adverse events.

Secondary outcome

Number of annual COPD exacerbations. Time to first exacerbation. Change from baseline for the St. George*s Respiratory Questionnaire total score and other SGRQ parameters. Lung function (FEV1, FEV1 % predicted, FVC, FEV1/FVC ratio). Rescue medication use. PK parameters.

Study description

Background summary

The morbidity and mortality of COPD are continuing to increase and worldwide, by the year 2020, COPD is expected to be the third leading cause of death and fifth leading cause of disability.

Despite several available therapies that have been shown to reduce COPD exacerbations and respiratory symptoms, many COPD patients continue to experience a high burden of respiratory symptoms and COPD exacerbations. Additionally, there is growing recognition that a high percentage of COPD patients with mild airflow limitation as well as smokers with preserved lung function suffer from a high burden of symptoms and COPD exacerbations. Therapies that effectively further reduce COPD exacerbations and improve respiratory symptoms could have a substantial impact on healthcare utilization and most importantly result in an improvement in COPD patients* quality of life. There is much evidence that the CXCR2 chemokine receptor plays a pivotal role in neutrophil activity in the lung. Danirixin has demonstrated potent antagonism of CXCR2 activity both in vitro and in vivo in preclinical and clinical studies. Its potency and duration of action supports its potential use as an oral, anti-inflammatory agent in the treatment of COPD. In clinical trials danirixin has been well-tolerated and most adverse events were mild to moderate.
The primary aim of this study is to evaluate the clinical activity and safety of 5 doses of danirixin compared with placebo in subjects with COPD.

Study objective

Primary:
To characterize the dose response of danirixin compared with placebo on the incidence and severity of respiratory symptoms in subjects with COPD and to compare the safety of danirixin with placebo.
Secondary:
To assess the annual rate of moderate/severe COPD exacerbations, to further characterize clinical activity, to characterize the pharmacokinetics of danirixin.

Study design

Double-blind (Sponsor Open), placebo-controlled, parallel group study.
Baseline assessments collected over a 7 day period (i.e. EXACT/E-RS:COPD, physical activity, and rescue medication use). Thereafter randomization (1:1:1:1:1:1):
* one of five dose strengths of danirixin (5, 10, 25, 35, 50 mg bid) or
* placebo for 24 weeks.
Three interim analyses are planned for the study: PK after 10 participants in each treatment group have completed Visit 3, futility analysis based on the E-RS:COPD after 150 participants have completed 3 months of study treatment, after 450 participants have completed 6 months of study treatment). The third interim analysis will be used to support GSK decisions regarding the further development of danirixin. The last interim analysis will include all clinical activity assessments and safety assessments.
Estimation 600 subjects (700 to be screened).

Intervention

Treatment with danirixin or placebo.

Study burden and risks

Risk: Adverse events of danirixin.
Burden:
11-12 visits in 32 weeks.
Physical examination: 5 times.
Blood draws: max. 11 times (175 ml blood in total).
Pregnancy test: 8 times.
Pulmonary function tests: 4 times.
ECG: 5 times.
Chest X-ray: once.
Entire study period: 1. Daily diary use of rescue medication, adverse events 2. Daily symptoms questionnaire.
Questionnaires: health resource utilization, symptoms and quality of life.
Optional: genetics blood sample (6 ml), PK sampling over 12 hours 9 blood draws (2 ml each).

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

* 40 to 80years of age inclusive.
* COPD based on ATS/ERS current guidelines.
* Symptoms including chronic cough, mucus hypersecretion, and dyspnea on most days for at least the previous 3 months.
* Documented history of COPD exacerbation(s) in the previous year. See protocol page 28 for details.
* Current and former smokers with a cigarette smoking history of *10 pack years. See protocol page 28 for details.
* Female participant of childbearing potential and male participant who agrees to follow the contraceptive guidance in appendix5 of the protocol during the treatment period and for at least 60 hours after the last dose of study treatment.

Exclusion criteria

* Diagnosis of other clinically relevant lung diseases (other than COPD).
* Alpha-1-antitrypsin deficiency.
* Less than 14 days have elapsed from the completion of a course of antibiotics or oral corticosteroids for a recent COPD exacerbation.
* Peripheral blood neutrophil count <1.5 x 109/L.
* Pneumonia (chest X-ray or CT confirmed) within the 3 months prior to screening.
* Chest x-ray or CT scan with evidence of a clinically significant abnormality not believed to be due to the presence of COPD (historic results up to 1 year prior to screening may be used).
* Current or chronic history of liver disease, or known hepatic or biliary abnormalities. Exceptions see protocol page 30.
* Abnormal and clinically significant 12-lead ECG finding. See protocol page 30 for details.
* Prior/Concomitant Therapy: see protocol page 30 for details.
* Prior/Concurrent Clinical Study Experience: see protocol page 31 for details.
* Pregnancy or breastfeeding.

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):	04-09-2017
Enrollment:	50
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Danirixin
Generic name:	Danirixin

Ethics review

Approved WMO Date:	18-04-2017
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	16-06-2017
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	11-08-2017

Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	18-08-2017
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	04-12-2017
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	21-12-2017
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	18-05-2018
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	20-06-2018
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
EudraCT	EUCTR2016-003675-21-NL
CCMO	NL60702.100.17
Other	www.gskclinicalstudyregister.com (205724); clinicaltrials.gov (registratienummer n.n.b.)