A Phase IIa Randomized, Placebo-Controlled, Double-Blind (Sponsor Open) Study to Investigate the Clinical Efficacy, Safety, and Tolerability of Nemiralisib (GSK2269557) in Symptomatic COPD Participants with a History of Exacerbations (205739)

Published: 04-06-2018
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Primary:To evaluate the clinical efficacy of nemiralisib compared with placebo to reduce the annual rate of moderate and severe exacerbations in participants with COPD.Secondary:Further efficacy parameters pertaining to exacerbations and aligned...

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

Summary

ID

NL-OMON45791

Source
ToetsingOnline

Brief title
study 205739

Condition

- Bronchial disorders (excl neoplasms)

Synonym
COPD; chronic obstructive airway disease

Research involving
Human

Sponsors and support

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

Intervention

Keyword: COPD, exacerbations, Nemiralisib, placebo

Outcome measures

Primary outcome

Annualized rate of moderate and severe exacerbations

Secondary outcome

Annualized rate of mild, moderate and severe exacerbations. Time to first moderate/severe exacerbation. Time to first mild/moderate/severe exacerbation. COPD Assessment Test (CAT). St. George*s Respiratory Questionnaire. Exacerbations of Chronic Pulmonary Disease Tool (EXACT). Trough IC, FEV1 and FVC measured pre and post-bronchodilator at Week 4, 12, 28, 52. Rescue medication use. PK parameters. Adverse events.

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. Phosphoinositide 3-Kinase Delta (PI3Kd) is thought to play a role in a number of epithelial responses relevant for the development of COPD. Therefore a PI3Kd inhibitor may be able to suppress a number of these processes. A greater proportion of macrophages appear to be alternatively activated in COPD and their ability to phagocytose infective pathogens is reduced as a result of this alternative activation. PI3Kd is one of the mediators involved in determining this alternative phenotype in macrophages and therefore it is proposed that inhibition of PI3Kd might rebalance macrophage activation towards a classic phagocytic phenotype facilitating clearance of bacteria, a major cause of exacerbation in COPD. The neutrophil and T cell are the two major inflammatory cell types involved in the pathogenesis of COPD and both are targeted by PI3Kd inhibitors.
Nemiralisib is a potent and highly selective inhaled PI3Kd inhibitor being developed as an anti-inflammatory for the treatment of inflammatory airways diseases. Nemiralisib will be administered via the ELLIPTA inhaler.
This placebo controlled study is designed to evaluate the clinical efficacy, safety, and tolerability of a single 500 mcg inhaled daily dose of nemiralisib for a period of 12 months. Nemiralisib will be added to the prescribed inhaled maintenance COPD therapy. Participants will be selected for the study on the basis that they are at an increased risk of exacerbation, having experienced *2 moderate or *1 severe COPD exacerbation(s) in the preceding 12 months despite the available maintenance therapy and are symptomatic and with COPD Assessment Test (CAT*10) at screening.

Study objective

Primary:
To evaluate the clinical efficacy of nemiralisib compared with placebo to reduce the annual rate of moderate and severe exacerbations in participants with COPD.
Secondary:
Further efficacy parameters pertaining to exacerbations and aligned with the primary objective. Symptoms and health related quality of life. Lung function. Usage of rescue medication. Pharmacokinetics. Safety and tolerability.

Study design

Phase IIa, multicenter, randomized, double-blind (sponsor open), placebo-controlled, parallel-group study.
Study medication (nemiralisib or placebo) on top of standard of care for COPD exacerbation. Randomization to 2 treatment groups: nemiralisib (500 mcg QD) and placebo (1:1).

Screening period (2 weeks), treatment period (12 months), follow-up period (up to 2 weeks).
Approx. 400 subjects.

Intervention

Treatment with nemiralisib or placebo.

Study burden and risks

Risk: Adverse events of nemiralisib.
Burden:
9-10 visits in 56 weeks.
Physical examination: 2 times.
Blood draws: 9 times (130 ml blood in total).
Pregnancy test: 9 times.
Pulmonary function tests with reversibility: 6 times.
ECG: 6 times.
Chest X-ray/CT-scan: once (if not performed in the past 3 months).
Entire study period: Electronic diary.
Questionnaires: COPD symptoms and exacerbations, work productivity.
Optional: genetics blood sample (6 ml), PK sampling over 1-6 hrs (twice) 3 blood draws (12 ml in total).

Contacts

Public
GlaxoSmithKline

Huis ter Heideweg 62
Zeist 3705 LZ
NL
Scientific
GlaxoSmithKline

Huis ter Heideweg 62
Zeist 3705 LZ
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

* Males and females * 40 and * 80 years of age.
* Established clinical history of COPD. See protocol page 37-38 for details.
* *2 moderate or *1 severe COPD exacerbation(s) in the preceding 12 months. See protocol page 38 for details.
* Current or former cigarette smoker with a history of *10 pack-years.
* A score of *10 on the COPD Assessment Test (CAT) at Screening.
* Existing prescribed inhaled COPD maintenance therapy must be a stable daily inhaled COPD maintenance therapy for at least 3 months prior to Screening. See protocol page 38 for details.
* Post-bronchodilator FEV1/FVC ratio * 0.70 and post-bronchodilator FEV1 * 80% of predicted in the past 5 years..
* No antibiotics and/or oral corticosteroids for a COPD exacerbation within 6 weeks prior to Screening.
* Female participant of childbearing potential who agrees to follow the contraceptive guidance in appendix 5 of the protocol. See protocol page 38-39 for details.

Exclusion criteria

* Asthma.
* Pneumonia (chest X-ray or CT confirmed) within the last 3 months prior to Screening
* Other respiratory disorders or other diseases, see protocol page 39-40 for details.
* Prior/Concomitant Therapies, see protocol page 40-42 for details.
* Prior/Concurrent Clinical Study Experience: see protocol page 42-43 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):	12-06-2018
Enrollment:	20
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Nemeralisib
Generic name:	Nemeralisib

Ethics review

Approved WMO Date:	04-06-2018
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	16-08-2018
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	24-09-2018

Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	25-09-2018
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	EUCTR2017-004564-35-NL
Other	gskclinicalstudyregister.com; registratienummer 205739
CCMO	NL65962.100.18