A randomised, double-blind (sponsor unblinded), placebocontrolled, parallel-group, multicentre study to evaluate the efficacy and safety of GSK2269557 administered in addition to standard of care in adult subjects diagnosed with an acute exacerbation of Chronic Obstructive Pulmonary Disease (PII116678)

Published: 01-12-2014
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Primary: To evaluate the effect of once daily repeat inhaled doses of GSK2269557 on lung parameters derived from HRCT scans in subjects with acute exacerbation of COPD,compared to placebo. Secondary: Other lung parameters derived from high...

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

Summary

ID

NL-OMON43618

Source
ToetsingOnline

Brief title
PII116678

Condition

- Respiratory disorders NEC

Synonym
COPD; chronic obstructive pulmonary disease

Research involving
Human

Sponsors and support

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

Intervention

Keyword: COPD, exacerbation, GSK2269557, placebo

Outcome measures

Primary outcome

siVaw at FRC and TLC after 12 and 28 days of treatment.

Secondary outcome

Whole body plethysmography parameters (e.g. iVaw, (s)iRaw), trachea length and diameter, adverse events, PK parameters, FEV1 and PEF, questionnaires, number of treatment failures and time to next exacerbation (see protocol page 10 for details).

Study description

Background summary

GSK2269557 is a potent and highly selective inhaled Phosphoinositide 3-Kinase Delta (PI3Kd) inhibitor being developed as an anti-inflammatory and anti-infective agent for the treatment of inflammatory airways diseases. 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. 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.
Existing data suggests that repeat dosing with GSK2269557 could potentially reduce the impact of an acute exacerbation, or prevent the onset of a secondary exacerbation.
The purpose of this study is to evaluate the efficacy of GSK2269557 administered in addition to standard of care in adult subjects diagnosed with an acute exacerbation of COPD.
To date GSK2269557 has not been administered to subjects with an acute exacerbation of COPD, but has been safely administered to healthy volunteers and a study in stable COPD subjects is currently ongoing.

Study objective

Primary: To evaluate the effect of once daily repeat inhaled doses of GSK2269557 on lung parameters derived from HRCT scans in subjects with acute exacerbation of COPD,
compared to placebo.
Secondary: Other lung parameters derived from high resolution (HR) CT-scans, safety and tolerability, PK, number of treatment failures, time to next exacerbation.

Study design

Randomised, double-blind (sponsor unblended), placebo-controlled, parallel-group phase IIA study. Randomisation (1:1) upon diagnosis acute exacerbation of COPD to inhaled
• GSK2269557 once daily
• Placebo.
on top of standard treatment.
Screening max. 3 days. Treatment period 12 weeks. Follow-up period 1-2 weeks.
Approx. 120 patients.

Intervention

Treatment with GSK2269557 or placebo.

Study burden and risks

Risk: adverse events of study treatment.
Burden: 8 visits in approx. 14 weeks.
Physical examination 6-7 times.
Blood draws 6-7 times (approx. 100 ml in total).
Pregnancy test 3 times.
Whole body plethysmography 3 times.
HRCT-scans 3 times.
ECG 6-7 times.
3 times completion of 1 questionnaire.
Pulmonary function test (FEV1, PEF) daily (at home).
Paper diary for AEs, study medication and concomitant medication.
Optional:
- pharmacogenetic research (6 ml blood once).
- biomarker research (4 times sputum and 2,5 ml blood).

Contacts

Public
GlaxoSmithKline

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Scientific
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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Elderly (65 years and older)

Inclusion criteria

• Between 40 and 80 years of age inclusive.
• Confirmed diagnosis of COPD (GOLD guidelines) for at least 6 months.
• Post-bronchodilator FEV1/FVC < 0.7 and FEV1 <= 80 % of predicted, documented in the last 5 years.
• Acute exacerbation of COPD requiring an escalation in therapy to include corticosteroid and antibiotics. See protocol page 23-24 for details.
• Smoker or an ex-smoker with a smoking history of at least 10 pack years.
• Body weight >=45 kg and BMI within the range 18 - 32 kg/m2 (inclusive).
• Adequate contraception for females of childbearing potential. See protocol page 25-26 for details.

Exclusion criteria

• Severe COPD exacerbation. To avoid recruitment of subjects with a severe COPD exacerbation, the presence of any one of the following severity criteria will render the subject ineligible for inclusion in the study:
- Need for invasive mechanical ventilation (short term (< 48h) NIV or CPAP is acceptable)
- Haemodynamic instability or clinically significant heart failure
- Confusion
- Clinically significant pneumonia, identified by chest X-ray (if available) or on the CT scan performed during screening. See protocol page 28 for more details.
• ECG indicative of an acute cardiac event or demonstrating a clinically significant arrhythmia requiring treatment.
• QTc prolongation. See protocol page 27 for details.
• Chronic treatment with macrolides; long term oxygen therapy (>15 hours/day).
• Chronic treatment with anti-TNF, anti-IL1, or any other immunosuppressive therapy within 60 days prior to dosing.
• Exposure to more than 4 investigational medicinal products within 12 months prior to the first dosing day.
• 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):	21-05-2015
Enrollment:	15
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	GSK2269557
Generic name:	GSK2269557

Ethics review

Approved WMO Date:	01-12-2014
Application type:	First submission
Review commission:	METC Maxima Medisch Centrum (Veldhoven)
Approved WMO Date:	27-02-2015
Application type:	First submission
Review commission:	METC Maxima Medisch Centrum (Veldhoven)
Approved WMO Date:	13-04-2015
Application type:	Amendment
Review commission:	METC Maxima Medisch Centrum (Veldhoven)
Approved WMO Date:	22-04-2015
Application type:	Amendment

Review commission:	METC Maxima Medisch Centrum (Veldhoven)
Approved WMO Date:	29-06-2015
Application type:	Amendment
Review commission:	METC Maxima Medisch Centrum (Veldhoven)
Approved WMO Date:	23-07-2015
Application type:	Amendment
Review commission:	METC Maxima Medisch Centrum (Veldhoven)
Approved WMO Date:	21-08-2015
Application type:	Amendment
Review commission:	METC Maxima Medisch Centrum (Veldhoven)
Approved WMO Date:	26-01-2016
Application type:	Amendment
Review commission:	METC Maxima Medisch Centrum (Veldhoven)
Approved WMO Date:	28-01-2016
Application type:	Amendment
Review commission:	METC Maxima Medisch Centrum (Veldhoven)
Approved WMO Date:	24-02-2016
Application type:	Amendment
Review commission:	METC Maxima Medisch Centrum (Veldhoven)
Approved WMO Date:	01-03-2016
Application type:	Amendment
Review commission:	METC Maxima Medisch Centrum (Veldhoven)

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	EUCTR2014-001972-70-NL
Other	gsk-clinicalstudyregister.com; registratienummer 116678
CCMO	NL51467.015.14