A Randomized, Double-blind, Placebo-controlled Study to Evaluate the Efficacy and Safety of Dupilumab in Patients with Severe Steroid Dependent Asthma

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Primary objective: To evaluate the efficacy of dupilumab, compared with placebo, for reducing the use of maintenance oral corticosteroids (OCS) in patients with severe steroid-dependent asthma.Secondary objectives:To evaluate the safety and…

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Allergic conditions
Study type	Interventional

Summary

ID

NL-OMON44861

Source
ToetsingOnline

Brief title
VENTURE

Condition

- Allergic conditions
- Lower respiratory tract disorders (excl obstruction and infection)

Synonym
Asthma, Severe Steroid Dependent Asthma

Research involving
Human

Sponsors and support

Primary sponsor: Sanofi-aventis
Source(s) of monetary or material Support: Sanofi

Intervention

Keyword: Dupilumab, Phase III, Placebo-Controlled, Severe Steroid Dependent Asthma

Outcome measures

Primary outcome

Percentage change in OCS dose while maintaining asthma control

Secondary outcome

- Proportion of patients achieving a reduction of 50% or greater in their OCS

dose while maintaining asthma control.

- Absolute reduction of OCS dose while maintaining asthma control

- Proportion of patients achieving a reduction of OCS dose to <5 mg while

maintaining asthma control

- Proportion of patients achieving a reduction of OCS dose to 0 while

maintaining asthma control

- Proportion of patients achieving maximum possible OCS dose reduction while

maintaining asthma control

Study description

Background summary

Dupilumab is under development as a potential novel treatment for asthma. Dupilumab, a fully human monoclonal antibody, is directed against the IL-4 receptor alpha subunit (IL-4R*), which is a component of IL-4 receptors Type I and Type II, as well as the IL-13 receptor. The binding of dupilumab to IL-4R* results in blockade of downstream signaling initiated by both IL-4 and IL-13.

Up-regulation of IL-4 and IL-13 activity has been implicated as an important inflammatory component of asthma disease progression. Recently published clinical data from a Phase 2 clinical trial, demonstrated that dupilumab had a significant clinical effect in reducing asthma exacerbations, improving lung function and asthma control in patients with moderate to severe uncontrolled asthma in comparison with placebo.

Study objective

Primary objective: To evaluate the efficacy of dupilumab, compared with placebo, for reducing the use of maintenance oral corticosteroids (OCS) in patients with severe steroid-dependent asthma.

Secondary objectives:
To evaluate the safety and tolerability of dupilumab.
To evaluate the effect of dupilumab in improving patient-reported outcomes.
To evaluate dupilumab systemic exposure and the incidence of treatment-emergent antidrug
antibodies.

Study design

Phase III, Double blinded, Placebo controlled

Intervention

Dupilumab or placebo every 2 weeks (loading dose with a double dose) added to current controller medications.

Study burden and risks

Risks and burdens related to blood collection and possible adverse events of study medication

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

Adult patients with a physician diagnosis of asthma for *12 months, based on the Global Initiative for Asthma (GINA) 2014 guidelines and the following criteria:;* Patients with severe asthma and a well-documented requirement for regular treatment with maintenance systemic corticosteroids in the 6 months prior to Visit 1 and using a stable OCS dose for 4 weeks prior to Visit 1.
* Existing treatment with high dose inhaled corticosteroid in combination with a second controller for at least 3 months with a stable dose of ICS for *1 month prior to Visit 1. In addition, patients requiring a third controller for their asthma are considered eligible for this study.
* Forced expiratory volume in 1 second (FEV1) <80% of predicted normal.
* Evidence of asthma as documented by either: Reversibility of at least 12% and 200 mL in FEV1 after the administration of 200 to 400 mcg (2 to 4 puffs of albuterol/salbutamol) before randomization or documented in the 12 months prior to Visit 1 OR Airway hyperresponsiveness (methacholine: provocative concentration that causes a positive reaction [PC20] of <8 mg/mL) documented in the 12 months prior to Visit 1.

Exclusion criteria

* Patients <18 years of age.
* Patients who weigh <30 kg.
* Chronic obstructive pulmonary disease (COPD) or other lung diseases (eg, idiopathic pulmonary fibrosis, Churg-Strauss Syndrome, etc) which may impair lung function.
* Clinical evidence or imaging (eg, chest X-ray, computed tomography, magnetic resonance

imaging) within 12 months of Visit 1 with clinically significant findings of lung disease(s) other than asthma, as per local standard of care.
* A patient who experiences a severe asthma exacerbation (defined as a deterioration of asthma that results in emergency treatment, hospitalization due to asthma, or treatment with systemic steroids at least twice their current dose for at least 3 days) within 4 weeks before Visit 1.
* A subject who requires 12 puffs or more of rescue medication on any 1 day in the week prior to Visit 1.
* A subject who has experienced an upper or lower respiratory tract infection within the 4 weeks prior to Screening.
* Current smoker or cessation of smoking within 6 months prior to Visit 1.
* Previous smoker with a smoking history >10 pack-years.
* Comorbid disease that might interfere with the evaluation of the investigational medicinal product (IMP).

Study design

Design

Study phase:	3
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):	18-03-2016
Enrollment:	9
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	n.v.t.

Generic name:	dupilumab

Ethics review

Approved WMO Date:	11-08-2015
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	04-11-2015
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	16-12-2015
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	21-12-2015
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	06-01-2016
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	18-02-2016
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	29-02-2016
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	16-03-2016
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

Approved WMO Date:	15-04-2016
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	18-04-2016
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	11-07-2016
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	31-08-2016
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	14-09-2016
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	06-12-2016
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	13-03-2017
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	23-03-2017
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

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	EUCTR2015-001573-40-NL
Other	IND105379
CCMO	NL54335.091.15