A Phase 1, Randomized, Double-blind, Placebo-controlled Study Evaluating CNTO 3157 in Healthy Normal and Asthmatic Subjects Inoculated with Human Rhinovirus Type 16

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

Summary

ID

NL-OMON39844

Source
ToetsingOnline

Brief title
Phase 1 trial in asthma patients with medication CNTO3157 and HRV-16

Condition

- Lower respiratory tract disorders (excl obstruction and infection)

Synonym
asthma chronic lung inflammation

Research involving
Human

Sponsors and support

Primary sponsor: Janssen-Cilag
Source(s) of monetary or material Support: farmaceutische industrie

Intervention

Keyword: Asthmatic Subjects, CNTO3157, healthy normal Subjects, Human Rhinovirus Type 16

Outcome measures

Primary outcome

Efficacy in Part 2 will be assessed using standard assessments to evaluate asthma treatments (eg, FEV1, ACQ). Although these standard assessments are primarily meant to assess efficacy, changes in these assessments will also be used to monitor safety throughout the study.

Efficacy evaluations will include spirometry (including FEV1, etc.), collection of patient reported outcomes (ACQ), daily asthma symptom diaries collected on a handheld electronic device (including the number of nocturnal awakenings, rescue medication use, impact on activities, and PEF), and assessment of nasal and ocular symptoms using TNOSS. These evaluations are widely accepted as standard endpoints for demonstrating therapeutic efficacy in terms of reduction of signs and symptoms of asthma. TNOSS will be used to evaluate the potential effect of CNTO 3157 on nasal and ocular symptoms which often co exist in subjects with asthma.

Secondary outcome

see general description of study parameters in paragraph: "primary study parameters/outcome of the study"

Study description

Background summary

CNTO 3157 is a fully human, sequence-adapted, IgG4* monoclonal antibody (mAb) that binds the extracellular domain (ECD) of human Toll-like receptor 3 (TLR3).
Exacerbations of asthma are frequently due to respiratory viral infections, in particular those caused by human rhinoviruses (HRVs). While the underlying mechanisms driving viral-induced exacerbations of asthma are not fully understood, it is possible that activation of TLR3 by viral RNA could trigger or enhance immune-mediated pathologies associated with exacerbations of asthma.

Study objective

The primary objective of Part 2 of this study is to determine the efficacy of pretreatment with CNTO 3157 compared with placebo in attenuating the respiratory manifestations of inoculation with HRV-16 in adult subjects with mild to moderate asthma.

The secondary objectives are to assess the safety, tolerability, PK, PD, and immunogenicity of multiple IV administrations of CNTO 3157 compared with placebo in adult subjects with mild to moderate asthma inoculated with HRV-16.

Study design

The study is randomized, multi-center, double-blind, parallel-design and placebo controlled
In Part 2, the severity of an upper respiratory tract infection due to inoculation with HRV-16 will be assessed
At the same time the efficacy will be assessed in part 2, using standard assessments to evaluate asthma treatments (eg, FEV1, PEFR, ACQ).
An independent Data Monitoring Committee will be commissioned for this study.

Intervention

Subjects in Part 2 will receive either 4 IV infusions of placebo at Week 1, Week 2, Week 3, and Week 4 (30 subjects), or 1 IV infusion of CNTO 3157 10 mg/kg at Week 1 followed by 3 infusions of 3 mg/kg of CNTO 3157 at Week 2, Week 3, and Week 4 (30 subjects). These infusions will also be administered over a period of not less than 30 minutes. After the last infusion (within 24 to 72 hours) at Week 4, subjects will be inoculated with HRV-16.

Study burden and risks

This is described in the information for the patient in the paragraph: "Which side effects can I expect?"
Summary from this paragraph:

Possible side effects from CNTO 3157:
Headache
Swelling of the nasal passages
Back pain
Generalized pain
Nausea
Diarrhea
Cough
Sore throat
Toothache

Most commond side effects of HRV-16 include:
Runny nose
Sneezing
Nasal Congestion
Rapid heartbeat
Ringing in the ears
Bronchitis
Jaw pain
Cough
Respiratory tract congestion
Tiredness

Possibility allergic reactions, possibility infusion reactions, risk vaccins and risks study procedures are also described in this paragraph

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

Be 18 (or the legal age of consent in the jurisdiction in which the study is taking place) to 75 years of age, inclusive at the time of signing the informed consent
-Have a body mass index (BMI) of 19 to 40 kg/m2 inclusive.
- Have a physician documented diagnosis of asthma for at least 6 months prior to Screening Visit 2.
- Have objective evidence of asthma by fulfilling 1 of the following 4 criteria below. Only 1 of these 4 criteria below needs to be fulfilled:
• An increase in FEV1 of 12% or greater and at least a 200 mL within 30 minutes after administration of up to 8 puffs of a short-acting β2-agonist (SABA) at Screening Visit 2,
• -documented increase in FEV1 of 12% or greater and at least a 200 mL within 30 minutes after administration of up to 8 puffs of a SABA within 36 months before Screening Visit 1
• -documented airway reactivity to histamine (PC20 histamine < or equal 8 mg/mL) or methacholine (PC20 methacholine < or equal 16 mg/mL) within 36 months prior to screening visit 1
• Airway reactivity to histamine (PC20 histamine < or equal 8mg/ml) or methacholine (PC20 methacholine < or equal 16 mg/ml assessed between screening visit 2 and prior to day 1.
- Have stable asthma based on physician assessment at Screening Visit 2.
• Permitted concomitant medications for asthma must have been at a stable dose for the 4 weeks prior to Screening Visit 1.
- Have a prebronchodilator forced expiratory volume in the first second (FEV1) >= 65% of predicted normal value at Screening Visit 2.

Exclusion criteria

- Has a history of any other chronic lung disease, including chronic obstructive pulmonary disease (COPD), bronchiolitis, bronchiectasis, allergic bronchopulmonary aspergillosis (mycosis), occupational asthma, sleep apnea, pulmonary hypertension, or any other

obstructive pulmonary disease, liver or renal insufficiency; significant unstable cardiac, vascular, pulmonary, gastrointestinal, endocrine, neurologic, hematologic, rheumatologic, psychiatric, or metabolic disturbances, or other body system disorders that are clinically significant in the opinion of the investigator.
- Has ever had an episode of life-threatening asthma defined as respiratory arrest or requiring intubation for asthma.
- Has been hospitalized (for greater than 24 hours) due to asthma in the 5 years prior to Screening Visit 1.
- Has experienced an asthma exacerbation in the 12 weeks prior to Screening Visit 1 requiring management with systemic steroids.
- Is receiving high dose ICS (>500 µg/day to fluticasone or equivalent). Use of low or medium dose ICS (<=500 µg/day fluticasone or equivalent) with or without permitted controller medications e.g LABA, LTRA is allowed.

Study design

Design

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):	03-05-2013
Enrollment:	12
Type:	Actual

Ethics review

Approved WMO

Date:	16-11-2012
Application type:	First submission

Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	18-12-2012
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	09-09-2013
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	18-09-2013
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	27-01-2014
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	05-02-2014
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	12-02-2014
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	05-06-2014
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

Approved WMO

Date:	12-06-2014
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	23-06-2014
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

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	EUCTR2011-005369-19-NL
ClinicalTrials.gov	NCT01704040
CCMO	NL42552.056.12