A Single-Center, Randomized, Observer-Blinded, Placebo-Controlled, Single-Ascending-Dose (SAD) Study to Investigate the Safety, Tolerability, Pharmacokinetics, and Pharmacodynamics of RO5469754, a Humanized Monoclonal Antibody, Following Intravenous or Subcutaneous Administration in Healthy Adults

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Primary:to assess the safety and tolerability of single doses of RO5469754 when administered as an intravenous (IV) infusion or subcutaneous (SC) injection(s), in healthy subjectsSecondary: to determine the single-dose pharmacokinetics (PK) of...

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

Summary

ID

NL-OMON37629

Source
ToetsingOnline

Brief title
RO5469754 monoclonal antibody study

Condition

- Bronchial disorders (excl neoplasms)

Synonym
Asthma, breathing difficulties

Research involving
Human

Sponsors and support

Primary sponsor: Hoffmann-La Roche
Source(s) of monetary or material Support: Farmaceutische Industrie

Intervention

Keyword: Asthma, Monoclonal Antibody

Outcome measures

Primary outcome

Safety

Pharmacokinetics

Pharmacodynamics

Secondary outcome

n.a.

Study description

Background summary

The drug to be given is a new, investigational compound that may eventually be used for the treatment of asthma.
In asthma , difficulty in breathing results from one or more different processes including spasm of the bronchial tubes, swelling of the bronchial tubes, mucus that is difficult to clear from the bronchial tubes, and thickening of the bronchial wall.
The compound is expected to realise a reduction in severe asthma exacerbations

and sustained improvements in measures of asthma control, including symptoms, lung function and use of rescue medications.
This new compound is not registered as a drug. This is the first time that this compound is being given to humans.

Study objective

Primary:
to assess the safety and tolerability of single doses of RO5469754 when administered as an intravenous (IV) infusion or subcutaneous (SC) injection(s), in healthy subjects

Secondary:
to determine the single-dose pharmacokinetics (PK) of RO5469754 when administered as an IV infusion or SC injection(s), in healthy subjects

Exploratory:
to explore potential changes in pharmacodynamic (PD) endpoints after single doses of RO5469754 in healthy subjects

Study design

Design:
an observer-blinded, randomized, placebo-controlled, single ascending dose study in 56 healthy male and/or female subject each receiving a single dose of RO5469754 or placebo (three active and one placebo) administered as an IV infusion or SC injection(s) in the fasted state; IV cohorts will be staggered; For the first three cohorts one subject will be dosed per Day, for the remaining IV dose cohorts two subject (one active and one placebo) will be dosed and monitored for 24 h before the remaining subjects will be dosed

Procedures and assessments
Screening and follow-up:
clinical laboratory, physical examination, 12-lead ECG (triplicate), vital signs, pregnancy test (females only), weight; at eligibility screening: medical history, ethanol and drug screen, HBsAg, anti HCV, anti-HIV 1/2 and TB test; clinical laboratory, physical examination, weight, vital signs, 12-lead ECG (triplicate), ethanol and drug screen and pregnancy test (females only) to be repeated upon admission

Observation period:
one period in clinic from -17 h up to 72 h after drug administration on Day 1 and ambulant visits on Days 5 (SC only) and 6 (SC only) and in Weeks 2, 3, 4, 5, 7, 10, 13 and 16 (follow-up). In Groups 9 - 11 extra ambulatory visits are possible in weeks 15, 17, 19, 21 and/or 22

Blood sampling:
for pharmacokinetics (IV cohorts): pre-dose up to 72 h post start of infusion, and at weeks 2, 3, 4, 5, 7, 10, 13 and 16; In Groups 9 - 11 extra samples are possible in weeks 15, 17, 19, and 21
for pharmacokinetics (SC cohorts): pre-dose and up to 120 h post-dose, and at weeks 2, 3, 4, 5, 7, 10, 13 and 16; In Groups 9 - 11 extra samples are possible in weeks 15, 17, 19, and 21

ADA (antibodies) sample: pre-dose on Day 1;
PD biomarker samples: pre-dose and 4 (IV cohorts only), 24, 48 and 72 h post-dose and at weeks 2, 3, 4, 5, 7, 10, 13 and 16; In Groups 9 - 11 extra samples are possible in weeks 15, 17, 19, and 21

for RCR (DNA): once at Day -1;
for RCR (RNA): once at Day -1 and pre-dose on Day 1;
for exploratory RNA biomarkers: pre-dose and up to 72 h post-dose and at weeks 2, 3, 4, 5, 7, 10, 13 and 16; In Groups 9 - 11 extra samples are possible in weeks 15, 17, 19, and 21
for exploratory PD biomarkers: pre-dose and up to 72 h post-dose and at weeks 2, 3, 4, 5, 7, 10, 13 and 16;In Groups 9 - 11 extra samples are possible in weeks 15, 17, 19, and 21

Safety assessments:
adverse events: throughout the study; at several timepoints abbreviated physical exam, vital signs, 12-lead ECG, clinical laboratory, a pregnancy test (females only), and tolerability of SC-injection (SC-cohorts only)

Bioanalysis:
analysis of RO5469754 samples using a validated method by Sponsor
analysis of ADA-sample using a validated method by Sponsor
analysis of PD biomarker samples using a validated method by PRA
analysis of RCR samples using a validated method by Sponsor
analysis of exploratory RNA biomarkers using a validated method by Sponsor
analysis of exploratory PD biomarkers using a validated method by Sponsor

Intervention

Active substance RO5469754

Study burden and risks

Procedures: pain, light bleeding, heamatoma, possibly an infection.

Contacts

Public
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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

Healthy male or female
age: 18-64 yrs, inclusive
BMI: 18-32 kg/m2, inclusive

Exclusion criteria

Suffering from: hepatitis B, cancer or HIV/Aids. In case of participation in another drug study within 60 days before the start of this study or being a blood donor within 90 days from the start of the study. In case of donating more than 1.5 liters blood in the 10 months preceding the start of the study (male)/ more than 1.0 liters of blood in the 10 months preceding the start of the study (female).

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):	01-11-2011
Enrollment:	56
Type:	Actual

Ethics review

Approved WMO Date:	18-10-2011
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	24-10-2011
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	15-03-2012
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

Approved WMO

Date:	19-03-2012
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	16-05-2012
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	24-05-2012
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	04-06-2012
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	06-06-2012
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	EUCTR2011-004194-91-NL
CCMO	NL38390.056.11