A Combined Clinical Phase I/IIa Study of the Safety and Efficacy of Nebulized RPL554 in Healthy Subjects, Allergic Asthmatics, and Allergic Rhinitics

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Aim of the study is to evaluate RPL554*s safety in healthy, non-asthmatic subjects and consequently to assess RPL 554 safety and efficacy in allergic asthmatics and in allergic rhinitics.

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

Summary

ID

NL-OMON32512

Source
ToetsingOnline

Brief title
Phase I/IIa evaluation of nebulised RPL554

Condition

- Respiratory disorders NEC

Synonym
bronchial asthma

Research involving
Human

Sponsors and support

Primary sponsor: Verona Pharma plc

Source(s) of monetary or material Support: verona Pharma

Intervention

Keyword: Pharmacodynamics, Pharmacokinetics, Phosphpdiesterase inhibitors, Safety

Outcome measures

Primary outcome

To assess the safety of nebulized RPL554 in healthy subjects, allergic asthmatics and allergic rhinitics using standard safety measures.

Secondary outcome

To investigate whether nebulized RPL554 possesses:

-Bronchodilator (increase in FEV1) and bronchoprotective activity (increase in PC20 to inhaled methacholine), respectively, in patients with clinically stable allergic asthma, not on controller medications and without regular use of bronchodilators.

-Anti-inflammatory effects in subjects with allergic rhinitis not on controller therapy following a standardized nasal challenge with a relevant allergen (inhibition of the allergen-induced nasal eosinophilia in nasal brushes).

-To investigate RPL554*s effect on the following exploratory measures:

-Nasal composite symptom scores post-allergen (RPL554 versus placebo)

-To investigate RPL554*s pharmacokinetics in plasma and urine.

Study description

Background summary

RPL554, is an inhibitor of two subtypes (3 and 4) of phosphodiesterase (PDE) enzymes. These two subtypes are known to be involved in modulating inflammatory

respiratory diseases, including allergic asthma and rhinitis. PDE 3 inhibitors have bronchodilator effects, while PDE 4 inhibitors have anti-inflammatory properties. Pharmacological evidence from animal experiments suggests that RPL554 may have therapeutic potential in both allergic asthma and rhinitis.

Study objective

Aim of the study is to evaluate RPL554*s safety in healthy, non-asthmatic subjects and consequently to assess RPL 554 safety and efficacy in allergic asthmatics and in allergic rhinitics.

Study design

Stage 1: a randomized, placebo controlled, parallel and double blind study in healthy volunteers.
Stage 2: an adaptive study with up to 4 potential dose levels in asthmatic patients.
Stage 3A: a randomized, placebo-controlled, double blind cross over study with two identical occasions in asthmatic patients.
Stage 3R: a randomized, placebo-controlled, double blind, crossover study with two identical occasions in patients with allergic rhinits.

Intervention

RPL554 or placebo

Study burden and risks

During the screening clinical significant abnormalities might be discovered, while during the study after the methacholine and nasal allergen challenge the patients respectively get dyspnoea and local allergic reactions.

Contacts

Public
Verona Pharma plc

Suite 21 Alpha House, 100 Borough High Street
London SE1 1LB
United Kingdom
Scientific
Verona Pharma plc

Suite 21 Alpha House, 100 Borough High Street

London SE1 1LB
United Kingdom

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

Male volunteers: healthy, non-smokers
Female volunteers: healthy, post-menopausal, non-smokers
Asthmatic patients: history of allergic asthma for at least 6 months, stable allergic asthma, Pre-bronchodilator FEV1 >=70% of predicted, documented bronchial hyper-responsiveness to inhaled Methacholine bromide (MCh) with a PC20MCh of <=4 mg/mL, documented allergy by a standardized Skin Prick Test (SPT)
Patients with allergic rhinitis: Documented allergy by a standardized Skin Prick Test (SPT), History of allergic rhinitis for at least 6 months, clinically stable allergic rhinitis

Exclusion criteria

Volunteers: clinical significant abonormalities (females: potential fertile)
Asthmatic patients: unstable asthma, recent (<4 weeks) treatment with inhaled corticosteroids or with systemic corticosteriods (within 8 weeks), recent (within 4 weeks) or actual airways viral infection, clinical significant abonormalities (females potential fertile).
Rhinitic patients: unstable allergic rhinitis, history of nasal surgery, evidence of nasal polyps, clinical significant abonrmalities (females potential fertile)

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):	05-03-2009
Enrollment:	62
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	none
Generic name:	none

Ethics review

Approved WMO Date:	21-11-2008
Application type:	First submission
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	27-01-2009
Application type:	First submission
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	18-02-2009
Application type:	Amendment
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)

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	EUCTR2008-005048-17-NL
CCMO	NL25696.058.08