A Phase I study to assess in vitro and in vivo immunoreactivity of Ruconest in Subjects with cow's milk allergy (CMA) and/or rabbit allergy (RA)

Published: 01-09-2011
Last updated: 01-05-2024

The primary objective of this study is to assess the negative predictive value of a Skin Prick Test protocol in subjects with clinical CMA and/or RA.

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

Summary

ID

NL-OMON39068

Source
ToetsingOnline

Brief title
Ruconest skin prick test validation protocol

Condition

- Allergic conditions

Synonym
Cow's milk allergy and rabbit allergy

Research involving
Human

Sponsors and support

Primary sponsor: Pharming Technologies B.V.
Source(s) of monetary or material Support: Pharming Technologies B.V.

Intervention

Keyword: Cow's milk allergy, Immunoreactivity, Rabbit allergy, Ruconest

Outcome measures

Primary outcome

Reactivity by both skin test procedures and severity of adverse events (AEs)

following subcutaneous challenge.

Number of subjects who experienced a positive skin reaction, as measured by a >=

3-mm wheal over the negative control (SPT) and/or an erythema that equals or

exceeds in mean diameter the positive control (ICT).

Endpoint will be evaluated by recording local reactions and systemic symptoms

of type I hypersensitivity. The negative predictive value of the skin test

protocol will be assessed as the number of subjects without systemic reaction

upon subcutaneous challenge over the number of subjects having tested negative

for the SPT and ICT.

Secondary outcome

NVT

Study description

Background summary

Ruconest has been approved for the treatment of acute HAE attacks, a rare genetic disorder typified by a deficiency or dysfunction of the plasmatic protein C1INH. The active ingredient in Ruconest is a recombinant human protein secreted in the milk of transgenic rabbits expressing the human gene for C1-esterase inhibitor (C1INH). Ruconest contains low levels of HRI, i.e. rabbit milk proteins or fragments there-off.
A SPT has been proposed to screen subjects with increased risk of hypersensitivity reaction to Ruconest. Subjects with RA and subjects with

clinical CMA have an increased risk of hypersensitivity: although cow*s milk proteins differ from rabbit milk proteins, cross-reaction between the Ruconest HRIs with cow*s milk IgEs in subjects with clinical CMA, is certainly possible. Performing the skin testing in subjects with clinical CMA and subjects with RA will evaluate the negative predictive value of a Ruconest skin test protocol in a highly relevant population. The current population is relevant since it has the highest risk for allergic reactions to Ruconest. So if this study shows that Ruconest is safe for this specific group, this significantly adds to the safety profile of the drug for the total population.

Study objective

The primary objective of this study is to assess the negative predictive value of a Skin Prick Test protocol in subjects with clinical CMA and/or RA.

Study design

Subjects with clinical CMA and/or RA defined by a suggestive history of symptoms after exposure to cow*s milk and/or rabbit dander and sensitization, will be contacted for participation in the study. Subjects will attend the clinic for 3-3.5 hours to undergo 1) confirmation of sensitization by SPT with cow*s milk and/or rabbit dander 2) SPT with increasing concentrations of Ruconest, and 3) intracutaneous skin testing (ICT) with increasing concentrations of Ruconest, 4) a blood draw to test basophil activation.

Subjects who tested negatively to the SPT and ICT will be asked to present after two weeks or later for 9-9.5 hours for a subcutaneous challenge with 4 increasing doses with standard solution of Ruconest

Intervention

SPT, ICT, and subcuteanous test with Ruconest

Study burden and risks

Subjects will need to attend the clinic for approximately 14 hours. On the first testing day, during the skin tests, local allergic reactions may occur, which can be treated symptomatically with oral antihistamines. Systemic hypersensitivity reactions are unlikely, and if they might occur can be treated with systemic antihistamines, steroids and/or epinephrine. At the second testing day, the subcutaneous challenge visit, systemic hypersensitivity reactions are possible, which can be treated with systemic antihistamines (oral, intramuscular, intravenous), steroids (oral, intramuscular, intravenous) and or epinephrine (intramuscular). These subjects will have no direct benefit from the study. The current study population is relevant since it has the highest risk for allergic reactions to Ruconest. So, if this study shows that

Ruconest is safe for this specific group, this significantly adds to the safety profile of the drug for the total population

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

- Positive SPT and/or IgE >0.35 for CM and/or positive SPT and/or IgE >0.35 for rabbit dander
- Signed written informed consent
- Males and females between 18 and 65 years old
- Medical records documenting clinical CMA and/or RA or suggestive history of symptoms
- Physical examination findings within normal limits
- Willingness and ability to comply with all protocol procedures

Exclusion criteria

• Pregnancy or breastfeeding, or current intention to become pregnant
• Severe dermographism
• Other concurrent disease or condition that would interfere, or for which the treatment might interfere with the conduct of the study, or that would, in the opinion of the Investigator, pose an unacceptable risk to individuals in this study
• Treatment with drugs that interfere with skin test response
• History or symptoms of significant psychiatric disease, including depression and schizophrenia
• Known or suspected addiction to drug and/or alcohol abuse
• Participation in an investigational drug or device trial within the last 30 days prior to screening

Study design

Design

Study type: Interventional

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	10-04-2012
Enrollment:	25
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Ruconest
Generic name:	conestat alfa
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	01-09-2011
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	09-01-2012
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	17-07-2012
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	18-07-2012
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	16-10-2012
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	22-10-2012
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	08-11-2013
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	20-12-2013
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	26-09-2014

Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	01-10-2014
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Not approved Date:	07-01-2015
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	30-01-2015
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)

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	EUCTR2011-004048-23-NL
CCMO	NL37955.041.11