A Double-Blind, Randomised, Placebo-Controlled, Multi-Centre Field Study to Assess the Efficacy and Safety of HDM-SPIRE in Subjects with a History of House Dust Mite-Induced Rhinoconjunctivitis

Published: 23-09-2014
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To evaluate the efficacy of HDM-SPIRE in the reduction of symptoms and the use of allergy rescue medication associated with HDM allergy in subjects with clinically relevant symptoms.

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

Summary

ID

NL-OMON42005

Source
ToetsingOnline

Brief title
HDM-SPIRE TH005

Condition

- Allergic conditions

Synonym
House Dust Mite-Induced Rhinoconjunctivitis; House Dust Mite allergy

Research involving
Human

Sponsors and support

Primary sponsor: Circassia Ltd.
Source(s) of monetary or material Support: Pharmaceutical industry;Circassia Ltd.

Intervention

Keyword: Allergy, House Dust Mite, Rhinoconjunctivitis

Outcome measures

Primary outcome

Mean Combined Score (CS) during the PAC3 period in the HDM-SPIRE treatment groups compared with the mean CS in the placebo group.

Secondary outcome

- Clinical Global Impression of Change in Rhinoconjunctivitis Symptoms for the HDM-SPIRE treatment groups compared with placebo at the end of study.

- Mean TRSS in the HDM-SPIRE treatment groups compared with placebo during the PAC3 period.

- Mean component scores of the TRSS (nasal and non-nasal) in the HDM-SPIRE treatment groups compared with placebo during the PAC3 period.

- Mean RMS in the HDM-SPIRE treatment groups compared with placebo during the PAC3 period.

- Mean Rhinoconjunctivitis Quality of Life Questionnaire (RQLQ) score in the HDM-SPIRE treatment groups compared with placebo at the end of the PAC3 period.

- Number of days subjects in the HDM-SPIRE treatment groups have no moderate or severe RSS symptoms without rescue medication usage compared with placebo during the PAC3 period.

Study description

Background summary

Clinical manifestations of House Dust Mite allergy include rhinoconjunctivitis, asthma and eczema.
Allergic rhinitis affects between 10% and 30% of all adults and up to 40% of children, 400
million people in the world. In Europe, the prevalence of HDM allergy varies according to geographical region but an
increase in the prevalence of sensitisation to HDM is occurring across Europe correlating
with the increase in allergic diseases.
The management of House Dust Mite-induced rhinoconjunctivitis, asthma and eczema includes allergen
avoidance and medication. However, it can be difficult to avoid indoor allergens and there is
no medication available that provides a definitive treatment for the symptoms of rhinoconjunctivitis, asthma or eczema.
HDM Synthetic Peptide Immuno-Regulatory Epitopes (HDM-SPIRE) is being developed for
the treatment of HDM allergy. It has been designed on the basis of the selection of a set of
seven peptides that on the one hand interact with T cells to induce tolerance but, on the other,
are too short to cross-link IgE on mast cells and basophils, thereby greatly reducing the
unwanted side effects of traditional immunotherapy using whole allergen extracts.

Study objective

To evaluate the efficacy of HDM-SPIRE in the reduction of symptoms and the use of allergy rescue medication associated with HDM allergy in subjects with clinically relevant symptoms.

Study design

The study will be a randomised, double-blind, placebo-controlled, parallel group,
multi-centre field assessment of 3 dose regimens of HDM-SPIRE administered at 4 weekly intervals for 28 weeks.
Subjects will attend the investigative site for screening and administration of study
medication and for periodic assessments of safety and efficacy. Subjects will

also
complete an electronic diary (eDiary) during four 3-week periods. These diaries will
capture the primary efficacy variable data (symptom scores and medication use) as
well as other patient reported data.

Intervention

- 8 x placebo 4 weeks apart
- 4 x 12 nmol HDM-SPIRE followed by 4 x placebo 4 weeks apart
- 4 x 12 nmol HDM-SPIRE 4 weeks apart followed by a second course of
4 x 12 nmol HDM-SPIRE 4 weeks apart
- 4 x 20 nmol HDM-SPIRE followed by 4 x placebo 4 weeks apart

Study burden and risks

HDM-SPIRE has been investigated in two clinical trials, both conducted in Canada. These
studies have recruited about 200 subjects in total.
A dose escalation study (Circassia TH001) evaluated 4 administrations of HDM-SPIRE
(0.03-12 nmol) 4 weeks apart and demonstrated that all doses up to and including 12 nmol
were well tolerated with no safety concerns identified. A second study (Circassia TH002),
involving exposure to HDM allergen in an Environmental Exposure Chamber (EEC), found
that a unit dose of 12 nmol HDM-SPIRE was effective in treating rhinoconjunctivitis
symptoms and appeared to be more effective than lower doses (3 or 6 nmol unit doses).
All doses and regimens evaluated in this study were well tolerated and no safety concerns
were raised.
The subjects will get 8 intradermal injections with 100µlHDM-SPIRE. Safety and tolerability will be assessed by recording of Adverse Events, physical examination, vital signs, laboratory values, pulmonary function and local reactions at the injection site over a period of 52 weeks.

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

- Male or female, aged 18-70 years.
- A reliable history consistent with moderate to severe rhinoconjunctivitis (sneezing, rhinorrhoea, itchy nose, nasal blockage and/or itchy eyes, red eyes, watering eyes and/or itchy ear/palate) on exposure to HDM for at least 1 year and which has required symptomatic treatment on at least one occasion during the last year.
- Mean TRSS *10 from 4 nasal and 4 non-nasal symptoms over a consecutive 7 day period before the Screening Visit 1B/C.
- Either Der p or Der f specific IgE *0.35 kU/L measured by ImmunoCAP®.
- Positive skin prick test (preferably using the ALK-Abello Allergen Extract test) to either Der p or Der f with a wheal diameter at least 5 mm (average of longest and orthogonal) larger than that produced by the negative control. The negative control must be <2 mm for the test to be
valid.
- Provide written informed consent.
Additional Inclusion Criteria at End of BAE
- Mean TRSS *12 from 4 nasal and 4 non-nasal symptoms during the BAE period (3-week period before randomisation).

- Completed the eDiary during the BAE on at least 16 days (>75% of occasions).

Exclusion criteria

- Diagnosis of asthma requiring GINA Step 3 or higher treatment.
- If asthmatic, experienced a deterioration of asthma that resulted in emergency treatment or hospitalisation in the 12 months before randomisation, or experienced a lifethreatening asthma attack (e.g. one requiring intubation and mechanical ventilation) at any time in the past.
- Used any oral or parenteral corticosteroids at any time within 1 month prior to Screening Visit 1B/C.
- Asthma requiring high-dose inhaled corticosteroids (ICS) or anti-IgE therapy within 6 months prior to Screening Visit 1B/C.
- Forced expiratory volume in 1 second (FEV1) <80% of predicted, or other evidence of partly controlled or uncontrolled asthma.
- Clinically significant confounding symptoms of allergy to relevant local seasonal allergens (e.g. ragweed, mugwort, tree, grass or mould) and cannot complete the BAE and the final PAC period at 50-52 weeks (PAC3) outside the respective allergy seasons.
- IgE *0.35 kU/l to other perennial allergens (e.g. animal dander, cockroach, mould) which cannot be avoided during the study or where sampling for these allergens demonstrates significant levels within the subject?s home from dust and/or vacuum cleaner samples, analysed using Indoor Biotechnologies Allergen Analysis Service.
- Intends to be away for 7 days or more during the final PAC period at 50-52 weeks (PAC3), or whose lifestyle means that there is a high likelihood of them
being away from home for more than 7 days during the PAC3 period.
- Received an immunosuppressive treatment within 3 months prior to screening (except steroids for allergic and asthma symptoms).
- Previous immunotherapy treatment with any HDM allergen for more than 1 month within 5 years prior to screening.
- History of significant recurrent acute sinusitis, defined as 2 episodes per year for the last 2 years, all of which required antibiotic treatment, or a history of chronic sinusitis, defined as sinus symptoms lasting greater than 12 weeks that include 2 or more major factors or 1 major factor and 2 minor factors. Major factors are defined as facial pain or pressure, nasal obstruction or blockage, nasal discharge or purulence or discoloured postnasal discharge, purulence in nasal cavity, or impaired or loss of smell. Minor factors are defined as headache, fever, halitosis, fatigue, dental pain, cough, and ear pain, pressure, or fullness.
Additional Exclusion Criteria at end of BAE
- Used any oral or parenteral corticosteroid during the BAE period.

Study design

Design

Study phase:	2
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-12-2014
Enrollment:	20
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	N/A
Generic name:	HDM-SPIRE 12nmol

Ethics review

Approved WMO Date:	23-09-2014
Application type:	First submission
Review commission:	IRB Nijmegen: Independent Review Board Nijmegen (Wijchen)
Approved WMO Date:	24-10-2014
Application type:	First submission
Review commission:	IRB Nijmegen: Independent Review Board Nijmegen (Wijchen)
Approved WMO Date:	20-01-2015

Application type:	Amendment
Review commission:	IRB Nijmegen: Independent Review Board Nijmegen (Wijchen)
Approved WMO Date:	23-01-2015
Application type:	Amendment
Review commission:	IRB Nijmegen: Independent Review Board Nijmegen (Wijchen)
Approved WMO Date:	09-07-2015
Application type:	Amendment
Review commission:	IRB Nijmegen: Independent Review Board Nijmegen (Wijchen)
Approved WMO Date:	30-07-2015
Application type:	Amendment
Review commission:	IRB Nijmegen: Independent Review Board Nijmegen (Wijchen)
Approved WMO Date:	09-12-2015
Application type:	Amendment
Review commission:	IRB Nijmegen: Independent Review Board Nijmegen (Wijchen)
Approved WMO Date:	05-01-2016
Application type:	Amendment
Review commission:	IRB Nijmegen: Independent Review Board Nijmegen (Wijchen)
Approved WMO Date:	04-05-2016
Application type:	Amendment
Review commission:	IRB Nijmegen: Independent Review Board Nijmegen (Wijchen)
Approved WMO Date:	25-05-2016
Application type:	Amendment
Review commission:	IRB Nijmegen: Independent Review Board Nijmegen (Wijchen)

Approved WMO Date:	10-10-2016
Application type:	Amendment
Review commission:	IRB Nijmegen: Independent Review Board Nijmegen (Wijchen)
Approved WMO Date:	20-10-2016
Application type:	Amendment
Review commission:	IRB Nijmegen: Independent Review Board Nijmegen (Wijchen)

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	EUCTR2014-001662-94-NL
ClinicalTrials.gov	NCT02150343
CCMO	NL49602.072.14