A double-blind, placebo-controlled, randomized trial to study the Viaskin® Peanut*s Efficacy and Safety for treating peanut allergy in children and adults.

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· To determine the efficacy of several doses of Viaskin® Peanut to significantlydesensitize peanut-allergic subjects to peanut after 12 months of EPIT treatment .· To evaluate the safety of a long-term EPIT with Viaskin® Peanut.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Food intolerance syndromes
Study type	Interventional

Summary

ID

NL-OMON39142

Source
ToetsingOnline

Brief title
VIPES

Condition

- Food intolerance syndromes

Synonym
peanut allergie

Research involving
Human

Sponsors and support

Primary sponsor: DBV Technologies

Source(s) of monetary or material Support: DBV Technologies

Intervention

Keyword: double-blind, Peanut allergy, placebo, Viaskin

Outcome measures

Primary outcome

The primary efficacy endpoint will be the percentage of treatment responders

for each active

treatment compared to placebo. A treatment responder is defined as a subject

with a peanut

protein eliciting dose equal to or greater than 1,000 mg peanut proteins based

on the results

of the DBPC peanut challenge after 12 months of treatment or a subject with a >=

10-fold

increase of the eliciting dose at 12 months, compared to their initial

eliciting dose.

Secondary outcome

Secondary Efficacy Endpoints:

The following secondary efficacy endpoints will be assessed:

1. The mean eliciting doses of peanut proteins at Month 12 in the 50 µg, 100 µg

and 250 µg groups versus the placebo group.

2 The mean cumulative reactive dose of peanut proteins at Month 12 in the 50

µg, 100 µg and 250 µg groups versus the placebo group.

3 The change in the severity of symptoms elicited during the peanut DBPCFCs from baseline to Month 12 for each treatment group. Symptoms will be graded according to the Oral Food Challenge (OFC) Symptom Score Sheet (Appendix 3) described by the Work Group Report on
OFC testing (1).

4 Time of appearance of the very first objective symptom during the DBPCFC at Month 12 in the 50 µg, 100 µg and 250 µg groups versus the placebo group.

5.The change in peanut end point titration by skin prick testing at baseline and at Months 3, 6 and 12.

6. The change in peanut-specific IgE, and immunoglobulin G subtype 4 (IgG4) at baseline and at Months 3, 6 and 12.

7 The correlation between the presence of peanut protein component(s) and response to Viaskin® Peanut immunotherapy.

8 The mean fold reduction of basophil activation, assessed by CD203c expression, at Months 3, 6 and 12. These results will be correlated with the primary efficacy criterion.

9. Primary efficacy endpoint in each age stratum.

10. Secondary efficacy endpoints in each age stratum for the mean eliciting dose in each treatment group, time of appearance of the 1st objective symptom, for the change in peanut-specific IgE and in IgG4 and the mean fold reduction of basophil activation of CD203c expression.

Safety Endpoints:

The following safety criteria will be determined:

1. Adverse events (AEs) by system organ class and relatedness to Viaskin® Peanut (all subjects and by age strata).

2. Incidence, duration and severity of local Viaskin® Peanut-induced AEs as assessed by the subjects all subjects and by age strata).

3. Systemic allergic symptoms and relatedness to Viaskin® Peanut (all subjects and by age strata).

4. Serious AEs (SAEs) and relatedness to Viaskin® Peanut (all subjects and by age strata).

5. Severity of AEs or SAEs elicited during the study and during the DBPCFCs at entry and after treatment (all subjects).

6. Laboratory data, physical examinations and vital signs (all subjects).

7. Spirometry results (all subjects and by age strata).

8. Safety sub-analysis in subjects with mutations in the filaggrin gene versus wild type subjects on the following parameters: Incidence, duration and severity of local Viaskin® Peanut-induced AEs, systemic allergic symptoms related to Viaskin® Peanut, SAEs related to Viaskin® Peanut, spirometry results.

Specific reactions triggered by an accidental consumption of peanut and the conditions around that accidental consumption will be collected. These AEs will be classified and analyzed separately.

Study description

Background summary

The Investigational New Drug, Viaskin® Peanut (DBV712), is a dry deposit of a formulation of peanut Protein extract intended for EPIT. EPIT is an emerging allergen-Specific ImmunoTherapy (known as SIT) approach for the treatment of atopic diseases. Recently, EPIT was successfully used for the treatment of grass pollen allergy (21), and also tested in a pilot 3-month clinical study in IgE-mediated cow*s milk allergy conducted in France (22).

The Investigational New Drug Viaskin® Peanut is a ready-to-use and easy-to-administer form ofallergen immunotherapy. Viaskin® Peanut is intended to induce clinical desensitization/tolerization to peanut in subjects moderately to severely allergic to peanut. Viaskin® Peanut includes the natural and complete set of peanut proteins that can interact with the local antigen presenting cells such as the epidermic Langerhans and dendritic cells and can initiate the process of clinical desensitization/tolerization. Moreover, by utilizing the epicutaneous route of administration, Viaskin® Peanut is able to initiate these immunomodulatory processes while minimizing the potential safety concerns associated with systemic exposure to food allergens.

Based on the results of the Phase Ib study, the doses of 50 µg, 100 µg and 250 µg are considered for this Phase IIb study for all ages of patient population, i.e. 18 to 55 years of age.

Study objective

· To determine the efficacy of several doses of Viaskin® Peanut to significantly desensitize peanut-allergic subjects to peanut after 12 months of EPIT treatment .
· To evaluate the safety of a long-term EPIT with Viaskin® Peanut.

Study design

This is a 12-month double-blind, placebo-controlled, randomized trial to study the efficacy and safety of Viaskin® Peanut, an allergen extract of peanut administered epicutaneously using the Viaskin® epicutaneous delivery system in subjects from 18 to 55 years old with a history of immediate hypersensitive reaction to peanut protein. The trial will be conducted at approximately 20-25 sites with Investigators and staff trained and experienced in the diagnosis and the management of peanut allergy and anaphylaxis, and who are capable of performing a doubleblind placebo-controlled food challenge (DBPCFC) in adult subjects. Three doses of peanut proteins, i.e. 50 µg, 100 µg and 250 µg per patch will be evaluated in the study.
Following the confirmation of peanut allergy at screening with a dose-escalating DBPCFC and provided that they reacted with an eliciting dose below or equal to 300 mg peanut proteins, subjects will be randomized in a 1:1:1:1 ratio into four different treatment groups, including 50 µg, 100 µg and 250 µg peanut proteins versus placebo. Treatment will last 12 months. Each subject will undergo two DBPCFCs: one at screening and one at 12 months at the end of the treatment period. Doses of peanut proteins will be given during the challenge every 30 minutes starting with a starting dose of 1 mg peanut proteins and proceeding up to a highest dose of 2,000 mg of peanut proteins for the challenge conducted at the end of treatment.
In addition to DBPCFC assessments, subjects will undergo other efficacy parameter assessments at months 3, 6 and 12 including skin prick tests (SPTs), titrated SPTs, determination of the changes in immunological

markers and basophil activation tests. Key assessments of safety, will be performed at each study visit by
the investigators including spirometry, peak flow measurements, vital signs, physical
examinations, clinical laboratory assessments. In between visits, subjects will report safety data on the diary
cards.

A follow-up visit will be performed 2 weeks after completion of treatment and after the last DBPCFC only for subjects who do not roll-over into the follow-up study (called OLFUS-VIPES study for Open- Label Follow-Up Study of VIPES). All subjects who completed the VIPES study up to Visit 11 (inclusive) will be eligible for participation in the OLFUS-VIPES study. At Visit 11, eligible subjects who have decided to enroll into the OLFUS-VIPES study can roll-over into the OLFUS-VIPES study, unless in the opinion of the investigator, it is not in the best interest of the subjects to continue receiving EPIT with Viaskin® Peanut.. Subjects who roll-over into the OLFUS-VIPES study will have their last visit at Visit 11 in VIPES. Those subjects who do not roll-over into the OLFUS-VIPES study will have their last visit at Visit 12 as initially planned. In total, during this study, subjects who roll-over into the OLFUS-VIPES study will be required to attend 11 study visits and subjects who do not roll-over into the OLFUS-VIPES study will be required to attend 12 study visits.

Intervention

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Study burden and risks

Patients with peanut allergy have to be watchful with food intake at all times. We believe that the intended benefits outweigh the possible disadvantages and burden. A number of study procedures that the patient will undergo are standard procedures that is done for these patients.

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

1. Peanut-allergic subjects between 18 and 55 years of age, with a well-documented medical history of systemic reactions after ingestion of peanut and currently following a strict peanut-free diet.
2. Peanut-specific immunoglobulin E (IgE) level (Phadia CAP-system) > 0.7 kU/L AND a positive peanut SPT with a largest wheal diameter >= 8 mm.;3. Positive DBPCFC at <= 300 mg of peanut proteins: the eliciting dose of peanut proteins during the DBPCFC is capped at 300 mg, i.e. subjects must react to peanut before reaching or at the dose of 300 mg peanut proteins.;4. Negative pregnancy test for women of childbearing potential. Females of childbearing age must use effective methods of contraception to prevent pregnancy and agree to continue to practice an acceptable method of contraception for the duration of participation in the study.
5. Ability to perform spirometry maneuvers in accordance with the American Thoracic Society guidelines (2005) .
6. Subjects willing to comply with all study requirements during their participation in the study.;7. Signed informed consent from adult subjects.

Exclusion criteria

1. Subjects with a history of severe anaphylaxis to peanut with the following symptoms: hypotension, hypoxia, neurological compromise (collapse, loss of consciousness or incontinence) (see Appendix 2: Anaphylaxis Staging System).;2. Pregnancy or lactation.;3.

Forced expiratory volume in one second (FEV1) < 80% of the predicted value at screening (Visit 1).
4. Subjects who did not react at or below the dose of 300 mg of peanut proteins during the DBPCFC at screening.;5. Subjects allergic to chocolate or who do not consume chocolate.;6. Subjects reacting objectively to the placebo formula at screening.;7. Severe reaction during the screening food challenge, defined as need for intubation, hypotension persisting after epinephrine administration, or the need for more than two doses of epinephrine.;8. Subjects with symptomatic allergy to pollens whose symptoms during the corresponding pollen season might interfere with the recording of symptoms during the DBPCFC, if the DBPCFC is conducted during the pollen season. The Investigator will have to ensure that the period for conducting the DBPCFC for such a subject will be outside of the pollen season.;9. Inability to discontinue short-acting antihistamines for three days or long-acting antihistamines for five to seven days (depending on half-life) prior to skin prick testing or food challenges. ;10. Subjects treated with systemic long-acting corticosteroids (depot corticosteroids) within 12 weeks prior to Visit 1 and/or systemic short-acting corticosteroid within 4 weeks prior to Visit 1 or any systemic corticosteroid at screening. ;11. Subjects with asthma defined as follows: ;a. uncontrolled persistent asthma by National Asthma Education and Prevention Program Asthma guidelines (2007) or by Global Initiative for Asthma (2011) or being treated with combination therapy of medium dose inhaled corticosteroid with a long acting inhaled β2-agonists (See Appendix 5: dosages of inhaled corticosteroids); ;b.at least two systemic corticosteroid courses for asthma in the past year or one oral corticosteroid course for asthma in the past three months; ;c.prior intubation for asthma in the past two years.;12. Subjects on β-blocking agents, angiotensin-converting enzyme inhibitors, angiotensin-receptor blockers, calcium channel blockers or tricyclic antidepressant therapy. ;13. Subjects undergoing any type of immunotherapy to any food (oral immunotherapy, sublingual immunotherapy, specific oral tolerance induction) within one year prior to Visit 1.;14. Subjects presently on aeroallergen immunotherapy and unwilling or unable to discontinue.;15. Subjects currently treated with anti-tumor necrosis factor drugs or anti-IgE drugs (such as omalizumab) or any biologic immunomodulatory therapy within one year prior to Visit 1.;16. Subjects suffering from generalized dermatologic diseases (e.g. severe atopic dermatitis, uncontrolled generalized eczema, keratosis pilaris, ichthyosis vulgaris) with no intact skin zones to apply the Viaskins. ;17. Subjects (or parents of subjects) with obvious excessive anxiety and unlikely to cope with the conditions of a food challenge.;18. Past or current disease(s), which in the opinion of the Investigator or the Sponsor, may affect the subject*s participation in this study, including but not limited to active eosinophilic gastrointestinal disorders, autoimmune disorders, uncontrolled diseases (hypertension, psychiatric, cardiac), or other disorders (e.g., liver, gastrointestinal, kidney, cardiovascular, pulmonary disease, or blood disorders).;19. Any disorder in which epinephrine is contraindicated such as coronary artery disease, uncontrolled hypertension, or serious ventricular arrhythmias.;20. Subjects unable to follow the protocol and the protocol requirements.;25. Participation in another clinical intervention study in the three months prior to Visit 1.

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:	Recruitment stopped
Start date (anticipated):	28-02-2013
Enrollment:	16
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Viaskin® Peanut
Generic name:	/

Ethics review

Approved WMO Date:	22-06-2012
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	21-12-2012
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)

Approved WMO

Date:	13-06-2013
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	02-08-2013
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	23-10-2013
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	24-03-2014
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	EUCTR2011-002550-32-NL
CCMO	NL38911.041.12