Open-label follow-up study of the VIPES study to evaluate long-term efficacy and safety of the Viaskin Peanut

Published: 07-10-2013
Last updated: 22-04-2024

The objectives of this follow-up/extension study of the VIPES study are:• To assess the efficacy of Viaskin® Peanut after up to 36 months of Epicutaneous Immunotherapy (EPIT) in peanut-allergic subjects.• To evaluate the safety of long-term...

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

Summary

ID

NL-OMON40279

Source
ToetsingOnline

Brief title
OLFUS-VIPES

Condition

- Food intolerance syndromes

Synonym
peanut allergy

Research involving
Human

Sponsors and support

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

Intervention

Keyword: long term safety, Open label, Peanut allergy, Viaskin

Outcome measures

Primary outcome

The OLFUS-VIPES study will have two treatment groups: Treatment Group 1 will consist of subjects who had received placebo in the VIPES study; Treatment Group 2 will consist of subjects who had received Viaskin® Peanut in the VIPES study.

Efficacy Endpoints:

The following efficacy endpoints will be assessed:

• At Month 12 in the OLFUS-VIPES study and by treatment group, the proportion of subjects with a peanut protein eliciting dose equal to or greater than 1000 mg peanut or with a >=10-fold increase of the eliciting dose compared to their baseline eliciting dose observed in the VIPES study. Subjects having received active treatment with Viaskin® Peanut for a total of 12 months (Treatment Group 1) and a total of 24 months (Treatment Group 2) will be analyzed separately.

• At Month 24 in the OLFUS-VIPES study and by treatment group 1 or 2, the proportion of subjects with a peanut protein eliciting dose equal to or greater than 1000 mg peanut or with a >=10-fold increase of the eliciting dose compared to their baseline eliciting dose observed in the VIPES study. Subjects having received active treatment with Viaskin® Peanut (DBV712) for a total of 24 months and a total of 36 months (since the VIPES study) will be analyzed separately.

• The proportion of subjects unresponsive (i.e. showing no objective symptoms during DBPCFC) to a cumulative dose of 1440 mg peanut protein or above at Month 12 and Month 24 in the OLFUS VIPES study.

• The proportion of subjects with a sustained unresponsiveness (i.e. showing no objective symptoms during DBPCFC after a period of 2 months without treatment) to a cumulative dose of 1440 mg peanut protein or above at Month 26.

• The median and mean cumulative reactive dose of peanut protein at Month 12 and Month 24 by treatment group.

• The change from baseline in peanut-specific IgE and IgG4 at Month 6, Month 12, Month 18 and Month 24 by treatment group.

• The change from baseline in the average wheal diameter during the skin prick testing (undiluted) at Month 6, Month 12, Month 18 and Month 24 by treatment group.

• Change in the Quality of Life (the FAQLQ/FAIM) at Month 12 and Month 24 compared to Day 1 for those countries where the questionnaires were available, globally and by treatment group.

Safety Endpoints:

The following safety endpoints will be assessed:

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

• Serious AEs (SAEs) by system organ class, severity and relatedness to Viaskin® Peanut (all subjects and by age strata).

• Systemic allergic symptoms and relatedness to Viaskin® Peanut (all subjects

and by age strata).

• Severity of AEs or SAEs elicited during the study and the DBPCFCs (all

subjects).

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

• Spirometry or Peak Expiratory Flow (PEF) results (all subjects).

Secondary outcome

Exploratory Criteria:

• Enumeration and characterization of reactions triggered by accidental

consumption of peanut during the follow-up study.

• Analysis of *Risk-taking behavior* of subjects (voluntary peanut consumption)

during the follow-up study.

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-touse 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

The objectives of this follow-up/extension study of the VIPES study are:
• To assess the efficacy of Viaskin® Peanut after up to 36 months of Epicutaneous Immunotherapy (EPIT) in peanut-allergic subjects.
• To evaluate the safety of long-term treatments with Viaskin® Peanut.
• To evaluate the sustained unresponsiveness to peanut after a period of 2 months without treatment in subjects showing desensitization to peanut after EPIT with Viaskin® Peanut.

Study design

This is an open-label follow-up study or extension study for subjects who previously were randomized and have completed the VIPES study. Subjects will be offered enrollment in this follow-up study to receive an additional 24 months of Viaskin® Peanut treatment followed by a period of 2 months without treatment and a peanut-free diet.

In Protocol 2.0 (incorporating Protocol Amendment 1), all subjects enrolling into the OLFUS-VIPES study after having completed the VIPES study will receive the highest dose of Viaskin® Peanut, i.e. 250 µg peanut protein, regardless of prior treatment (placebo, 50 µg, 100 µg or 250 µg Viaskin® Peanut) they were receiving in the VIPES study.

Subjects who entered already the OLFUS-VIPES study under the initial protocol design (Protocol Version 1.1 dated 27 May 2013) will all switch to receive the 250 µg dose at their protocol visit at Month 6 (Visit 3) or at Month 12 (Visit 4) after the approval of Amendment 1 at their sites.

The transition from the VIPES study to the OLFUS-VIPES study or the transition from the initial OLFUS-VIPES design to the amended OLFUS-VIPES design will be performed keeping the blinding in the VIPES study until the VIPES study results are obtained. The same Interactive Web Response System (IWRS) used to allocate treatment to subjects in the VIPES study will be used in the OLFUS-VIPES study. Hence, all subjects should receive the 250 µg dose in the OLFUS-VIPES study but none of them will be unblinded until the VIPES study is unblinded.

During the lifetime of the OLFUS-VIPES study, the VIPES study results will be revealed and an optimal clinical dose of Viaskin® Peanut for future studies will be determined.

However, in the OLFUS-VIPES study, all subjects would already be treated at the 250 µg dose at that time, and they will remain under the 250 µg dose to the end

of the study, whatever the optimal clinical dose is. This will prevent subjects from having to switch to another dose again during the OLFUS-VIPES study.

After the overall 24 months of active treatment with Viaskin® Peanut, a period of 2 months without treatment will be considered for those subjects being assessed for sustained unresponsiveness.

Repeated daily application of Viaskin® Peanut will continue as in the VIPES study, i.e. a new patch will be applied every 24 hours on the inner side of both upper arms for adults (>=18 years) and adolescents (12-17 years), or on the inter-scapular area of the back for children (7-11 years).

In order not to unblind the treatment arms until the results of the VIPES study are known and to better assure safety in particular for placebo subjects crossing over to receive the 250 µg dose of Viaskin® Peanut, the duration of application of the Viaskin® Peanut patch will be progressively increased for the first 2 weeks of treatment in all subjects entering the OLFUS VIPES study (one week shorter than what was done at the start of the VIPES study): patches will be applied for 6 hours every day during the first week, 12 hours every day during the second week, and for the entire 24 hours of daily application from the third week or the 15th day onwards.

Subjects enrolled in the OLFUS-VIPES study before approval of Protocol Amendment 1 and who will switch to the 250 µg dose after Protocol Amendment 1 is approved may apply the new 250 µg patch for the whole 24 hours starting on the very first day. They have been receiving Viaskin® Peanut at one of the three doses for at least 6 months: no safety concerns are expected. However, at the discretion of the Investigator, the 2-week period of progressive increase of time of daily application described above may be repeated.

The first double-blind placebo-controlled food challenge (DBPCFC) in the OLFUS-VIPES study will be conducted after 12 months of treatment up to a cumulative dose of 5040 mg peanut protein.

The second DBPCFC in the OLFUS-VIPES study will be conducted after 24 months of treatment for all subjects up to a cumulative dose of 5040 mg peanut protein.

- Subjects who react objectively below or at a cumulative dose of 1440 mg of peanut protein during this second DBPCFC at 24 months in the OLFUS-VIPES study will have their last visit at Visit 8 (Month 24 + 1 week).
- Subjects who are unresponsive to the cumulative dose of 1440 mg of peanut protein or above during this second DBPCFC at 24 months in the OLFUS-VIPES study will continue to a Month 26 visit as described below.

Subjects who are unresponsive at a cumulative dose of 1440 mg peanut protein or above (unresponsiveness to the DBPCFC is defined as no objective reaction to peanut protein), will be taken off treatment and will continue for an

additional 2 months without treatment and will continue their peanut-free diet. This additional period will help to assess the **sustained unresponsiveness** i.e. to study whether the subjects will maintain this level of unresponsiveness to peanut protein even after 2 months without receiving any peanut EPIT treatment.

The third DBPCFC in the study will then be conducted after a period of 2 months without treatment, i.e. at Month 26 (Visit 9 and Visit 10), only for those subjects who were unresponsive to a cumulative dose of 1440 mg peanut protein or above at Month 24. Visit 10 will be the End of Study Visit for these subjects.

Throughout the OLFUS-VIPES study period, subjects will be instructed to remain on a peanut-free diet. The re-introduction or not of peanut into the subject*s diet at the end of their participation in the study will be left to the Investigator*s decision.

Intervention

Repeated daily application of Viaskin® Peanut will continue as in the VIPES study, i.e. a new patch will be applied every 24 hours on the inner side of both upper arms for adults (>=18 years) and adolescents (12-17 years), or on the inter-scapular area of the back for children (7-11 years).
In order not to unblind the treatment arms until the results of the VIPES study are known and to better assure safety in particular for placebo subjects crossing over to receive the active treatment at the 250 µg dose of Viaskin® Peanut, the duration of application of the Viaskin® Peanut patch will be progressively increased for the first 2 weeks of treatment in all subjects entering the OLFUS VIPES study (one week shorter than what was done at the start of the VIPES study): patches will be applied for 6 hours every day during the first week, 12 hours every day during the second week, and for the entire 24 hours of daily application from the third week or the 15th day onwards.

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

Public

DBV Technologies

reu des Meuniers 80/84
Bagneux 92220
FR
Scientific
DBV Technologies

reu des Meuniers 80/84
Bagneux 92220
FR

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

1. Signed informed consent from adult subjects or parent(s)/guardian(s) of children <18 years + children*s assent for children >7 years or as per country-specific regulations or laws. This consent should be signed no later than Visit 11 in the VIPES study.
2. Adult and pediatric subjects (>=7 years) who completed the VIPES study, with a mandatory and
documented DBPCFC at Month 12 in the VIPES study.
3. Negative pregnancy test for women of childbearing potential at Visit 10 in the VIPES study.
4. Female subject of childbearing potential 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. Documented sexual abstinence will be accepted as an effective method of contraception for girls below 15 years of age.
5. Subjects and/or parents/guardians willing to comply with all study requirements during their
participation in the study.

Exclusion criteria

1. Severe reaction during the DBPCFC at Month 12 in the VIPES study, defined as need for intubation, hypotension persisting after epinephrine administration, and/or the need for more than two doses of epinephrine.
2. Pregnancy or lactation.
3. Females of childbearing potential planning a pregnancy in the coming 2 to 3 years.
4. Subjects who became allergic to chocolate or who do not want to consume the chocolate study challenge vehicle anymore.
5. Subjects who developed hypersensitivity to excipients of the Viaskin patches or of the food challenge formula used during the VIPES study.
6. 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.
7. Subjects with asthma that has evolved and now fulfills any of the criteria 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.
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 year.
8. Subjects receiving β-blocking agents, angiotensin-converting enzyme inhibitors, angiotensin-receptor blockers, calcium channel blockers or tricyclic antidepressant therapy.
9. Subjects receiving or planning to receive anti-tumor necrosis factor drugs or anti-IgE drugs (such as omalizumab) or any biologic immunomodulatory therapy.
10. Subjects receiving or planning to receive any type of immunotherapy to any food (e.g. oral immunotherapy, sublingual immunotherapy, specific oral tolerance induction) during their participation in the study.
11. Subjects receiving or planning to receive any aeroallergen immunotherapy during their participation in the study.
12. Allergy or know history of reaction to Tegaderm® with no possibilities to use an alternative dressing approved by the Sponsor.
13. Subjects suffering from generalized dermatologic disease (e.g. severe atopic dermatitis, uncontrolled generalized eczema, ichthyosis vulgaris) with no intact zones to apply the Viaskin® patches.
14. Subjects or parent(s)/guardian(s) of subjects with obvious excessive anxiety and unlikely to cope with the conditions of a food challenge.
15. 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, immunodeficiency, malignancy, uncontrolled diseases (e.g. hypertension, psychiatric, cardiac), or other disorders (e.g. liver, gastrointestinal, kidney, cardiovascular, pulmonary disease, or blood disorders).
16. Any new disorder in which epinephrine is contraindicated such as coronary artery disease, uncontrolled hypertension, or serious ventricular arrhythmias.

17. A history of drug or alcohol abuse while in the VIPES study.
18. A history of non compliance in the VIPES study. Non compliance is defined as subjects not applying the patch at all for 60 days or more (this can be either consecutive or intermittent non application of the patches) during the whole VIPES study duration.
19. Subjects unable to follow the protocol requirements.
20. Participation in another clinical intervention study in the past year, other than the VIPES study.
21. Subjects on any experimental drugs in the past year, other than those used in the VIPES study.

Study design

Design

Study phase:	2
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	22-05-2014
Enrollment:	9
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Viaskin Peanut
Generic name:	peanut allergen extract

Ethics review

Approved WMO

Date:	07-10-2013

Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	24-02-2014
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	10-04-2014
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	05-05-2014
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	24-06-2015
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	10-07-2015
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	EUCTR2013-001754-10-NL
ClinicalTrials.gov	NCT01955109
CCMO	NL45417.041.13