EPITOPE OPEN-LABEL EXTENSION STUDY TO EVALUATE THE LONG-TERM CLINICAL BENEFIT AND SAFETY OF DBV712 IN PEANUT-ALLERGIC CHILDREN (EPOPEX)

Published: 15-09-2020
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This study has been transitioned to CTIS with ID 2024-515703-19-00 check the CTIS register for the current data. The objectives of this follow-up study of the EPITOPE study are:• To assess the clinical benefit of Viaskin Peanut after up to 3 years...

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

Summary

ID

NL-OMON56419

Source
ToetsingOnline

Brief title
EPOPEX

Condition

- Allergic conditions

Synonym
Peanut-allergy

Research involving
Human

Sponsors and support

Primary sponsor: /
Source(s) of monetary or material Support: DBV Technologies S.A.

Intervention

Keyword: Open-label, peanut-allergy, Viaskin Peanut

Outcome measures

Primary outcome

The following endpoints will be explored for the assessment of the sustained clinical benefit of Viaskin Peanut 250 µg after 1, 2 and 3 years of treatment in each group (VP+VP group, Placebo+VP group) and overall:

• Proportion of subjects reaching an ED >=1000 mg;

• Proportion of treatment responders, using the treatment response definition of the EPITOPE study, i.e., a subject is defined as a treatment responder if:

o The baseline ED was >10 mg peanut protein and the ED is >=1000 mg peanut protein at the post-baseline DBPCFCs or;

o The baseline ED was <=10 mg and the ED is >=300 mg peanut protein at the post-baseline DBPCFCs.

For the VP+VP group, the baseline ED is defined as the ED reached at the EPITOPE study entry.

For the Placebo+VP group, the baseline ED is defined as the latest, valid ED in the EPITOPE study (i.e., Month 12).

• Proportion of subjects reaching a cumulative dose of at least 1444 mg peanut protein at the post-baseline DBPCFCs;

• Proportion of subjects reaching a cumulative dose of at least 3444 mg peanut

protein at the post-baseline DBPCFCs;

• Proportion of subjects unresponsive (i.e., showing no symptoms leading to stopping the DBPCFC) to the highest dose of peanut protein (i.e. 2000 mg), which is the percentage of subjects who pass the post-baseline DBPCFCs;

• Mean and median CRD of peanut protein;

• Mean and median ED of peanut protein.

Secondary outcome

The following safety endpoints will be analyzed:

• Adverse Events and Treatment-emergent adverse events (TEAEs) by System Organ Class (SOC) and Preferred Term (PT);

• Treatment-emergent adverse events by maximum severity and by maximum duration and relatedness to the IP;

• Serious adverse events (SAEs) by SOC and PTs, maximum severity and relatedness to the IP;

• Treatment-emergent adverse events leading to treatment discontinuation;

• Local adverse events of special interest (AESIs) (i.e., reactions at patch sites potentially leading to skin barrier disruption) and systemic AESIs (i.e., anaphylaxis, or systemic hypersensitivity reactions leading to epinephrine intake), whatever the causal relationship to the IP;

• Incidence, duration and maximum severity of local cutaneous reactions as assessed by the subjects;

• Incidence and severity of local cutaneous reactions as assessed by the Investigator;

• Laboratory data, physical examinations and vital signs;

The following study procedure safety criteria will be assessed over 3 years of treatment:

• Symptoms elicited during the DBPCFCs by severity;

• Severity of symptoms score during the DBPCFCs;

• Serious AEs elicited during the DBPCFCs.

The safety endpoints will be evaluated in the overall Safety population using the rescheduling rules and by treatment group (VP+VP / Placebo+VP).

The following exploratory endpoints will be evaluated over 3 years of treatment in each group (VP+VP group, Placebo+VP group) and overall using the rescheduling rules:

• Total IgE, peanut-specific IgE and IgG4 levels and levels of IgE and IgG4 specific to peanut protein components (Ara h 1, Ara h 2, Ara h 3);

• Peanut SPT average wheal diameters;

• Description of the quality of life (QoL) questionnaires (FAQLQ/FAIM/ EQ-5D-5L) data and QoL scores;

• Enumeration and characterization of reactions triggered by accidental consumption of peanut and analysis of *risk-taking behavior* of subjects (voluntary peanut consumption) during the study;

• Epigenetic modifications of the promoters of some specific genes;

• Sensitization status to other allergens and their evolution over the study period;

• Scoring atopic dermatitis index evolution over time.

Study description

Background summary

see protocol on pages 26-27/135.

Study objective

This study has been transitioned to CTIS with ID 2024-515703-19-00 check the CTIS register for the current data.

The objectives of this follow-up study of the EPITOPE study are:
• To assess the clinical benefit of Viaskin Peanut after up to 3 years of epicutaneous immunotherapy (EPIT) to induce/maintain desensitization to peanut in peanut-allergic children;
• To evaluate the safety of long-term treatment with Viaskin Peanut in peanut-allergic children.

Study design

This is an open-label, follow-up study for subjects who completed the EPITOPE study.
Eligible subjects will be offered enrollment in this follow-up study to receive Viaskin Peanut treatment at the dose selected in EPITOPE study (250 µg). Additional treatment duration will be 2 years, if subjects were previously randomized to active treatment in the EPITOPE study, or 3 years if subjects were randomized to placebo in the EPITOPE study. The treatment group during the EPITOPE study will remain blinded until the EPITOPE database is locked and the study results are unblinded.
Eligible subjects who decide to participate in the EPOPEX follow-up study will transition into this study during Visit 11 of the EPITOPE study. Subjects continuing into the EPOPEX study will not perform Visit 12 of EPITOPE study. Visit 11 of the EPITOPE study and Visit 1 of the EPOPEX study will be conducted concurrently, as far as possible; however, considering practical aspects for the center and for the subject*s family, Visit 1 might be conducted within a week of Visit 11.
The EPOPEX study population will consist of 2 sub-groups, based on the treatment received during the EPITOPE study:

• Subjects who received placebo in the EPITOPE study (Placebo+VP group);
• Subjects who received Viaskin Peanut (any dose) in the EPITOPE study (VP+VP group).

The overall maximum study duration for each subject is approximately 2 years and 1 month for subjects previously randomized to Viaskin Peanut (any dose) in

the EPITOPE study and 3 years and 1 month for subjects previously randomized to placebo in the EPITOPE study (including visit windows).
Double-Blind, Placebo-Controlled Food Challenges (DBPCFCs) will be conducted after 1, 2 and 3 years of EPIT treatment with Viaskin Peanut. As such, subjects in the Placebo+VP group will undergo 3 DBPCFCs in the EPOPEX study, after 1, 2 and 3 years of active treatment. Subjects in the VP+VP group will undergo 2 DBPCFCs in the EPOPEX study, after 2 and 3 years of active treatment (the DBPCFC performed at the end of the EPITOPE study corresponds to the DBPCFC after 1 year of active treatment).

The starting dose of the challenge will be 1 mg of peanut protein and will escalate up to the highest dose of 2000 mg peanut protein.

Key assessments of global safety will include adverse events (AEs), skin observation of the areas of patch application, vital signs, physical examinations, clinical laboratory assessments.

In between visits, the occurrence of any AE or local skin reactions and the use of concomitant medications will be recorded by the subject*s parent(s)/guardian(s) in a diary. The subject diary will be reviewed by the site medical staff at each visit. When reviewing the diary data, the Investigator will use her/his clinical judgment to validate the AEs and concomitant medications to be reported in the e-CRF. If the diary data entries are not reported in the e-CRF by the Investigator based on her/his clinical judgment, this will be documented in the source documents.

The adhesion and the occlusion of the condensation chamber of the patch will be assessed at each site visit by site staff.

Additional assessments will include total Immunoglobulin E (IgE), peanut-specific IgE and Immunoglobulin G4 (IgG4), IgE and IgG4 specific to peanut protein components, skin prick tests (SPTs), quality of life (Food Allergy Quality of Life Questionnaire [FAQLQ]/Food Allergy Independent Measure [FAIM]/EQ-5D-5L), IgE specific to other allergens (i.e., cow*s milk, egg white, house dust mite, Timothy grass pollen), description of accidental consumption of peanut and risk-taking behavior, epigenetic modifications and assessment of atopic dermatitis using the scoring atopic dermatitis (SCORAD) index.

A Data and Safety Monitoring Board (DSMB) composed of independent experts in food allergy will review study safety data at specific intervals during the study and on an ad hoc basis.
During their participation in the study, subjects will be instructed to remain on a strict peanut-free diet. Reintroducing peanut into the subject*s diet at the end of their participation in the study will be left to the Investigator*s decision. This decision will be collected in the electronic case report from (e-CRF).

Intervention

This study will be conducted in an *open-label* manner. This means that in the EPOPEX study, the treatment and the dose that your child will receive are known. All children in EPOPEX will receive the active patch: Viaskin* Peanut 250 µg. However, until the end of the EPITOPE study in April 2022, in which the child participated previously, it was not possible to know if the child received the active or the placebo patch in EPITOPE.

There is no approved treatment other than strict avoidance for peanut food allergy. If the subject is not enrolled, there
is no treatment proposed. Therefore, he/she will receive the standard-of-care treatment, that is to say, *strict
avoidance*.

Study burden and risks

As with all research studies, the study medication and study procedures may involve unknown risks. Any medication can have temporary and permanent side effects and can cause unforeseen adverse reactions. The study medication may not control/reduce your child*s peanut allergy. The procedures in this study are routine in medical practice for peanut allergy except for the patch application itself. Participation in this study does not have a special risk except for the food challenge. In some cases, examinations and study treatment administration may cause some discomfort.

Known Side effects of Viaskin* Peanut
The study medication may cause some side effects. These could include:
• Skin reactions:
o At treatment initiation the subjects reported very commonly (>= 10%) mild or moderate skin reactions (Pruritus, erythema and swelling)
o During the study, skin reactions (for example application site pruritus (itching), erythema (redness), macule (small circumscribed changes in the colour of skin that are neither raised (elevated) nor depressed), papule (small solid rounded bumps rising from the skin), irritation and application site eczema (redness, swelling, crusting, and thickening of the skin) are the most frequently reported adverse reactions, occurring in more than 10% of subjects; other skin reaction at application site: swelling, urticaria and darkened coloring of the skin are commonly reported adverse reaction, occurring in less than 10% of subjects (>=1% and <10%). The less frequently reported skin application site adverse reaction (Uncommon: >=0.1% and <1%) are application site excoriation, application site bleeding (mainly due to scratching), application site infection and application site pain. Most of local adverse reactions associated with patch application were mild to moderate in severity.
• Severe skin reactions (pruritus, erythema, swelling) at the patch application site or possibly extending beyond the patch application area may also occur.

• Reactions distant from the site of patch application such as symptoms that may suggest a local transitory allergic reaction due to presence of peanut allergen trace amount on fingers following contact with the patch and further touching of the eyes have been reported. These reactions include conjunctivitis allergic, eye swelling and redness of eyes. These distant symptoms occur in less than 10% of subjects (>=1% and <10%);
• Anaphylaxis, include distant symptoms, such as hives, itchy throat, lip swelling, rash, difficult breathing, coughing, sneezing, vomiting, abdominal pain and general feeling of uneasiness. The most severe cases, which can potentially be life-threatening may lead to severe hypotension and loss of consciousness. Anaphylaxis has been reported in less than 10% of subjects (>=1% and <10%) during testing of study treatment. In completed studies, systemic allergic reactions reported as anaphylactic reactions were reported in slightly numerically more subjects treated with Viaskin* Peanut than with placebo (5.1% vs 2.8%). All anaphylactic reaction reported as related to Viaskin* Peanut were mild to moderate, characterized mainly by skin reactions as well as subjective respiratory symptoms with no cardiovascular nor respiratory compromise. In Viaskin* Peanut treated subjects, these anaphylactic reactions tended to occur early during the treatment (within 2 months from treatment initiation), led to brief treatment interruption and did not recur while continuing treatment. The majority resolved either without epinephrine or following one injectable epinephrine administered at home.
If your child experienced any other symptoms you can talk with your investigator. Please ask the investigator if you have any questions about the known and possible side effects of Viaskin* Peanut.
Please talk to your child*s investigator for more details on side effects. You can also find them detailed in Appendix D.

Contacts

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/

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Children (2-11 years)
Babies and toddlers (28 days-23 months)

Inclusion criteria

All subjects who completed the EPITOPE study up to Visit 11 (inclusive) will be offered enrollment into the EPOPEX study, provided that all selection criteria are met. Subjects will be enrolled in this study only if they meet, among others, the following key inclusion criteria: completion of the EPITOPE study, with a completed and documented DBPCFC at Month 12 (i.e., both Visit 10 and Visit 11 performed).

Exclusion criteria

Subjects will not be enrolled, if they meet, among others, the following exclusion criteria: development of severe anaphylactic reaction during the Month 12 DBPCFC (at Visit 10 or Visit 11) in the EPITOPE study requiring a tracheal intubation or leading to a cardiac arrest and/or to coma; other cases of severe anaphylaxis will be considered eligible to enter the EPOPEX study.

Study design

Design

Study phase:	3
Study type:	Interventional
Masking:	Open (masking not used)

Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	02-03-2021
Enrollment:	6
Type:	Actual

Medical products/devices used

Registration:	No
Product type:	Medicine
Brand name:	Viaskin Peanut (DBV712)
Generic name:	na

Ethics review

Approved WMO Date:	15-09-2020
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	27-01-2021
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	21-04-2021
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	28-07-2021
Application type:	Amendment

Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	08-03-2022
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	06-07-2022
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	21-01-2024
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	20-02-2024
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	18-06-2024
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	31-07-2024
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

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
EU-CTR	CTIS2024-515703-19-00
EudraCT	EUCTR2018-003323-10-NL
CCMO	NL74575.078.20