# PEANUT ALLERGY ORAL IMMUNOTHERAPY STUDY OF AR101 FOR DESENSITIZATION IN CHILDREN AND ADULTS (THE PALISADE STUDY)

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The primary objective is to demonstrate the efficacy of AR101, a pharmaceutical-grade peanut allergen formulation, through reduction in clinical reactivity to limited amounts of peanut allergen in peanut-allergic children (ages 4-17 years, inclusive...

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

## Summary

### ID

NL-OMON47055

**Source**
ToetsingOnline

**Brief title**
PALISADE

### Condition

- Allergic conditions

**Synonym**
peanut allergy

**Research involving**
Human

### Sponsors and support

**Primary sponsor:** Aimmune Therapeutics Inc.

**Source(s) of monetary or material Support:** Industry

## Intervention

**Keyword:** AR101, IMMUNOTHERAPY, PEANUT ALLERGY

## Outcome measures

### Primary outcome

The primary clinical efficacy endpoint is the proportion of subjects aged 4 to 17 years who tolerate a single highest dose of at least 1000 mg (2043 mg cumulative) of peanut protein with no more than mild symptoms at the Exit DBPCFC

### Secondary outcome

Key Secondary Endpoints:

* The proportion of subjects aged 4 to 17 years who tolerate a single highest dose of at least 600 mg (1043 mg cumulative) of peanut protein with no more than mild symptoms at the Exit DBPCFC

* The proportion of subjects aged 4 to 17 years who tolerate a single highest dose of at least 300 mg (443 mg cumulative) of peanut protein with no more than mild symptoms at the Exit DBPCFC

* The maximum severity of symptoms in subjects aged 4 to 17 years occurring at any challenge dose of peanut protein during the Exit DBPCFC

* The proportion of subjects aged 18 to 55 years who tolerate a single highest dose of at least 1000 mg (2043 mg cumulative) of peanut protein with no more than mild symptoms at the Exit DBPCFC

Other Secondary Endpoints:

* Maximum dose achieved with no or mild symptoms at Exit DBPCFC in subjects aged 4 to 17 years

* Change from baseline in maximum tolerated dose (MTD) of peanut protein at DBPCFC in subjects aged 4 to 17 years

* Use of epinephrine as a rescue medication at Exit DBPCFC and comparison to its use at Screening DBPCFC in subjects aged 4 to 17 years

* Changes in peanut-specific serum IgE and IgG4 levels in subjects aged 4 to 17 years

* Changes in peanut skin prick test (SPT) mean wheal diameters in subjects aged 4 to 17 years

* Quality of life assessment using the food allergy related quality of life questionnaire (FAQLQ), and the food allergy independent measure (FAIM) questionnaire in subjects aged 4 to 17 years

Secondary Safety Endpoints:

* The safety of peanut OIT based on adverse events (AEs) including serious adverse events (SAEs) in the following 5 age groups: 4 to 17 years, 4 to 11 years, 12 to 17 years, 18 to 55 years, and 4 to 55 years, inclusive

* Use of epinephrine as a rescue medication during OIT (Initial Escalation, Up-dosing, and Maintenance Periods) in the following 5 age groups: 4 to 17 years, 4 to 11 years, 12 to 17 years, 18 to 55 years, and 4 to 55 years, inclusive

* Frequency of anaphylaxis during OIT (Initial Escalation, Up-dosing, and Maintenance Periods) in the following 5 age groups: 4 to 17 years, 4 to 11

years, 12 to 17 years, 18 to 55 years, and 4 to 55 years, inclusive

* Frequency of allergic reaction (hypersensitivity) AEs occurring during the Up-dosing versus the Maintenance Period, normalized for duration of treatment in the following 5 age groups: 4 to 17 years, 4 to 11 years, 12 to 17 years, 18 to 55 years, and 4 to 55 years, inclusive
* Frequency of accidental ingestions of peanut and other allergenic foods in the following 5 age groups: 4 to 17 years, 4 to 11 years, 12 to 17 years, 18 to 55 years, and 4 to 55 years, inclusive
* Severity of adverse events associated with accidental ingestions of peanut and other allergenic foods in the following 5 age groups: 4 to 17 years, 4 to 11 years, 12 to 17 years, 18 to 55 years, and 4 to 55 years, inclusive
* Frequency of premature discontinuation of dosing due to AEs; and frequency of premature discontinuation of dosing due to chronic/recurrent gastrointestinal (GI) AEs in the following 5 age groups: 4 to 17 years, 4 to 11 years, 12 to 17 years, 18 to 55 years, and 4 to 55 years, inclusive
* Assessment of asthma control using the Asthma Control Test questionnaire in in the following 5 age groups: 4 to 17 years, 4 to 11 years, 12 to 17 years, 18 to 55 years, and 4 to 55 years, inclusive

Exploratory Endpoints:

* The primary endpoints identified above will be repeated in the following 3 age groups: 4 to 11 years, 12 to 17 years, and 4 to 55 years, inclusive
* The first 3 key secondary endpoints and all other secondary endpoints

identified above will be repeated in the following 4 age groups: 4 to 11 years,

12 to 17 years, 18 to 55 years, and 4 to 55 years, inclusive

* Treatment satisfaction assessment using the Treatment Satisfaction

Questionnaire for Medication (TSQM-9), an exit questionnaire, and palatability

questions

# Study description

### Background summary

Peanut allergy is a common and serious condition that often affects children, and is commonly associated with severe reactions, including life-threatening anaphylaxis. Despite efforts at strict peanut avoidance, accidental exposure continues to be a major concern in peanut allergy because allergic responses can be triggered after ingestion of just milligram quantities of peanut protein. Accidental exposures may result from commercial food product mislabeling as well as inattention to, or mistrust of, food warning labels. Oral immunotherapy for peanut allergy has been widely studied in recent years and has demonstrated encouraging safety and efficacy results in early clinical trials. In practical terms, this state of desensitization should be sufficient to protect a patient with peanut allergy in case of an accidental exposure to peanut while the patient is attempting to maintain a peanut- avoidant diet.

### Study objective

The primary objective is to demonstrate the efficacy of AR101, a pharmaceutical-grade peanut allergen formulation, through reduction in clinical reactivity to limited amounts of peanut allergen in peanut-allergic children (ages 4-17 years, inclusive).
The secondary objectives are:
* To demonstrate the safety of AR101 as measured by the incidence of adverse events, including serious adverse events in children (ages 4-17 years, inclusive).
* To evaluate the immunological effects of peanut OIT therapy in children (ages 4-17 years, inclusive).

### Study design

This is an international, multicenter, randomized, double-blind, placebo-controlled study of the efficacy and safety of AR101 in a characterized

desensitization OIT regimen in peanut-allergic individuals. The study will consist of a screening phase, that includes a Screening double-blind, placebo-controlled food challenge (DBPCFC), and a double-blind OIT treatment phase that includes an initial escalation period, an up-dosing period, and a maintenance period, followed by an Exit DBPCFC.
An open-label safety follow-on study (ARC004) is planned after completion of ARC003.
All eligible subjects will receive escalating doses of either AR101 or placebo. Eligible subjects who reach the targeted dose of 300 mg/d and maintain that dose for approximately 24 weeks will undergo an Exit DBPCFC. Subjects who do not reach 300 mg/d will be considered escalation failures and nonresponders for the primary analysis.
A DBPCFC will be performed for those subjects achieving the target dose of 300 mg/d and continuing to receive that dose throughout the maintenance period (~24 weeks). Each subject will be unblinded when he/she completes the DBPCFC at the end of the ~24-week maintenance period, provided regulatory and IRB/EC approval for ARC004 have been received, the availability of IP for ARC004, and all major data queries for the subject have been resolved. If this is not the case, the subject shall remain on blinded treatment until these requirements are satisfied. The subject should continue his or her maintenance visits (completed as unscheduled visits), every 30 days and complete all protocol procedures at each visit until study completion and rollover to ARC004.
All placebo subjects who complete ARC003 are eligible for rollover into the ARC004 protocol. Placebo subjects from ARC003 will, in ARC004, undergo an escalation schedule identical to that for active subjects in the ARC003 protocol. All subjects on active treatment in ARC003 who pass the DBPCFC at the 300 mg (443 mg cumulative) challenge dose level of peanut protein are eligible to proceed to ARC004. Those who do not pass DBPCFC at the 300 mg (443 mg cumulative) challenge dose level will be considered endpoint failures and nonresponders for the primary analysis. They will not be eligible for rollover into the ARC004 protocol due to safety concerns. Those subjects who pass DBPCFC at the 300 mg (443 mg cumulative) challenge dose level, but fail at the 600 mg (1043 mg cumulative) or 1000 mg (2043 mg cumulative) challenge dose level, will also be considered endpoint failures and nonresponders for the primary analysis for North America or Europe, respectively; however, they will be eligible for rollover into the ARC004 protocol because tolerating a 300 mg (443 mg cumulative) dose of peanut protein is considered a clinically relevant level of desensitization in the event of accidental exposure.
A Data Safety Monitoring Committee (DSMC) will be established to monitor the study for safety.

**Intervention**

AR101 or placebo. Doses characterized and normalized for total protein and specific peanut allergen ratios will ascend per the dosing regimen outlined below. Study product will be provided in pull-apart capsules formulated to contain 0.5, 1, 10, 20, and 100 mg of peanut protein. Matching placebo capsules

identical to the active capsules will be used to maintain double-blinded conditions. For the Maintenance Period, 300 mg of peanut protein will be formulated in foil-laminate sachets. Matching placebo sachets will be used to maintain the double-blind. Study products will be shipped directly to the investigational site or the investigational site*s pharmacy, depending on the investigational site*s institutional requirements. Trained investigational site personnel will dispense the study product to the subject or the subject*s parent or guardian in a manner consistent with the assigned dose level. Study product will be dispensed in double-blinded fashion according to subject randomization number, using an interactive voice/web response system.

**Study burden and risks**

Oral food challenges are expected to induce an allergic response in food-allergic individuals. Allergic reactions can be severe, including life-threatening allergic reactions; however, the risk of an allergic reaction is reduced by initiating the challenge with a very small amount of the food, gradually increasing the dose, and stopping the challenge at the first definitive sign of a significant reaction.
There may be a risk that during participation in the trial the subjects may decrease their vigilance against accidental peanut ingestion because they believe they are protected from it. This phenomenon has been reported in previous trials. Subjects in the trial and their participating family will be warned that they should continue to practice their usual vigilance against accidental ingestion of peanuts or peanut-containing foods.

# Contacts

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# Trial sites

## Listed location countries

Netherlands

# Eligibility criteria

**Age**
Adolescents (12-15 years)
Adolescents (16-17 years)
Adults (18-64 years)
Children (2-11 years)
Elderly (65 years and older)

## Inclusion criteria

Age 4 through 55 years (inclusive);Clinical history of allergy to peanuts or peanut-containing foods;Serum IgE to peanut of *0.35 kUA/L [determined by UniCAPTM within the past 12 months] and/or a SPT to peanut *3 mm compared to control;Experience dose-limiting symptoms at or before the 100 mg challenge dose of peanut protein (measured as 200 mg of peanut flour) on Screening DBPCFC conducted in accordance with PRACTALL (Practical Issues in Allergology, Joint United States/European Union Initiative) guidelines;Written informed consent from adult subjects;Written informed consent from parent/guardian for minor subjects;Written assent from minor subjects as appropriate (e.g., above the age of 7 years or the applicable age per local regulatory requirements);Use of effective birth control by female subjects of child-bearing potential;Not be residing at the same address as another subject in this or any peanut OIT study

## Exclusion criteria

History of cardiovascular disease, including uncontrolled or inadequately controlled hypertension;History of severe or life-threatening episode of anaphylaxis or anaphylactic shock within 60 days of Screening DBPCFC;History of chronic disease (other than asthma, atopic dermatitis, or allergic rhinitis) that is, or is at significant risk of becoming, unstable or requiring a change in chronic therapeutic regimen;History of eosinophilic esophagitis (EoE), other eosinophilic gastrointestinal disease, gastroesophageal reflux disease (GERD), symptoms of dysphagia (difficulty swallowing, food *getting stuck*), or recurrent gastrointestinal symptoms of undiagnosed etiology;Current participation in any other interventional study;Subject is in *build-up phase* of immunotherapy to another allergen ( has not reached maintenance dosing);Severe asthma (2007 NHLBI Criteria Steps 5 or 6, see

Appendix 2);Mild or moderate asthma (2007 NHLBI Criteria Steps 1-4), if uncontrolled or difficult to control as defined by any of the following:;Forced expiratory volume in 1 second (FEV1) < 80% of predicted, or ratio of FEV1 to forced vital capacity (FEV1/FVC) < 75% of predicted, with or without controller medications (only for age 6 or greater and able to do spirometry) or;Inhaled corticosteroid (ICS) dosing of > 500 mcg daily fluticasone (or equivalent ICSs based on National Heart, Lung, and Blood Institute [NHLBI] dosing chart) or;* 1 hospitalization in the past year prior to screening for asthma or ;* Emergency room (ER) visit for asthma within 6 months prior to screening;History of steroid medication use (via intravenous [IV], intramuscular [IM] or oral administration) in any of the following manners: ;* history of daily oral steroid dosing for >1 month during the past year or;* burst oral steroid course in the past 3 months prior to randomization or;* >2 burst oral steroid courses in the past year *1 week in duration;Inability to discontinue antihistamines 5 half-lives before the initial day of escalation, skin prick testing, or DBPCFC;Lack of an available palatable vehicle food to which the subject is not allergic;Use of any therapeutic antibody (eg omalizumab, mepolizumab, reslizumab, etc.), any investigational peanut immunotherapy (eg oral, sublingual, epicutaneous), or any other immunomodulatory therapy excluding corticosteroids within the past 6 months ;Use of beta-blockers (oral), angiotensin-converting enzyme (ACE) inhibitors, angiotensin-receptor blockers (ARB) or calcium channel blockers;Pregnancy or lactation;Having the same place of residence as another subject in the study;Participation in another clinical trial within 30 days or 5 half-lives of the investigational product, whichever is longer, prior to randomization;Developing dose limiting symptoms in reaction to the placebo part of the Screening DBPCFC

# Study design

## Design

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| Study phase: | 3 |
| Study type: | Interventional |
| Intervention model: | Parallel |
| Allocation: | Randomized controlled trial |
| Masking: | Double blinded (masking used) |
| Control: | Placebo |
| Primary purpose: | Treatment |

## Recruitment

NL

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|---|---|
| Recruitment status: | Recruitment stopped |
| Start date (anticipated): | 22-06-2016 |

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| Enrollment: | 20 |
| Type: | Actual |

### Medical products/devices used

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|---|---|
| Product type: | Medicine |
| Brand name: | AR101 |
| Generic name: | AR101 |
| Product type: | Medicine |
| Brand name: | Placebo |
| Generic name: | Placebo |

## Ethics review

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|---|---|
| Approved WMO Date: | 08-12-2015 |
| Application type: | First submission |
| Review commission: | METC Universitair Medisch Centrum Groningen (Groningen) |
| Approved WMO Date: | 11-04-2016 |
| Application type: | First submission |
| Review commission: | METC Universitair Medisch Centrum Groningen (Groningen) |
| Approved WMO Date: | 15-08-2016 |
| Application type: | Amendment |
| Review commission: | METC Universitair Medisch Centrum Groningen (Groningen) |
| Approved WMO Date: | 02-11-2016 |
| Application type: | Amendment |
| Review commission: | METC Universitair Medisch Centrum Groningen (Groningen) |
| Approved WMO Date: | 30-11-2016 |
| Application type: | Amendment |
| Review commission: | METC Universitair Medisch Centrum Groningen (Groningen) |
| Approved WMO Date: | 25-04-2017 |

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| Application type: | Amendment |
| Review commission: | METC Universitair Medisch Centrum Groningen (Groningen) |
| Approved WMO Date: | 18-05-2017 |
| Application type: | Amendment |
| Review commission: | METC Universitair Medisch Centrum Groningen (Groningen) |
| Approved WMO Date: | 18-10-2017 |
| Application type: | Amendment |
| Review commission: | METC Universitair Medisch Centrum Groningen (Groningen) |
| Approved WMO Date: | 20-11-2017 |
| Application type: | Amendment |
| Review commission: | METC Universitair Medisch Centrum Groningen (Groningen) |
| Approved WMO Date: | 22-02-2018 |
| Application type: | Amendment |
| Review commission: | METC Universitair Medisch Centrum Groningen (Groningen) |
| Approved WMO Date: | 30-03-2018 |
| Application type: | Amendment |
| Review commission: | METC Universitair Medisch Centrum Groningen (Groningen) |

# 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 | EUCTR2015-004257-41-NL |
| ClinicalTrials.gov | NCT02635776 |
| CCMO | NL55395.042.15 |