



Clinical trial results: Oral Desensitization to Peanut in Peanut-Allergic Children and Adults Using Characterized Peanut Allergen Oral Immunotherapy.

Summary

EudraCT number	2021-002087-47
Trial protocol	Outside EU/EEA
Global end of trial date	07 January 2015

Results information

Result version number	v1 (current)
This version publication date	19 February 2022
First version publication date	19 February 2022

Trial information

Trial identification

Sponsor protocol code	ARC001
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01987817
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Aimmune Therapeutics Inc.
Sponsor organisation address	8000 Marina Blvd, Suite 300, Brisbane, United States, 94005
Public contact	Director of Regulatory Affairs, Aimmune Therapeutics Inc, +1 650-409-5164, RegulatoryAffairs@aimmune.com
Scientific contact	Director of Regulatory Affairs, Aimmune Therapeutics Inc, +1 650-409-5164, RegulatoryAffairs@aimmune.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMA-001734-PIP01-14
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	18 February 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	07 January 2015
Global end of trial reached?	Yes
Global end of trial date	07 January 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective is to demonstrate the efficacy of Characterized Peanut Allergen through reduction in clinical reactivity to limited amounts of peanut allergen in peanut-allergic children and young adults (ages 4-26 years, inclusive)

Protection of trial subjects:

Protocol and ICF were approved by IECs or IRBs and FDA in conformance with US code of Federal Regulations and ICH guidelines. Study was conducted per GCP and Declaration of Helsinki guidelines. Patients or parents /legal guardians of patients were educated on study and to notify sites of allergic symptoms occurring at home. Diary logs for completion at home by patients/families to measure IP compliance and alert sites of Adverse Events of Interest, including accidental exposure or Epi pen use.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	06 February 2014
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy, Ethical reason
Long term follow-up duration	23 Months
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United States: 55
Worldwide total number of subjects	55
EEA total number of subjects	0

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	41
Adolescents (12-17 years)	13
Adults (18-64 years)	1

From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

67 subjects were initially enrolled. 11 subjects failed screening, resulting in 56 subjects being initially randomized and enrolled in the study. The randomized population comprised 29 subjects in the AR101 group and 27 subjects in the placebo group. The final intent-to-treat (ITT) population had one fewer subject in the placebo group (n=26).

Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	AR101

Arm description:

A peanut-derived oral immunotherapy drug.

Arm type	Experimental
Investigational medicinal product name	AR101
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral powder
Routes of administration	Oral use

Dosage and administration details:

Pull-apart capsules at 4 dosage strengths (0.5, 1, 10, 100 mg)

Arm title	Placebo
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Arm description:

Matching placebo

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral powder
Routes of administration	Oral use

Dosage and administration details:

Equivalent amount of placebo powder containing inactive ingredients.

Number of subjects in period 1	AR101	Placebo
Started	29	26
Completed	23	26
Not completed	6	0
Consent withdrawn by subject	1	-
Physician decision	1	-
Adverse event, non-fatal	4	-

Baseline characteristics

Reporting groups

Reporting group title	AR101
Reporting group description: A peanut-derived oral immunotherapy drug.	
Reporting group title	Placebo
Reporting group description: Matching placebo	

Reporting group values	AR101	Placebo	Total
Number of subjects	29	26	55
Age categorical			
Units: Subjects			
Children (2-11 years)	20	21	41
Adolescents (12-17 years)	8	5	13
Adults (18-64 years)	1	0	1
Age continuous			
Units: years			
median	7	8	
full range (min-max)	4 to 21	4 to 14	-
Gender categorical			
Units: Subjects			
Female	9	10	19
Male	20	16	36

Subject analysis sets

Subject analysis set title	AR101 intent-to-treat population
Subject analysis set type	Intention-to-treat
Subject analysis set description: Intent-to-treat population is defined as subjects who received at least 1 dose of randomized study treatment.	
Subject analysis set title	Placebo intent-to-treat population
Subject analysis set type	Intention-to-treat
Subject analysis set description: The final intent-to-treat (ITT) population consists of subjects who received at least 1 dose of randomized study treatment.	

Reporting group values	AR101 intent-to-treat population	Placebo intent-to-treat population	
Number of subjects	29	26	
Age categorical			
Units: Subjects			
Children (2-11 years)	20	21	
Adolescents (12-17 years)	8	5	
Adults (18-64 years)	1	0	

Age continuous			
Units: years			
median	7	8	
full range (min-max)	4 to 21	4 to 14	
Gender categorical			
Units: Subjects			
Female	9	10	
Male	20	16	

End points

End points reporting groups

Reporting group title	AR101
Reporting group description: A peanut-derived oral immunotherapy drug.	
Reporting group title	Placebo
Reporting group description: Matching placebo	
Subject analysis set title	AR101 intent-to-treat population
Subject analysis set type	Intention-to-treat
Subject analysis set description: Intent-to-treat population is defined as subjects who received at least 1 dose of randomized study treatment.	
Subject analysis set title	Placebo intent-to-treat population
Subject analysis set type	Intention-to-treat
Subject analysis set description: The final intent-to-treat (ITT) population consists of subjects who received at least 1 dose of randomized study treatment.	

Primary: The Proportion of Subjects Who Tolerate at Least 300 mg (443 mg Cumulative) of Peanut Protein With no More Than Mild Symptoms at the Exit DBPCFC

End point title	The Proportion of Subjects Who Tolerate at Least 300 mg (443 mg Cumulative) of Peanut Protein With no More Than Mild Symptoms at the Exit DBPCFC
End point description: The primary endpoint was the percentage of subjects who achieved desensitization, as determined by tolerating at least 300 mg (443 mg cumulative) of peanut protein at the Exit Double Blind Placebo Controlled Food Challenge (DBPCFC) with no more than mild symptoms (i.e., desensitization responders).	
End point type	Primary
End point timeframe: 6-9 months.	

End point values	AR101 intent-to-treat population	Placebo intent-to-treat population		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	29	26		
Units: Number of subjects	23	5		

Statistical analyses

Statistical analysis title	Treatment difference at 300 mg
Statistical analysis description: Fisher Exact test for the difference (AR101 - Placebo) in proportion of subjects who tolerated a single highest dose of at least 300 mg.	
Comparison groups	Placebo intent-to-treat population v AR101 intent-to-treat

	population
Number of subjects included in analysis	55
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Fisher exact
Parameter estimate	Risk difference (RD)
Point estimate	60
Confidence interval	
level	95 %
sides	2-sided
lower limit	35
upper limit	79

Secondary: Change From Baseline in Maximum Tolerated Dose of Peanut Protein at the Exit DBPCFC

End point title	Change From Baseline in Maximum Tolerated Dose of Peanut Protein at the Exit DBPCFC
End point description:	The change in maximum tolerated dose of peanut protein from baseline (screening) to the Exit DBPCFC.
End point type	Secondary
End point timeframe:	6-9 months.

End point values	AR101 intent-to-treat population	Placebo intent-to-treat population		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	29	26		
Units: milligram(s)				
least squares mean (confidence interval 95%)	1.254 (0.984 to 1.523)	0.341 (0.057 to 0.626)		

Statistical analyses

Statistical analysis title	Change From Baseline in Maximum Tolerated Dose
Statistical analysis description:	MTD for the baseline and Exit DBPCFC are transformed back to log10 scale before calculations. A value of 0.3 mg is substituted for subjects who could not tolerate the lowest DBPCFC dose before log10 transformation.
Comparison groups	AR101 intent-to-treat population v Placebo intent-to-treat population

Number of subjects included in analysis	55
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 ^[1]
Method	ANCOVA
Parameter estimate	Treatment Difference
Point estimate	0.912
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.5184
upper limit	1.3065

Notes:

[1] - The p-value is based on the F-test for treatment effect adjusted for MTD from baseline (log10 mg). The p-value and confidence intervals are based on the normality assumption.

Secondary: Maximum Dose Achieved With no or Mild Symptoms at Exit DBPCFC

End point title	Maximum Dose Achieved With no or Mild Symptoms at Exit DBPCFC
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End point description:

The number of participants analyzed per outcome measure reflects the intent-to-treat (ITT) population (subjects who received at least 1 dose of randomized study treatment).

End point type	Secondary
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End point timeframe:

6-9 months

End point values	AR101 intent-to-treat population	Placebo intent-to-treat population		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	29	26		
Units: Number of subjects				
0.3 g	0	1		
3 mg	2	2		
10 mg	3	7		
30 mg	1	5		
100 mg	0	6		
300 mg	5	5		
600 mg	18	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Changes in Peanut-Specific IgE From Baseline to Exit DBPCFC

End point title	Changes in Peanut-Specific IgE From Baseline to Exit DBPCFC
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End point description:

The number of participants analyzed per outcome measure reflects the intent-to-treat (ITT) population

(subjects who received at least 1 dose of randomized study treatment).

Relative change from baseline is calculated as the ratio of exit visit result to the baseline result, within treatment group.

End point type	Secondary
End point timeframe:	
6-9 months.	

End point values	AR101 intent-to-treat population	Placebo intent-to-treat population		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	29	26		
Units: kUA/L				
geometric mean (confidence interval 95%)				
Baseline	32.571 (18.626 to 56.957)	53.839 (34.952 to 82.934)		
Exit	36.889 (21.258 to 64.015)	57.060 (37.186 to 87.557)		
Relative Change From Baseline	1.231 (1.027 to 1.475)	1.060 (1.001 to 1.112)		

Statistical analyses

No statistical analyses for this end point

Secondary: Changes in Peanut-Specific IgG4 From Baseline to Exit DBPCFC

End point title	Changes in Peanut-Specific IgG4 From Baseline to Exit DBPCFC
End point description:	
The number of participants analyzed per outcome measure reflects the intent-to-treat (ITT) population (subjects who received at least 1 dose of randomized study treatment)	
Relative change from baseline is calculated as the ratio of exit visit result to the baseline result, within treatment group.	
End point type	Secondary
End point timeframe:	
6-9 months.	

End point values	AR101 intent-to-treat population	Placebo intent-to-treat population		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	29	26		
Units: µg/mL				
geometric mean (confidence interval 95%)				
Baseline	0.734 (0.487 to 1.107)	0.510 (0.344 to 0.757)		

Exit	3.609 (2.074 to 6.281)	0.540 (0.377 to 0.775)		
Relative Change From Baseline	5.068 (3.640 to 7.055)	1.066 (0.905 to 1.255)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in Skin Prick Test (SPT) Mean Peanut Wheal Diameter Results From Baseline

End point title	Change in Skin Prick Test (SPT) Mean Peanut Wheal Diameter Results From Baseline
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End point description:

The number of participants analyzed per outcome measure reflects the intent-to-treat (ITT) population (subjects who received at least 1 dose of randomized study treatment).

End point type	Secondary
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End point timeframe:

6-9 months.

End point values	AR101 intent-to-treat population	Placebo intent-to-treat population		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	29	26		
Units: millimeter(s)				
arithmetic mean (confidence interval 95%)				
Baseline	14.1 (11.6 to 16.7)	13.7 (11.4 to 16.0)		
Exit	7.1 (5.7 to 8.6)	11.8 (9.3 to 14.4)		
Change from Baseline	-7.0 (-9.9 to -4.1)	-1.8 (-4.8 to 1.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Maximum Symptom Severity at Each Challenge Dose of Peanut Protein in All Subjects During Up-Dosing DBPCFC

End point title	Number of Participants With Maximum Symptom Severity at Each Challenge Dose of Peanut Protein in All Subjects During Up-Dosing DBPCFC
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End point description:

Maximum severity of symptoms that occurred at each challenge dose of peanut protein for all subjects during up-dosing DBPCFC.

End point type	Secondary
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End point timeframe:

Up to 36 weeks for up-dosing.

End point values	AR101 intent-to-treat population	Placebo intent-to-treat population		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	21	21		
Units: participants				
No symptoms at 3 mg	11	18		
Mild symptoms at 3 mg	0	3		
Moderate symptoms at 3 mg	0	0		
Severe symptoms at 3 mg	0	0		
Missing symptom at 3 mg	10	0		
No symptoms at 10 mg	10	21		
Mild symptoms at 10 mg	1	0		
Moderate symptoms at 10 mg	0	0		
Severe symptoms at 10 mg	0	0		
Missing symptom at 10 mg	10	0		
No symptoms at 30 mg	10	20		
Mild symptoms at 30 mg	2	1		
Moderate symptoms at 30 mg	0	0		
Severe symptoms at 30 mg	0	0		
Missing symptom at 30 mg	9	0		
No symptoms at 100 mg	11	18		
Mild symptoms at 100 mg	1	3		
Moderate symptoms at 100 mg	0	0		
Severe symptoms at 100 mg	0	0		
Missing symptom at 100 mg	9	0		
No symptoms at 300 mg	7	20		
Mild symptoms at 300 mg	4	1		
Moderate symptoms at 300 mg	0	0		
Severe symptoms at 300 mg	0	0		
Missing symptom at 300 mg	10	0		
No symptoms at 600 mg	6	12		
Mild symptoms at 600 mg	6	5		
Moderate symptoms at 600 mg	0	4		
Severe symptoms at 600 mg	0	0		
Missing symptom at 600 mg	9	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Maximum Symptom Severity at Each Challenge Dose of Peanut Protein in All Subjects During Maintenance DBPCFC

End point title	Number of Participants With Maximum Symptom Severity at
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End point description:

Up to 60 weeks (Up to 36 weeks for up-dosing; up to 24 weeks for maintenance).

End point type

Secondary

End point timeframe:

Maximum severity of symptoms that occurred at each challenge dose of peanut protein for all subjects during maintenance DBPCFC.

End point values	AR101 intent-to-treat population	Placebo intent-to-treat population		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	20	20		
Units: participants				
No symptoms at 3 mg	7	9		
Mild symptoms at 3 mg	0	1		
Moderate symptoms at 3 mg	0	0		
Severe symptoms at 3 mg	0	0		
Missing symptom at 3 mg	13	10		
No symptoms at 10 mg	6	9		
Mild symptoms at 10 mg	0	0		
Moderate symptoms at 10 mg	0	0		
Severe symptoms at 10 mg	0	0		
Missing symptom at 10 mg	14	11		
No symptoms at 30 mg	6	9		
Mild symptoms at 30 mg	0	1		
Moderate symptoms at 30 mg	0	0		
Severe symptoms at 30 mg	0	0		
Missing symptom at 30 mg	14	10		
No symptoms at 100 mg	6	9		
Mild symptoms at 100 mg	1	0		
Moderate symptoms at 100 mg	0	0		
Severe symptoms at 100 mg	0	0		
Missing symptom at 100 mg	13	11		
No symptoms at 300 mg	6	8		
Mild symptoms at 300 mg	0	1		
Moderate symptoms at 300 mg	0	0		
Severe symptoms at 300 mg	0	0		
Missing symptom at 300 mg	14	11		
No symptoms at 600 mg	7	7		
Mild symptoms at 600 mg	2	3		
Moderate symptoms at 600 mg	0	1		
Severe symptoms at 600 mg	0	0		
Missing symptom at 600 mg	11	9		
No symptoms at 1000 mg	5	7		
Mild symptoms at 1000 mg	7	4		
Moderate symptoms at 1000 mg	2	2		
Severe symptoms at 1000 mg	0	1		
Missing symptom at 1000 mg	6	6		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

6-9 months

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	16.0
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Reporting groups

Reporting group title	AR101
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Reporting group description:

A peanut-derived oral immunotherapy drug

Reporting group title	Placebo
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Reporting group description:

Matching Placebo

Serious adverse events	AR101	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 29 (3.45%)	1 / 26 (3.85%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	1 / 29 (3.45%)	1 / 26 (3.85%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	AR101	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	28 / 29 (96.55%)	22 / 26 (84.62%)	
Injury, poisoning and procedural complications			
Ligament sprain			
subjects affected / exposed	0 / 29 (0.00%)	2 / 26 (7.69%)	
occurrences (all)	0	2	
Nervous system disorders			

Headache subjects affected / exposed occurrences (all)	3 / 29 (10.34%) 3	3 / 26 (11.54%) 3	
Somnolence subjects affected / exposed occurrences (all)	2 / 29 (6.90%) 2	0 / 26 (0.00%) 0	
General disorders and administration site conditions Pyrexia subjects affected / exposed occurrences (all)	5 / 29 (17.24%) 5	4 / 26 (15.38%) 4	
Malaise subjects affected / exposed occurrences (all)	0 / 29 (0.00%) 0	2 / 26 (7.69%) 2	
Ear and labyrinth disorders Ear pain subjects affected / exposed occurrences (all)	2 / 29 (6.90%) 2	0 / 26 (0.00%) 0	
Immune system disorders Hypersensitivity subjects affected / exposed occurrences (all)	26 / 29 (89.66%) 341	13 / 26 (50.00%) 68	
Gastrointestinal disorders Vomiting subjects affected / exposed occurrences (all)	4 / 29 (13.79%) 8	2 / 26 (7.69%) 3	
Diarrhoea subjects affected / exposed occurrences (all)	1 / 29 (3.45%) 1	3 / 26 (11.54%) 3	
Nausea subjects affected / exposed occurrences (all)	3 / 29 (10.34%) 9	1 / 26 (3.85%) 1	
Abdominal pain subjects affected / exposed occurrences (all)	2 / 29 (6.90%) 3	1 / 26 (3.85%) 1	
Abdominal pain upper			

subjects affected / exposed occurrences (all)	1 / 29 (3.45%) 1	2 / 26 (7.69%) 4	
Respiratory, thoracic and mediastinal disorders			
Nasal congestion subjects affected / exposed occurrences (all)	2 / 29 (6.90%) 2	3 / 26 (11.54%) 4	
Cough subjects affected / exposed occurrences (all)	2 / 29 (6.90%) 2	2 / 26 (7.69%) 2	
Oropharyngeal pain subjects affected / exposed occurrences (all)	3 / 29 (10.34%) 4	1 / 26 (3.85%) 1	
Skin and subcutaneous tissue disorders			
Urticaria subjects affected / exposed occurrences (all)	3 / 29 (10.34%) 3	2 / 26 (7.69%) 2	
Infections and infestations			
Upper respiratory tract infection subjects affected / exposed occurrences (all)	2 / 29 (6.90%) 2	5 / 26 (19.23%) 9	
Viral infection subjects affected / exposed occurrences (all)	3 / 29 (10.34%) 3	1 / 26 (3.85%) 1	
Pharyngitis streptococcal subjects affected / exposed occurrences (all)	2 / 29 (6.90%) 2	1 / 26 (3.85%) 1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
02 December 2013	Protocol Amendment 1: Clarification of study design.
06 February 2014	Protocol Amendment 2: Changes in study procedures and various clarifications including dosage, primary efficacy endpoint and eligibility criteria.
14 May 2014	Protocol Amendment 3: Changes in study design and study procedures. the Exit DBPCFC was changed from up to 1000 mg (1443 mg cumulative) to up to 600 mg (1043 mg cumulative) peanut protein or placebo.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported