



Clinical trial results: AR101 Trial in Europe Measuring Oral Immunotherapy Success in Peanut Allergic Children (ARTEMIS)

Summary

EudraCT number	2016-005004-26
Trial protocol	GB FR DE ES SE IE IT
Global end of trial date	15 February 2019

Results information

Result version number	v1 (current)
This version publication date	15 August 2020
First version publication date	15 August 2020

Trial information

Trial identification

Sponsor protocol code	ARC010
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03201003
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	Clinical Operations, Aimmune Therapeutics Inc., +1 6503963822, amarcantonio@aimmune.com
Scientific contact	Clinical Operations, Aimmune Therapeutics Inc., +1 6503963822, amarcantonio@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	17 May 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	15 February 2019
Global end of trial reached?	Yes
Global end of trial date	15 February 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective was 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 and adolescents (ages 4 to 17 years, inclusive).

Protection of trial subjects:

- Education of patients to notify sites of allergic symptoms occurring at home.
- Patient emergency card, dos and don't card, home dosing card.
- Patients/caregivers asked to carry epi-pen with them at all times during study.
- Patient advised to go to local emergency unit outside of normal clinical working hours.
- Patient advised to report rare or unforeseen AEs immediately.
- Advised to practice usual peanut avoidance
- Specific reporting/monitoring of AEs, Gastrointestinal AEs (monitoring and follow-up for EOE), capture of AEs in patient diaries, EDC, SAE reporting, study and individual stopping rules & in clinic, supervised up-dosing, including observation timelines prior to Clinic departure.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	26 June 2017
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy, Regulatory reason, Scientific research
Long term follow-up duration	12 Months
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Spain: 26
Country: Number of subjects enrolled	Sweden: 11
Country: Number of subjects enrolled	United Kingdom: 59
Country: Number of subjects enrolled	France: 17
Country: Number of subjects enrolled	Germany: 28
Country: Number of subjects enrolled	Ireland: 26
Country: Number of subjects enrolled	Italy: 8
Worldwide total number of subjects	175
EEA total number of subjects	175

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)	127
Adolescents (12-17 years)	48
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

A total of 227 subjects between the ages of 4 and 17 years with suspected peanut allergy were screened for inclusion of which 175 were randomised and enrolled in the study.

Pre-assignment

Screening details:

Selection criteria included the following prior to randomisation:

- a clinical history of peanut allergy
- a mean peanut skin prick test wheal diameter ≥ 3 mm larger than the control and/or a serum peanut-specific IgE ≥ 0.35 kUA/L
- experiencing dose-limiting symptoms at or before the 300 mg dose of peanut protein during the screening DBPCFC

Period 1

Period 1 title	Post- randomisation (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:

AR101 drug product was supplied in 2 presentations. These were capsules containing 0.5, 1, 10, 20 and 100mg of peanut protein and sealed sachets containing 300mg of peanut protein. The capsules were used during the Initial Escalation and Up-dosing phases of the study. The sachets were used during the Maintenance phase. These 3, post-randomisation, phases are described below.

Initial escalation: Comprised of dose-escalation (from 0.5mg to a maximum of 6 mg at 20 to 30-minute intervals) on Day 1 and confirmation of the tolerability of a single 3 mg dose on Day 2.

Up-dosing: Following initial escalation, subjects received daily doses of AR101 and are up-dosed every 2 weeks for approximately 20 weeks. Dosing commenced at 3mg and progressed to 300mg via 10 incremental dosing steps at 2 weekly intervals.

Maintenance: All subjects who reach and tolerate 300 mg/d will continue to take a daily maintenance dose of 300mg/d for 12 to 16 weeks. Maintenance visits occur every 4 weeks.

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:

A placebo matching the AR101 drug product was supplied in 2 presentations. These were capsules matching the 0.5, 1, 10, 20 and 100mg peanut capsules but containing no peanut protein and sealed sachets matching the peanut protein sachets but without any peanut protein. The capsules were used during the Initial Escalation and Up-dosing phases of the study. The sachets were used during the Maintenance phase. These 3, post-randomisation, phases are described above but utilising the placebo presentations.

Number of subjects in period 1	AR101	Placebo
Started	132	43
Completed	106	40
Not completed	26	3
Consent withdrawn by subject	4	1
Adverse event, non-fatal	14	1
Other	5	1
Lost to follow-up	2	-
Protocol deviation	1	-

Baseline characteristics

Reporting groups

Reporting group title	AR101
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Reporting group description:

A peanut-derived oral immunotherapy drug
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Reporting group title	Placebo
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Reporting group description:

Matching Placebo

Reporting group values	AR101	Placebo	Total
Number of subjects	132	43	175
Age categorical			
Units: Subjects			
Children (2-11 years)	97	30	127
Adolescents (12-17 years)	35	13	48
Gender categorical			
Units: Subjects			
Female	64	16	80
Male	68	27	95

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 ITT/ Safety Population Ages 4-17
Subject analysis set type	Intention-to-treat
Subject analysis set description: The pre-specified primary efficacy population includes subjects Ages 4-17 in the ITT Population	
Subject analysis set title	Placebo ITT / Safety Population Ages 4-17
Subject analysis set type	Intention-to-treat
Subject analysis set description: The pre-specified primary efficacy population includes subjects Ages 4-17 in the ITT Population	

Primary: Primary Efficacy End point: Percentage of subjects ages 4-17 who tolerated a single highest dose of at least 1000 mg in the Exit Oral Food Challenge

End point title	Primary Efficacy End point: Percentage of subjects ages 4-17 who tolerated a single highest dose of at least 1000 mg in the Exit Oral Food Challenge
End point description: The pre-specified primary efficacy population includes subjects Ages 4-17 in the ITT Population	
End point type	Primary
End point timeframe: Exit oral food challenge (after approximately 9 months of blinded therapy)	

End point values	AR101 ITT/ Safety Population Ages 4-17	Placebo ITT / Safety Population Ages 4-17		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	132	43		
Units: Percentage of Patients				
number (confidence interval 95%)				
Responder %	58.3 (49.4 to 66.8)	2.3 (0.1 to 12.3)		

Statistical analyses

Statistical analysis title	Treatment difference at 1000 mg
Statistical analysis description: The 95% CIs for difference in binomial proportions were based on exact unconditional confidence limits using the score statistic. p-values were based on Fisher's exact test.	

Comparison groups	AR101 ITT/ Safety Population Ages 4-17 v Placebo ITT / Safety Population Ages 4-17
Number of subjects included in analysis	175
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Fisher exact
Parameter estimate	Risk difference (RD)
Point estimate	56
Confidence interval	
level	95 %
sides	2-sided
lower limit	44.1
upper limit	65.2

Secondary: Secondary Efficacy End point: Percentage of subjects ages 4-17 who tolerated a single highest dose of at least 600 mg in the Exit Oral Food Challenge

End point title	Secondary Efficacy End point: Percentage of subjects ages 4-17 who tolerated a single highest dose of at least 600 mg in the Exit Oral Food Challenge
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End point description:

The pre-specified efficacy population includes subjects Ages 4-17 in the ITT Population

End point type	Secondary
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End point timeframe:

Exit oral food challenge (after approximately 9 months of blinded therapy)

End point values	AR101 ITT/ Safety Population Ages 4-17	Placebo ITT / Safety Population Ages 4-17		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	132	43		
Units: Percentage of Patients				
number (confidence interval 95%)				
Responder %	68.2 (59.5 to 76.0)	9.3 (2.6 to 22.1)		

Statistical analyses

Statistical analysis title	Treatment difference at 600 mg
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Statistical analysis description:

The 95% CIs for difference in binomial proportions were based on exact unconditional confidence limits using the score statistic. p-values were based on Fisher's exact test.

Comparison groups	AR101 ITT/ Safety Population Ages 4-17 v Placebo ITT / Safety Population Ages 4-17
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Number of subjects included in analysis	175
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Fisher exact
Parameter estimate	Risk difference (RD)
Point estimate	58.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	44.2
upper limit	69.3

Secondary: Secondary Efficacy End point: Percentage of subjects ages 4-17 who tolerated a single highest dose of at least 300 mg in the Exit Oral Food Challenge

End point title	Secondary Efficacy End point: Percentage of subjects ages 4-17 who tolerated a single highest dose of at least 300 mg in the Exit Oral Food Challenge
End point description:	The pre-specified secondary efficacy population includes subjects Ages 4-17 in the ITT Population
End point type	Secondary
End point timeframe:	Exit oral food challenge (after approximately 9 months of blinded therapy)

End point values	AR101 ITT / Safety Population Ages 4-17	Placebo ITT / Safety Population Ages 4-17		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	132	43		
Units: Percentage of Patients				
number (confidence interval 95%)				
Responder %	73.5 (65.1 to 80.8)	16.3 (6.8 to 30.7)		

Statistical analyses

Statistical analysis title	Treatment difference at 300 mg
Statistical analysis description:	The 95% CIs for difference in binomial proportions were based on exact unconditional confidence limits using the score statistic. p-values were based on Fisher's exact test.
Comparison groups	AR101 ITT / Safety Population Ages 4-17 v Placebo ITT / Safety Population Ages 4-17

Number of subjects included in analysis	175
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Fisher exact
Parameter estimate	Risk difference (RD)
Point estimate	57.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	41.2
upper limit	69.1

Secondary: Secondary Efficacy Endpoint: Maximum severity of symptoms at any challenge dose during the peanut exit DBPCFC

End point title	Secondary Efficacy Endpoint: Maximum severity of symptoms at any challenge dose during the peanut exit DBPCFC
End point description:	
End point type	Secondary
End point timeframe:	
Exit oral food challenge (after approximately 9 months of blinded therapy)	

End point values	AR101 ITT/ Safety Population Ages 4-17	Placebo ITT / Safety Population Ages 4-17		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	132	43		
Units: Percentage of Subjects				
number (not applicable)				
None	35.6	0		
Mild	41.7	37.2		
Moderate	18.2	46.5		
Severe or Higher	4.5	16.3		

Statistical analyses

Statistical analysis title	Treatment difference in Maximum Severity
Statistical analysis description:	
Tested using the Cochran-Mantel-Haenszel statistic (with equally spaced scores) stratified by country.	
Comparison groups	AR101 ITT/ Safety Population Ages 4-17 v Placebo ITT / Safety Population Ages 4-17

Number of subjects included in analysis	175
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Cochran-Mantel-Haenszel

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Through study completion (approximately 9 months)

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	19.1
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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 / 132 (0.76%)	2 / 43 (4.65%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Injury, poisoning and procedural complications			
Intentional overdose	Additional description: Paracetamol and a combination hormone birth control medication.		
subjects affected / exposed	1 / 132 (0.76%)	0 / 43 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Bronchospasm			
subjects affected / exposed	0 / 132 (0.00%)	1 / 43 (2.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Bronchitis bacterial			
subjects affected / exposed	0 / 132 (0.00%)	1 / 43 (2.33%)	
occurrences causally related to treatment / all	0 / 0	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	130 / 132 (98.48%)	42 / 43 (97.67%)	
Vascular disorders			
Flushing			
subjects affected / exposed	15 / 132 (11.36%)	1 / 43 (2.33%)	
occurrences (all)	42	3	
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	29 / 132 (21.97%)	14 / 43 (32.56%)	
occurrences (all)	41	19	
Fatigue			
subjects affected / exposed	13 / 132 (9.85%)	5 / 43 (11.63%)	
occurrences (all)	36	5	
Malaise			
subjects affected / exposed	8 / 132 (6.06%)	3 / 43 (6.98%)	
occurrences (all)	12	3	
Chest discomfort			
subjects affected / exposed	7 / 132 (5.30%)	1 / 43 (2.33%)	
occurrences (all)	15	1	
Immune system disorders			
Systemic allergic reaction			
subjects affected / exposed	16 / 132 (12.12%)	1 / 43 (2.33%)	
occurrences (all)	2	22	
Seasonal allergy			
subjects affected / exposed	10 / 132 (7.58%)	2 / 43 (4.65%)	
occurrences (all)	20	2	
Respiratory, thoracic and mediastinal disorders			
Throat irritation			
subjects affected / exposed	57 / 132 (43.18%)	8 / 43 (18.60%)	
occurrences (all)	659	25	
Sneezing			
subjects affected / exposed	43 / 132 (32.58%)	7 / 43 (16.28%)	
occurrences (all)	157	24	

Cough			
subjects affected / exposed	66 / 132 (50.00%)	24 / 43 (55.81%)	
occurrences (all)	166	53	
Rhinorrhoea			
subjects affected / exposed	34 / 132 (25.76%)	10 / 43 (23.26%)	
occurrences (all)	89	22	
Nasal congestion			
subjects affected / exposed	23 / 132 (17.42%)	8 / 43 (18.60%)	
occurrences (all)	63	12	
Dyspnoea			
subjects affected / exposed	15 / 132 (11.36%)	3 / 43 (6.98%)	
occurrences (all)	40	11	
Wheezing			
subjects affected / exposed	22 / 132 (16.67%)	3 / 43 (6.98%)	
occurrences (all)	45	8	
Throat tightness			
subjects affected / exposed	10 / 132 (7.58%)	1 / 43 (2.33%)	
occurrences (all)	31	8	
Nasal pruritus			
subjects affected / exposed	11 / 132 (8.33%)	3 / 43 (6.98%)	
occurrences (all)	19	3	
Oropharyngeal pain			
subjects affected / exposed	37 / 132 (28.03%)	12 / 43 (27.91%)	
occurrences (all)	99	18	
Pharyngeal paraesthesia			
subjects affected / exposed	7 / 132 (5.30%)	2 / 43 (4.65%)	
occurrences (all)	37	3	
Asthma			
subjects affected / exposed	7 / 132 (5.30%)	3 / 43 (6.98%)	
occurrences (all)	12	7	
Injury, poisoning and procedural complications			
Arthropod bite			
subjects affected / exposed	6 / 132 (4.55%)	5 / 43 (11.63%)	
occurrences (all)	7	6	
Nervous system disorders			

Headache subjects affected / exposed occurrences (all)	46 / 132 (34.85%) 128	19 / 43 (44.19%) 65	
Dizziness subjects affected / exposed occurrences (all)	4 / 132 (3.03%) 4	3 / 43 (6.98%) 3	
Blood and lymphatic system disorders Lymphadenopathy subjects affected / exposed occurrences (all)	8 / 132 (6.06%) 10	1 / 43 (2.33%) 1	
Ear and labyrinth disorders Ear pain subjects affected / exposed occurrences (all)	14 / 132 (10.61%) 21	0 / 43 (0.00%) 0	
Motion sickness subjects affected / exposed occurrences (all)	4 / 132 (3.03%) 5	3 / 43 (6.98%) 4	
Eye disorders Eye pruritus subjects affected / exposed occurrences (all)	24 / 132 (18.18%) 37	8 / 43 (18.60%) 12	
Eye swelling subjects affected / exposed occurrences (all)	11 / 132 (8.33%) 18	3 / 43 (6.98%) 7	
Gastrointestinal disorders Abdominal pain subjects affected / exposed occurrences (all)	88 / 132 (66.67%) 835	19 / 43 (44.19%) 126	
Nausea subjects affected / exposed occurrences (all)	58 / 132 (43.94%) 437	11 / 43 (25.58%) 31	
Paraesthesia oral subjects affected / exposed occurrences (all)	52 / 132 (39.39%) 961	9 / 43 (20.93%) 49	
Vomiting subjects affected / exposed occurrences (all)	53 / 132 (40.15%) 120	10 / 43 (23.26%) 17	

Oral pruritus			
subjects affected / exposed	28 / 132 (21.21%)	1 / 43 (2.33%)	
occurrences (all)	236	1	
Lip swelling			
subjects affected / exposed	20 / 132 (15.15%)	4 / 43 (9.30%)	
occurrences (all)	112	6	
Lip pruritus			
subjects affected / exposed	16 / 132 (12.12%)	2 / 43 (4.65%)	
occurrences (all)	97	2	
Abdominal discomfort			
subjects affected / exposed	17 / 132 (12.88%)	2 / 43 (4.65%)	
occurrences (all)	120	3	
Tongue pruritus			
subjects affected / exposed	12 / 132 (9.09%)	5 / 43 (11.63%)	
occurrences (all)	133	11	
Lip oedema			
subjects affected / exposed	7 / 132 (5.30%)	1 / 43 (2.33%)	
occurrences (all)	20	2	
Diarrhoea			
subjects affected / exposed	16 / 132 (12.12%)	8 / 43 (18.60%)	
occurrences (all)	26	19	
Abdominal pain upper			
subjects affected / exposed	14 / 132 (10.61%)	5 / 43 (11.63%)	
occurrences (all)	44	6	
Lip pain			
subjects affected / exposed	7 / 132 (5.30%)	0 / 43 (0.00%)	
occurrences (all)	21	0	
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	67 / 132 (50.76%)	14 / 43 (32.56%)	
occurrences (all)	300	62	
Urticaria			
subjects affected / exposed	48 / 132 (36.36%)	9 / 43 (20.93%)	
occurrences (all)	156	27	
Erythema			

subjects affected / exposed	34 / 132 (25.76%)	5 / 43 (11.63%)	
occurrences (all)	69	5	
Rash			
subjects affected / exposed	21 / 132 (15.91%)	8 / 43 (18.60%)	
occurrences (all)	38	18	
Angioedema			
subjects affected / exposed	13 / 132 (9.85%)	4 / 43 (9.30%)	
occurrences (all)	87	7	
Eczema			
subjects affected / exposed	12 / 132 (9.09%)	11 / 43 (25.58%)	
occurrences (all)	25	18	
Dry skin			
subjects affected / exposed	6 / 132 (4.55%)	4 / 43 (9.30%)	
occurrences (all)	8	5	
Dermatitis atopic			
subjects affected / exposed	3 / 132 (2.27%)	4 / 43 (9.30%)	
occurrences (all)	3	5	
Musculoskeletal and connective tissue disorders			
Pain in extremity			
subjects affected / exposed	11 / 132 (8.33%)	1 / 43 (2.33%)	
occurrences (all)	15	1	
Infections and infestations			
Conjunctivitis			
subjects affected / exposed	15 / 132 (11.36%)	5 / 43 (11.63%)	
occurrences (all)	31	25	
Nasopharyngitis			
subjects affected / exposed	44 / 132 (33.33%)	12 / 43 (27.91%)	
occurrences (all)	77	21	
Rhinitis			
subjects affected / exposed	20 / 132 (15.15%)	7 / 43 (16.28%)	
occurrences (all)	51	17	
Viral infection			
subjects affected / exposed	18 / 132 (13.64%)	7 / 43 (16.28%)	
occurrences (all)	24	10	
Upper respiratory tract infection			

subjects affected / exposed	17 / 132 (12.88%)	11 / 43 (25.58%)	
occurrences (all)	21	12	
Gastroenteritis			
subjects affected / exposed	12 / 132 (9.09%)	5 / 43 (11.63%)	
occurrences (all)	13	6	
Gastroenteritis viral			
subjects affected / exposed	7 / 132 (5.30%)	0 / 43 (0.00%)	
occurrences (all)	8	0	
Influenza			
subjects affected / exposed	4 / 132 (3.03%)	3 / 43 (6.98%)	
occurrences (all)	4	3	
Respiratory tract infection			
subjects affected / exposed	3 / 132 (2.27%)	3 / 43 (6.98%)	
occurrences (all)	4	5	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
16 January 2017	Amendment 1 Main Changes: <ul style="list-style-type: none">• Revised inclusion criteria• Optional substudy added as exploratory endpoint
26 September 2017	Amendment 2 Main Changes: <ul style="list-style-type: none">• Added end of study definition.• Modified exclusion criteria• Modified contraception procedures• Moved basophil activation test from optional substudy to main study• Added: Details on emergency unblinding procedure, protocol deviations and adverse event reporting.
28 August 2018	Amendment 3 Main Changes: <ul style="list-style-type: none">• Removed basophil activation test as a study objective and endpoint.• Clarified subject eligibility for enrollment in ARC008• Modified dose adjustment guidelines• Removed requirement for a daily diary during 6-month GI AE safety follow-up• Provided instructions in the event of early study closure.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported