# 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 |

**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) | EMEA-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 AEIs, 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 |

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 |
| 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 | 132 | 43 | 175 |
| Age categorical<br>Units: Subjects | | | |
| Children (2-11 years) | 97 | 30 | 127 |
| Adolescents (12-17 years) | 35 | 13 | 48 |
| Gender categorical<br>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 |

End point description:

The pre-specified 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 % | 68.2 (59.5 to 76.0) | 9.3 (2.6 to 22.1) | | |

## Statistical analyses

| **Statistical analysis title** | Treatment difference at 600 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 | 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 |

| Dictionary used | |
|---|---|
| Dictionary name | MedDRA |
| Dictionary version | 19.1 |

| Reporting groups | |
|---|---|
| Reporting group title | AR101 |
| Reporting group description: | |
| A peanut-derived oral immunotherapy drug | |
| Reporting group title | Placebo |
| 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 | 46 / 132 (34.85%) | 19 / 43 (44.19%) | |
| occurrences (all) | 128 | 65 | |
| Dizziness | | | |
| subjects affected / exposed | 4 / 132 (3.03%) | 3 / 43 (6.98%) | |
| occurrences (all) | 4 | 3 | |
| Blood and lymphatic system disorders | | | |
| Lymphadenopathy | | | |
| subjects affected / exposed | 8 / 132 (6.06%) | 1 / 43 (2.33%) | |
| occurrences (all) | 10 | 1 | |
| Ear and labyrinth disorders | | | |
| Ear pain | | | |
| subjects affected / exposed | 14 / 132 (10.61%) | 0 / 43 (0.00%) | |
| occurrences (all) | 21 | 0 | |
| Motion sickness | | | |
| subjects affected / exposed | 4 / 132 (3.03%) | 3 / 43 (6.98%) | |
| occurrences (all) | 5 | 4 | |
| Eye disorders | | | |
| Eye pruritus | | | |
| subjects affected / exposed | 24 / 132 (18.18%) | 8 / 43 (18.60%) | |
| occurrences (all) | 37 | 12 | |
| Eye swelling | | | |
| subjects affected / exposed | 11 / 132 (8.33%) | 3 / 43 (6.98%) | |
| occurrences (all) | 18 | 7 | |
| Gastrointestinal disorders | | | |
| Abdominal pain | | | |
| subjects affected / exposed | 88 / 132 (66.67%) | 19 / 43 (44.19%) | |
| occurrences (all) | 835 | 126 | |
| Nausea | | | |
| subjects affected / exposed | 58 / 132 (43.94%) | 11 / 43 (25.58%) | |
| occurrences (all) | 437 | 31 | |
| Paraesthesia oral | | | |
| subjects affected / exposed | 52 / 132 (39.39%) | 9 / 43 (20.93%) | |
| occurrences (all) | 961 | 49 | |
| Vomiting | | | |
| subjects affected / exposed | 53 / 132 (40.15%) | 10 / 43 (23.26%) | |
| occurrences (all) | 120 | 17 | |

| | | | |
|---|---|---|---|
| 0ral 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:<br>• Revised inclusion criteria<br>• Optional substudy added as exploratory endpoint |
| 26 September 2017 | Amendment 2 Main Changes:<br>• Added end of study definition.<br>• Modified exclusion criteria<br>• Modified contraception procedures<br>• Moved basophil activation test from optional substudy to main study<br>• Added: Details on emergency unblinding procedure, protocol deviations and adverse event reporting. |
| 28 August 2018 | Amendment 3 Main Changes:<br>• Removed basophil activation test as a study objective and endpoint.<br>• Clarified subject eligibility for enrollment in ARC008<br>• Modified dose adjustment guidelines<br>• Removed requirement for a daily diary during 6-month GI AE safety follow-up<br>• 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