Clinical trial results:
A Multicenter, Open-Label, Longer-Term Study of AR101 Characterized Oral Desensitization Immunotherapy in Subjects Who Participated in a Prior AR101 Study

Summary

EudraCT number	2017-001334-26
Trial protocol	GB IE SE ES DE FR NL IT
Global end of trial date	27 April 2023

Results information

Result version number	v1
This version publication date	26 October 2024
First version publication date	26 October 2024

Trial information

Trial identification

Sponsor protocol code	ARC008

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03292484
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Aimmune Therapeutics, a Nestlé Health Science Company
Sponsor organisation address	1007 US Hwy 202/206, Bldg JR2, Suite E102 Bridgewater, New Jersey, United States, 08807
Public contact	Jay Patel , Aimmune Therapeutics, a Nestlé Health Science Company, jay.patel@uk.nestle.com
Scientific contact	Jay Patel , Aimmune Therapeutics, a Nestlé Health Science Company, jay.patel@uk.nestle.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
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	27 April 2023
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	27 April 2023
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To describe safety and tolerability during longer-term administration of AR101 and follow-up observation after the last dose of AR101.

Protection of trial subjects:

The study was conducted in conformance with the principles of the Declaration of Helsinki (2013) or with the laws and regulations of the country in which the research was conducted, whichever provided greater protection of the individual. In addition, the study was conducted in accordance with Good Clinical Practice (GCP) and International Council for Harmonisation (ICH) of Technical Requirements for Pharmaceuticals for Human Use guidelines, EU (European Union) Directive 2001/20/EC, EU Directive 2005/28/EC, EU Clinical Trials Regulation (CTR) 536/2014, local applicable legislation including but not limited to the United Kingdom (UK) SI 2004/1031 Medicines for Human Use (Clinical Trials) Regulations 2004 as amended, Council for International Organizations of Medical Sciences International Ethical Guidelines, and national and local regulations and directives as appropriate including the archiving of essential records. The study was conducted under a protocol reviewed and approved by an ethics committee and conducted by scientifically and medically qualified persons.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	02 November 2017
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Canada: 67
Country: Number of subjects enrolled	France: 18
Country: Number of subjects enrolled	Germany: 48
Country: Number of subjects enrolled	Ireland: 36
Country: Number of subjects enrolled	Italy: 10
Country: Number of subjects enrolled	Netherlands: 3
Country: Number of subjects enrolled	Spain: 31
Country: Number of subjects enrolled	Sweden: 10
Country: Number of subjects enrolled	United Kingdom: 96
Country: Number of subjects enrolled	United States: 592
Worldwide total number of subjects	911
EEA total number of subjects	156

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)	607
Adolescents (12-17 years)	274
Adults (18-64 years)	30
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This Phase 3, open-label study was conducted in participants who participated in a prior AR101 study at 89 investigational sites in 10 countries (Canada, France, Germany, Ireland, Italy, Netherlands, Spain, Sweden, United Kingdom, and the United States).

Pre-assignment

Screening details:

A total of 911 participants were enrolled in this study.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	AR101

Arm description:

Eligible participants who received AR101 in a prior AR101 study continued their dosing regimen (extended maintenance at 300 milligrams[mg] daily/nondaily dosing)[Treatment Pathway 4 for participants from study ARC005, or Treatment Pathway 1 for all other participants], or had up-dosing/repeat up-dosing to 300mg daily;initial and extended maintenance at 300mg daily[Treatment Pathway 2]. Eligible participants who received placebo in prior AR101 study received initial dose escalation(Day 1:0.5-3mg for participants from study ARC005[Treatment Pathway 5], 0.5-6mg for all other participants[Treatment Pathway 3]; Day 2:1 mg for participants from study ARC005, 3mg for all other participants), up-dosing(1-300 milligrams per day{mg/day} for participants from study ARC005 [Treatment Pathway 5]; 3-300mg/day for all other participants[Treatment Pathway 3]);initial and extended maintenance at 300mg daily.Participants received AR101 until discontinuation criteria was met (maximum exposure:4.8years).

Arm type	Experimental
Investigational medicinal product name	AR101
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, Modified-release granules
Routes of administration	Oral use

Dosage and administration details:

AR101 was administered as pull-apart capsules formulated to contain 0.5, 1, 10, 20, or 100 mg of peanut protein or as foil-laminate sachets containing 300 mg of peanut protein.

Number of subjects in period 1	AR101
Started	911
Safety Population	908
Completed	18
Not completed	893
Investigator decision (unrelated to AE)	13
Protocol Violation	2
Coronavirus Disease 2019	1

Unspecified	20
Withdrew consent (unrelated to adverse event [AE])	86
Sponsor decision	349
Lost to follow-up	7
Participants did not have Study Exit Forms	415

Baseline characteristics

Reporting groups	
Reporting group title	AR101

Reporting group description:

Eligible participants who received AR101 in a prior AR101 study continued their dosing regimen (extended maintenance at 300 milligrams[mg] daily/nondaily dosing)[Treatment Pathway 4 for participants from study ARC005, or Treatment Pathway 1 for all other participants], or had up-dosing/repeat up-dosing to 300mg daily;initial and extended maintenance at 300mg daily[Treatment Pathway 2]. Eligible participants who received placebo in prior AR101 study received initial dose escalation(Day 1:0.5-3mg for participants from study ARC005[Treatment Pathway 5], 0.5-6mg for all other participants[Treatment Pathway 3]; Day 2:1 mg for participants from study ARC005, 3mg for all other participants), up-dosing(1-300 milligrams per day{mg/day} for participants from study ARC005 [Treatment Pathway 5]; 3-300mg/day for all other participants[Treatment Pathway 3]);initial and extended maintenance at 300mg daily.Participants received AR101 until discontinuation criteria was met (maximum exposure:4.8years).

Reporting group values	AR101	Total	
Number of subjects	911	911	
Age categorical Units: Subjects			
In utero		0	
Preterm newborn infants (gestational age < 37 wks)		0	
Newborns (0-27 days)		0	
Infants and toddlers (28 days-23 months)		0	
Children (2-11 years)		0	
Adolescents (12-17 years)		0	
Adults (18-64 years)		0	
From 65-84 years		0	
85 years and over		0	
Age continuous Units: years			
arithmetic mean	9.8		
standard deviation	± 4.75	-	
Gender categorical Units: Subjects			
Female	359	359	
Male	552	552	
Ethnicity Units: Subjects			
Hispanic or Latino	38	38	
Not Hispanic or Latino	842	842	
Not collected	31	31	
Race Units: Subjects			
Asian	106	106	
Black or African American	18	18	
Native Hawaiian or Other Pacific Islander	3	3	
White	664	664	

Other	65	65	
Multiple Races Reported	53	53	
Not Collected	2	2	

End points

End points reporting groups

Reporting group title	AR101

Reporting group description:

Eligible participants who received AR101 in a prior AR101 study continued their dosing regimen (extended maintenance at 300 milligrams[mg] daily/nondaily dosing)[Treatment Pathway 4 for participants from study ARC005, or Treatment Pathway 1 for all other participants], or had up-dosing/repeat up-dosing to 300mg daily;initial and extended maintenance at 300mg daily[Treatment Pathway 2]. Eligible participants who received placebo in prior AR101 study received initial dose escalation(Day 1:0.5-3mg for participants from study ARC005[Treatment Pathway 5], 0.5-6mg for all other participants[Treatment Pathway 3]; Day 2:1 mg for participants from study ARC005, 3mg for all other participants), up-dosing(1-300 milligrams per day{mg/day} for participants from study ARC005 [Treatment Pathway 5]; 3-300mg/day for all other participants[Treatment Pathway 3]);initial and extended maintenance at 300mg daily.Participants received AR101 until discontinuation criteria was met (maximum exposure:4.8years).

Subject analysis set title	AR101
Subject analysis set type	Safety analysis

Subject analysis set description:

Eligible participants who received AR101 in a prior AR101 study continued their dosing regimen (extended maintenance at 300 mg daily/nondaily dosing) [Treatment Pathway 4 for participants from study ARC005, or Treatment Pathway 1 for all other participants], or had up-dosing/repeat up-dosing to 300 mg daily; initial and extended maintenance at 300 mg daily [Treatment Pathway 2]. Eligible participants who received placebo in a prior AR101 study received initial dose escalation (Day 1: 0.5-3 mg for participants from study ARC005 [Treatment Pathway 5], 0.5-6 mg for all other participants [Treatment Pathway 3]; Day 2: 1 mg for participants from study ARC005, 3 mg for all other participants), up-dosing (1-300 mg/day for participants from study ARC005 [Treatment Pathway 5]; 3-300 mg/day for all other participants [Treatment Pathway 3]); initial and extended maintenance at 300 mg daily. Participants received AR101 until discontinuation criteria was met (maximum exposure: 4.8 years).

Primary: Number of Participants With Treatment-emergent Adverse Events (TEAEs) and Treatment-emergent Serious Adverse Events (TESAEs)

End point title	Number of Participants With Treatment-emergent Adverse Events (TEAEs) and Treatment-emergent Serious Adverse Events (TESAEs)[1]

End point description:

An AE was any untoward medical occurrence in humans, whether or not considered related to the investigational product (IP), that occurred during the conduct of a clinical study. A SAE was any event that resulted in any of the following: death, life-threatening AE, inpatient hospitalization or prolongation of existing hospitalization, persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions, congenital abnormality or birth defect, or important medical event that did not result in one of the above outcomes, but jeopardized the health of the study participant or required medical or surgical intervention to prevent one of the outcomes listed above. TEAEs were defined as those AEs with onset after the first dose of AR101 in ARC008 and no more than 30 days after the last dose of study drug. The safety population consisted of all participants who received AR101 during ARC008.

End point type	Primary

End point timeframe:

From first dose of study drug through 30 days after last dose of study drug, up to 59 months

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: As the endpoint is descriptive in nature, no statistical analysis is provided.

End point values	AR101			
Subject group type	Subject analysis set			
Number of subjects analysed	908			
Units: participants				
TEAEs	866			
TESAEs	42			

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants With Premature Discontinuation of AR101 Dosing due to TEAEs

End point title	Number of Participants With Premature Discontinuation of AR101 Dosing due to TEAEs[2]

End point description:

An AE was any untoward medical occurrence in humans, whether or not considered related to the IP, that occurred during the conduct of a clinical study. TEAEs were defined as those AEs with onset after the first dose of AR101 in ARC008 and no more than 30 days after the last dose of study drug. The safety population consisted of all participants who received AR101 during ARC008.

End point type	Primary

End point timeframe:

From first dose of study drug through 30 days after last dose of study drug, up to 59 months

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: As the endpoint is descriptive in nature, no statistical analysis is provided.

End point values	AR101			
Subject group type	Subject analysis set			
Number of subjects analysed	908			
Units: participants	53			

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants With Premature Discontinuation of AR101 Dosing due to Chronic/Recurrent Gastrointestinal TEAEs

End point title	Number of Participants With Premature Discontinuation of AR101 Dosing due to Chronic/Recurrent Gastrointestinal TEAEs[3]

End point description:

An AE was any untoward medical occurrence in humans, whether or not considered related to the IP, that occurred during the conduct of a clinical study. TEAEs were defined as those AEs with onset after the first dose of AR101 in ARC008 and no more than 30 days after the last dose of study drug. Gastrointestinal (GI) AEs, typically chronic/recurrent GI AEs, that resulted in prolonged interruption of dosing are reported. The safety population consisted of all participants who received AR101 during ARC008.

End point type	Primary

End point timeframe:

From first dose of study drug through 30 days after last dose of study drug, up to 59 months

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: As the endpoint is descriptive in nature, no statistical analysis is provided.

End point values	AR101			
Subject group type	Subject analysis set			
Number of subjects analysed	908			
Units: participants	25			

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants With TEAEs That led to a Change in Treatment Regimen

End point title	Number of Participants With TEAEs That led to a Change in Treatment Regimen[4]

End point description:

An AE was any untoward medical occurrence in humans, whether or not considered related to the IP, that occurred during the conduct of a clinical study. TEAEs were defined as those AEs with onset after the first dose of AR101 in ARC008 and no more than 30 days after the last dose of study drug. Number of participants with TEAEs requiring dose interruption and dose reduction of study treatment are reported. The safety population consisted of all participants who received AR101 during ARC008.

End point type	Primary

End point timeframe:

From first dose of study drug through 30 days after last dose of study drug, up to 59 months

Notes:

[4] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: As the endpoint is descriptive in nature, no statistical analysis is provided.

End point values	AR101			
Subject group type	Subject analysis set			
Number of subjects analysed	908			
Units: participants				
TEAEs requiring dose interruption of treatment	669			
TEAEs requiring dose reduction of treatment	167			

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants With TEAEs That led to Early Withdrawal

End point title	Number of Participants With TEAEs That led to Early Withdrawal[5]

End point description:

An AE was any untoward medical occurrence in humans, whether or not considered related to the IP, that occurred during the conduct of a clinical study. TEAEs were defined as those AEs with onset after the first dose of AR101 in ARC008 and no more than 30 days after the last dose of study drug. The safety population consisted of all participants who received AR101 during ARC008.

End point type	Primary

End point timeframe:

From first dose of study drug through 30 days after last dose of study drug, up to 59 months

Notes:

[5] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: As the endpoint is descriptive in nature, no statistical analysis is provided.

End point values	AR101			
Subject group type	Subject analysis set			
Number of subjects analysed	908			
Units: participants	27			

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants Who Experienced a Treatment-emergent Anaphylactic Reaction

End point title	Number of Participants Who Experienced a Treatment-emergent Anaphylactic Reaction[6]

End point description:

Anaphylaxis was defined by a number of signs and symptoms that occurred alone or in combination within minutes up to a few hours after exposure to a provoking agent. Treatment-emergent anaphylactic reactions included anaphylactic reactions that occurred after first dose of AR101 in ARC008 through 30 days after last dose of study product but excluding anaphylactic reactions that occurred during or related to a food challenge. The safety population consisted of all participants who received AR101 during ARC008.

End point type	Primary

End point timeframe:

From first dose of study drug through 30 days after last dose of study drug, up to 59 months

Notes:

[6] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: As the endpoint is descriptive in nature, no statistical analysis is provided.

End point values	AR101			
Subject group type	Subject analysis set			
Number of subjects analysed	908			
Units: participants	192			

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants With use of Epinephrine as a Rescue Medication

End point title	Number of Participants With use of Epinephrine as a Rescue Medication[7]

End point description:

Rescue medications were any medication used to treat individual acute allergic reactions during ARC008 and were according to recognized standards of care for allergy practice. The safety population consisted of all participants who received AR101 during ARC008.

End point type	Primary

End point timeframe:

From first dose of study drug through 30 days after last dose of study drug, up to 59 months

Notes:

[7] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: As the endpoint is descriptive in nature, no statistical analysis is provided.

End point values	AR101			
Subject group type	Subject analysis set			
Number of subjects analysed	908			
Units: participants	234			

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants Who Experienced Accidental or Non-accidental Food Allergy Episodes

End point title	Number of Participants Who Experienced Accidental or Non-accidental Food Allergy Episodes[8]

End point description:

An accidental food allergen exposure was any known or suspected exposure to a food to which the participant was allergic, including peanut, whether or not it resulted in an AE. A non-accidental food allergen exposure was an intentional exposure to a food to which the participant was allergic, including peanut, whether or not it resulted in an AE. Treatment-emergent food allergy episodes included food allergy episodes that occurred after first dose of AR101 in ARC008 through 30 days after last dose of study product but excluding food allergy episodes that occurred during or related to a food challenge. The safety population consisted of all participants who received AR101 during ARC008.

End point type	Primary

End point timeframe:

From first dose of study drug through 30 days after last dose of study drug, up to 59 months

Notes:

[8] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: As the endpoint is descriptive in nature, no statistical analysis is provided.

End point values	AR101			
Subject group type	Subject analysis set			
Number of subjects analysed	908			
Units: participants				
Accidental Food Allergy Episodes	208			
Non-accidental Food Allergy Episodes	35			

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants With TEAEs Following Accidental or Non-accidental Exposure to Peanut and Other Allergenic Foods

End point title	Number of Participants With TEAEs Following Accidental or Non-accidental Exposure to Peanut and Other Allergenic Foods[9]

End point description:

An accidental food allergen exposure was any known or suspected exposure to a food to which the participant was allergic, including peanut, whether or not it resulted in an AE. A non-accidental food allergen exposure was an intentional exposure to a food to which the participant was allergic, including peanut, whether or not it resulted in an AE. An AE was any untoward medical occurrence in humans, whether or not considered related to the IP, that occurred during the conduct of a clinical study. Treatment-emergent food allergy episodes included food allergy episodes that occurred after first dose of AR101 in ARC008 through 30 days after last dose of study product but excluding food allergy episodes that occurred during or related to a food challenge. The safety population consisted of all participants who received AR101 during ARC008.

End point type	Primary

End point timeframe:

From first dose of study drug through 30 days after last dose of study drug, up to 59 months

Notes:

[9] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: As the endpoint is descriptive in nature, no statistical analysis is provided.

End point values	AR101			
Subject group type	Subject analysis set			
Number of subjects analysed	908			
Units: participants	227			

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants With Eosinophilic Esophagitis (EoE)

End point title	Number of Participants With Eosinophilic Esophagitis (EoE)[10]

End point description:

EoE was diagnosed by biopsy/endoscopy. The safety population consisted of all participants who received AR101 during ARC008.

End point type	Primary

End point timeframe:

From first dose of study drug through 30 days after last dose of study drug, up to 59 months

Notes:

[10] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: As the endpoint is descriptive in nature, no statistical analysis is provided.

End point values	AR101			
Subject group type	Subject analysis set			
Number of subjects analysed	908			
Units: participants	7			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Tolerating Each Challenge Dose in the Open-label Food Challenge (OLFC) and the Double-blind, Placebo-Controlled Food Challenge (DBPCFC)

End point title	Percentage of Participants Tolerating Each Challenge Dose in the Open-label Food Challenge (OLFC) and the Double-blind, Placebo-Controlled Food Challenge (DBPCFC)

End point description:

During the OLFC, single doses (300, 600, 1000, and 2000 mg) of peanut protein were conditionally tested using a food challenge mixture administered sequentially at 20- to 30-minute intervals. During the DBPCFC, single doses (3, 10, 30, 100, 300, 600, 1000, and 2000 mg) of peanut protein and placebo were conditionally tested using a food challenge mixture administered sequentially at 20- to 30-minute intervals up to a single highest challenge dose of 2000 mg. The safety population consisted of all participants who received AR101 during ARC008. Only those participants who had an OLFC or a DBPCFC are reported. Here, n=number of participants with data collected for each specified category

End point type	Secondary

End point timeframe:

OLFC: At Month 12 and yearly thereafter, up to 58 months; DBPCFC: End of treatment (Month 58)

End point values	AR101			
Subject group type	Subject analysis set			
Number of subjects analysed	517			
Units: percentage of participants				
number (confidence interval 95%)				
OLFC: Tolerated at least 300 mg (n=517)	98.6 (97.2 to 99.5)			
OLFC: Tolerated at least 600 mg (n=517)	94.2 (91.8 to 96.1)			

OLFC: Tolerated at least 1000 mg (n=517)	78.7 (74.9 to 82.2)			
OLFC: Tolerated at least 2000 mg (n=517)	55.9 (51.5 to 60.2)			
DBPCFC: Tolerated at least 3 mg (n=211)	100.0 (98.3 to 100.0)			
DBPCFC: Tolerated at least 10 mg (n=211)	100.0 (98.3 to 100.0)			
DBPCFC: Tolerated at least 30 mg (n=211)	99.5 (97.4 to 100.0)			
DBPCFC: Tolerated at least 100 mg (n=211)	99.1 (96.6 to 99.9)			
DBPCFC: Tolerated at least 300 mg (n=211)	94.8 (90.9 to 97.4)			
DBPCFC: Tolerated at least 600 mg (n=211)	88.2 (83.0 to 92.2)			
DBPCFC: Tolerated at least 1000 mg (n=211)	75.8 (69.5 to 81.4)			
DBPCFC: Tolerated at least 2000 mg (n=211)	60.2 (53.2 to 66.8)			

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum Tolerated Challenge Dose at Each Food Challenge

End point title	Maximum Tolerated Challenge Dose at Each Food Challenge

End point description:

The maximum tolerated challenge dose for a food challenge was defined as the maximum single dose of peanut protein resulting in no more than mild symptoms and assessed by the investigator to have been tolerated (i.e., the participant did not experience any dose-limiting symptoms). During the OLFC, single doses (300, 600, 1000, and 2000 mg) of peanut protein were conditionally tested using a food challenge mixture administered sequentially at 20- to 30-minute intervals. During the DBPCFC, single doses (3, 10, 30, 100, 300, 600, 1000, and 2000 mg) of peanut protein and placebo were conditionally tested using a food challenge mixture administered sequentially at 20- to 30-minute intervals up to a single highest challenge dose of 2000 mg. The safety population consisted of all participants who received AR101 during ARC008. Only those participants who had an OLFC or a DBPCFC are reported. Here, n=number of participants with data collected for each specified category.

End point type	Secondary

End point timeframe:

OLFC: At Month 12 and yearly thereafter, up to 58 months; DBPCFC: End of treatment (Month 58)

End point values	AR101			
Subject group type	Subject analysis set			
Number of subjects analysed	517			
Units: mg				
number (not applicable)				
OLFC (n=517)	2000			
DBPCFC (n=211)	2000			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With use of Epinephrine as a Rescue Medication During the Food Challenges

End point title	Number of Participants With use of Epinephrine as a Rescue Medication During the Food Challenges

End point description:

Rescue medications were any medication used to treat individual acute allergic reactions during ARC008 and were according to recognized standards of care for allergy practice. During the OLFC, single doses (300, 600, 1000, and 2000 mg) of peanut protein were conditionally tested using a food challenge mixture administered sequentially at 20- to 30-minute intervals. During the DBPCFC, single doses (3, 10, 30, 100, 300, 600, 1000, and 2000 mg) of peanut protein and placebo were conditionally tested using a food challenge mixture administered sequentially at 20- to 30-minute intervals up to a single highest challenge dose of 2000 mg. The safety population consisted of all participants who received AR101 during ARC008. Only those participants who had an OLFC or a DBPCFC are reported. Here, n=number of participants with data collected for each specified category.

End point type	Secondary

End point timeframe:

OLFC: At Month 12 and yearly thereafter, up to 58 months; DBPCFC: End of treatment (Month 58)

End point values	AR101			
Subject group type	Subject analysis set			
Number of subjects analysed	517			
Units: participants				
OLFC (n=517)	110			
DBPCFC (n=211)	35			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From first dose of study drug through 30 days after last dose of study drug, up to 59 months

Adverse event reporting additional description:

The safety population consisted of all participants who received AR101 during ARC008.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	26.0

Reporting groups

Reporting group title	AR101

Reporting group description:

Eligible participants who received AR101 in a prior AR101 study continued their dosing regimen (extended maintenance at 300 mg daily/nondaily dosing) [Treatment Pathway 4 for participants from study ARC005, or Treatment Pathway 1 for all other participants], or had up-dosing/repeat up-dosing to 300 mg daily; initial and extended maintenance at 300 mg daily [Treatment Pathway 2]. Eligible participants who received placebo in a prior AR101 study received initial dose escalation (Day 1: 0.5-3 mg for participants from study ARC005 [Treatment Pathway 5], 0.5-6 mg for all other participants [Treatment Pathway 3]; Day 2: 1 mg for participants from study ARC005, 3 mg for all other participants), up-dosing (1-300 mg/day for participants from study ARC005 [Treatment Pathway 5]; 3-300 mg/day for all other participants [Treatment Pathway 3]); initial and extended maintenance at 300 mg daily. Participants received AR101 until discontinuation criteria was met (maximum exposure: 4.8 years).

Serious adverse events	AR101		
Total subjects affected by serious adverse events			
subjects affected / exposed	42 / 908 (4.63%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Injury, poisoning and procedural complications			
Concussion			
subjects affected / exposed	2 / 908 (0.22%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Wrist fracture			
subjects affected / exposed	1 / 908 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Pyrexia			

subjects affected / exposed	1 / 908 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Immune system disorders			
Anaphylactic reaction			
subjects affected / exposed	8 / 908 (0.88%)		
occurrences causally related to treatment / all	4 / 8		
deaths causally related to treatment / all	0 / 0		
Ear and labyrinth disorders			
Vestibular disorder			
subjects affected / exposed	1 / 908 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	2 / 908 (0.22%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Coeliac disease			
subjects affected / exposed	1 / 908 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Constipation			
subjects affected / exposed	1 / 908 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Oral disorder			
subjects affected / exposed	1 / 908 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Asthma			

subjects affected / exposed	4 / 908 (0.44%)			
occurrences causally related to treatment / all	1 / 4			
deaths causally related to treatment / all	0 / 0			
Asthmatic crisis				
subjects affected / exposed	1 / 908 (0.11%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Atelectasis				
subjects affected / exposed	1 / 908 (0.11%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Dyspnoea				
subjects affected / exposed	1 / 908 (0.11%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumothorax				
subjects affected / exposed	1 / 908 (0.11%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Wheezing				
subjects affected / exposed	1 / 908 (0.11%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Skin and subcutaneous tissue disorders				
Angioedema				
subjects affected / exposed	1 / 908 (0.11%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Renal and urinary disorders				
Urinary retention				
subjects affected / exposed	1 / 908 (0.11%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Infections and infestations				

Appendicitis			
subjects affected / exposed	8 / 908 (0.88%)		
occurrences causally related to treatment / all	0 / 8		
deaths causally related to treatment / all	0 / 0		
Croup infectious			
subjects affected / exposed	2 / 908 (0.22%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Enterovirus infection			
subjects affected / exposed	1 / 908 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastroenteritis			
subjects affected / exposed	1 / 908 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastroenteritis viral			
subjects affected / exposed	1 / 908 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Influenza			
subjects affected / exposed	1 / 908 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Meningitis			
subjects affected / exposed	1 / 908 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Meningitis viral			
subjects affected / exposed	1 / 908 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumonia			

subjects affected / exposed	1 / 908 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumonia mycoplasmal			
subjects affected / exposed	1 / 908 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Rhinovirus infection			
subjects affected / exposed	1 / 908 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Salmonella bacteraemia			
subjects affected / exposed	1 / 908 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Sinusitis			
subjects affected / exposed	1 / 908 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Viral infection			
subjects affected / exposed	1 / 908 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	1 / 908 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Type 1 diabetes mellitus			
subjects affected / exposed	1 / 908 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	AR101		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	865 / 908 (95.26%)		
Nervous system disorders			
Headache			
subjects affected / exposed	240 / 908 (26.43%)		
occurrences (all)	816		
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	293 / 908 (32.27%)		
occurrences (all)	597		
Illness			
subjects affected / exposed	61 / 908 (6.72%)		
occurrences (all)	118		
Immune system disorders			
Anaphylactic reaction			
subjects affected / exposed	187 / 908 (20.59%)		
occurrences (all)	334		
Seasonal allergy			
subjects affected / exposed	50 / 908 (5.51%)		
occurrences (all)	87		
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	47 / 908 (5.18%)		
occurrences (all)	65		
Eye disorders			
Eye pruritus			
subjects affected / exposed	83 / 908 (9.14%)		
occurrences (all)	163		
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	293 / 908 (32.27%)		
occurrences (all)	769		
Abdominal pain			

subjects affected / exposed	271 / 908 (29.85%)		
occurrences (all)	2212		
Nausea			
subjects affected / exposed	183 / 908 (20.15%)		
occurrences (all)	1122		
Abdominal pain upper			
subjects affected / exposed	173 / 908 (19.05%)		
occurrences (all)	684		
Abdominal discomfort			
subjects affected / exposed	166 / 908 (18.28%)		
occurrences (all)	1028		
Diarrhoea			
subjects affected / exposed	127 / 908 (13.99%)		
occurrences (all)	272		
Oral pruritus			
subjects affected / exposed	88 / 908 (9.69%)		
occurrences (all)	739		
Lip swelling			
subjects affected / exposed	68 / 908 (7.49%)		
occurrences (all)	158		
Paraesthesia oral			
subjects affected / exposed	59 / 908 (6.50%)		
occurrences (all)	1215		
Lip pruritus			
subjects affected / exposed	53 / 908 (5.84%)		
occurrences (all)	253		
Dyspepsia			
subjects affected / exposed	51 / 908 (5.62%)		
occurrences (all)	173		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	302 / 908 (33.26%)		
occurrences (all)	949		
Throat irritation			

subjects affected / exposed	169 / 908 (18.61%)		
occurrences (all)	2368		
Oropharyngeal pain			
subjects affected / exposed	165 / 908 (18.17%)		
occurrences (all)	363		
Nasal congestion			
subjects affected / exposed	145 / 908 (15.97%)		
occurrences (all)	317		
Sneezing			
subjects affected / exposed	118 / 908 (13.00%)		
occurrences (all)	413		
Rhinorrhoea			
subjects affected / exposed	114 / 908 (12.56%)		
occurrences (all)	272		
Wheezing			
subjects affected / exposed	107 / 908 (11.78%)		
occurrences (all)	287		
Asthma			
subjects affected / exposed	85 / 908 (9.36%)		
occurrences (all)	160		
Oropharyngeal discomfort			
subjects affected / exposed	85 / 908 (9.36%)		
occurrences (all)	466		
Rhinitis allergic			
subjects affected / exposed	60 / 908 (6.61%)		
occurrences (all)	105		
Dyspnoea			
subjects affected / exposed	59 / 908 (6.50%)		
occurrences (all)	131		
Throat tightness			
subjects affected / exposed	50 / 908 (5.51%)		
occurrences (all)	71		
Skin and subcutaneous tissue disorders			
Urticaria			
subjects affected / exposed	251 / 908 (27.64%)		
occurrences (all)	862		

Pruritus			
subjects affected / exposed	191 / 908 (21.04%)		
occurrences (all)	827		
Rash			
subjects affected / exposed	121 / 908 (13.33%)		
occurrences (all)	182		
Eczema			
subjects affected / exposed	74 / 908 (8.15%)		
occurrences (all)	143		
Erythema			
subjects affected / exposed	65 / 908 (7.16%)		
occurrences (all)	125		
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	221 / 908 (24.34%)		
occurrences (all)	474		
Upper respiratory tract infection			
subjects affected / exposed	213 / 908 (23.46%)		
occurrences (all)	421		
Viral infection			
subjects affected / exposed	143 / 908 (15.75%)		
occurrences (all)	250		
Influenza			
subjects affected / exposed	108 / 908 (11.89%)		
occurrences (all)	134		
COVID-19			
subjects affected / exposed	102 / 908 (11.23%)		
occurrences (all)	114		
Gastroenteritis viral			
subjects affected / exposed	90 / 908 (9.91%)		
occurrences (all)	117		
Gastroenteritis			
subjects affected / exposed	88 / 908 (9.69%)		
occurrences (all)	118		
Rhinitis			

subjects affected / exposed	76 / 908 (8.37%)		
occurrences (all)	171		
Conjunctivitis			
subjects affected / exposed	54 / 908 (5.95%)		
occurrences (all)	79		
Pharyngitis streptococcal			
subjects affected / exposed	54 / 908 (5.95%)		
occurrences (all)	69		
Ear infection			
subjects affected / exposed	50 / 908 (5.51%)		
occurrences (all)	56		
Sinusitis			
subjects affected / exposed	47 / 908 (5.18%)		
occurrences (all)	60		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
19 December 2017	The primary purpose of this amendment was to modify the eligibility criteria to ensure that appropriate participants were enrolled in this follow-on study, remove changes in basophil activation as an objective and endpoint of the study, clarify contraceptive methods, clarify the study duration, and remove the requirement for medical monitor confirmation of participant eligibility.
11 May 2018	The primary purpose of this amendment was to modify exclusion criterion 2 to allow AR101 treated participants who did not successfully consume at least the 300 mg single dose of peanut protein at the exit DBPCFC of an originating study that required a food challenge to enroll in study ARC008, if specified in the originating study. This amendment also clarified additional participants from originating study ARC004 who might be eligible to receive daily dosing with AR101 in treatment pathway 2 of ARC008.
24 July 2018	The primary purpose of this amendment was to accommodate participants who did not complete their AR101 dosing regimen in an eligible originating study. Allowed one additional dosing kit to be dispensed in exceptional circumstances to provide flexibility for participants with scheduling issues who required continued dosing. Removed the requirement for repeat up-dosing to be completed within 26 weeks in treatment pathway 2 to provide flexibility and allowed more time for tolerability so participants could continue treatment. Allowed safety follow-up to continue for participants who discontinued early due to AEs from an eligible originating study.
01 November 2019	The primary purpose of this amendment was to add 2 new treatment pathways (Treatment Pathways 4 and 5) for eligible participants from prior study ARC005 to begin or continue treatment with AR101. This amendment also removed the optional real world peanut challenge, which was introduced to inform participants of their potential risk of allergic reaction from unintended ingestion of peanut-containing foods. Extended the study duration to allow assessment of long-term safety of AR101. Removed the daily diary from treatment pathways 1, 2, and 3 and from safety follow-up after early discontinuation to reduce burden for these participants who already have at least 9 months experience taking AR101. Consolidated the procedures for the end of the study. Added or removed telephone calls or expands the window for telephone calls after study site visits for safety follow-up, feasibility, or participant convenience, as appropriate. Added guidance for safety follow-up for participants diagnosed with EoE. Added an exclusion criterion for participants currently committed to an institution by virtue of an order issued by judicial or administrative authorities per some local requirements. Added total immunoglobulin G4 (IgG4) and IgE to immunology assessments. Added an exploratory objective and endpoint to evaluate changes in asthma or atopic dermatitis in participants from prior study ARC005.
28 May 2020	The primary purpose of this amendment was to provide guidance on changes to study conduct during a pandemic, epidemic, or other emergency not related to the study, when restrictions issued at the country, state, regional, and/or local level prevent the conduct of study site visits and access to study product for an extended period.

22 December 2020	The primary purpose of this amendment was to modify the study design to demonstrate a sustained clinical effect after 5 years total of AR101 treatment including all prior studies, and a 1-year observation period after stopping AR101 treatment per regulatory authority request. The study objectives, endpoints, duration, procedures, and schedules of events were updated in accordance with the study design changes. Removed the optional OLFC at the end of treatment as a DBPCFC was required per study design changes. Added guidance to assess the benefit-risk of continued AR101 treatment when a participant had several AR101-related systemic allergic reactions during maintenance treatment for safety reasons. Reduced time points for Asthma Control Test/Childhood Asthma Control Test, Total Nasal Symptom Score, and Test for Respiratory and Asthma Control in Kids during extended maintenance in all treatment pathways to reduce the burden for participants. Removed the Food Allergy Quality of Life – Parental Burden questionnaire from treatment pathways 1 and 2, as it was not administered in prior AR101 studies and changes from baseline cannot be assessed. Added a window for telephone calls after initial dose-escalation day 2, up-dosing visits, and initial maintenance visits in treatment pathway 5 for feasibility. Expanded the window for telephone call after the OLFC from the next day to within 2 days for feasibility.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported