Clinical trial results:
An Open-label Study to Evaluate the Pharmacokinetics and Pharmacodynamics and Long-term Safety of Benralizumab Administered Subcutaneously in Children with Severe Eosinophilic Asthma

Summary

EudraCT number	2019-004638-40
Trial protocol	Outside EU/EEA
Global end of trial date	12 September 2022

Results information

Result version number	v1 (current)
This version publication date	28 March 2023
First version publication date	28 March 2023

Trial information

Trial identification

Sponsor protocol code	D3250C00025

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04305405
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	AstraZeneca
Sponsor organisation address	Karlebyhusentren, B674 Astraallen, Södertälje, Sweden, 151 85
Public contact	Global Clinical Lead, AstraZeneca, +1 877-240-9479, information.center@astrazeneca.com
Scientific contact	Global Clinical Lead, AstraZeneca, +1 877-240-9479, information.center@astrazeneca.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-001214-PIP01-11
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?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	12 September 2022
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	12 September 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the pharmacokinetics (PK) of benralizumab administered subcutaneously (SC) in children from 6 to 11 years of age with severe eosinophilic asthma.

Protection of trial subjects:

This study was performed in accordance with the ethical principles that have their origin in the Declaration of Helsinki and that are consistent with International Council for Harmonisation/Good Clinical Practice, applicable regulatory requirements, and the AstraZeneca policy on Bioethics.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	21 November 2019
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United States: 19
Country: Number of subjects enrolled	Japan: 11
Worldwide total number of subjects	30
EEA total number of subjects	0

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	28
Adolescents (12-17 years)	2
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This Phase III, open-label, parallel group study was conducted in pediatric participants with severe eosinophilic asthma at 17 investigational sites.

Pre-assignment

Screening details:

The study consisted of a screening period (up to 4 weeks), treatment period [2 parts; Part A (16 weeks) followed by Part B (32 weeks)], and a safety follow-up visit at Week 52. A total of 30 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

Are arms mutually exclusive?	Yes
Arm title	Benralizumab Dose 1, Aged 6-14 Years

Arm description:

All participants with body weight <35 kilograms (kg) at screening received benralizumab Dose 1 subcutaneous (SC) injection once daily on Day 0 and at Weeks 4, 8, and 16 in Part A, followed by benralizumab Dose 1 at Weeks 24, 32, and 40 in Part B.

Arm type	Experimental
Investigational medicinal product name	Benralizumab
Investigational medicinal product code	
Other name	MEDI-563
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Benralizumab was administered as a sc injection in either upper arm, thighs, or the abdomen in rotation.

Arm title	Benralizumab Dose 2, Aged 6-14 Years

Arm description:

All participants with body weight >=35 kg or aged 12-14 years (irrespective of body weight) at screening received benralizumab Dose 2 SC injection once daily on Day 0 and at Weeks 4, 8, and 16 in Part A, followed by benralizumab Dose 2 at Weeks 24, 32, and 40 in Part B.

Arm type	Experimental
Investigational medicinal product name	Benralizumab
Investigational medicinal product code	
Other name	MEDI-563
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Benralizumab was administered as a sc injection in either upper arm, thighs, or the abdomen in rotation.

Number of subjects in period 1	Benralizumab Dose 1, Aged 6-14 Years	Benralizumab Dose 2, Aged 6-14 Years
Started	15	15
Completed	15	14
Not completed	0	1
Withdrawal by parent/guardian	-	1

Baseline characteristics

Reporting groups	
Reporting group title	Benralizumab Dose 1, Aged 6-14 Years
Reporting group description:	
All participants with body weight <35 kilograms (kg) at screening received benralizumab Dose 1 subcutaneous (SC) injection once daily on Day 0 and at Weeks 4, 8, and 16 in Part A, followed by benralizumab Dose 1 at Weeks 24, 32, and 40 in Part B.	
Reporting group title	Benralizumab Dose 2, Aged 6-14 Years
Reporting group description:	
All participants with body weight >=35 kg or aged 12-14 years (irrespective of body weight) at screening received benralizumab Dose 2 SC injection once daily on Day 0 and at Weeks 4, 8, and 16 in Part A, followed by benralizumab Dose 2 at Weeks 24, 32, and 40 in Part B.	

Reporting group values	Benralizumab Dose 1, Aged 6-14 Years	Benralizumab Dose 2, Aged 6-14 Years	Total
Number of subjects	15	15	30
Age categorical Units: Subjects			
Age Continuous Units: years			
arithmetic mean	8.3	9.8	
standard deviation	± 2.02	± 1.93	-
Sex: Female, Male Units: participants			
Female	4	7	11
Male	11	8	19
Race/Ethnicity, Customized Units: Subjects			
White	4	4	8
Black or African American	3	5	8
Asian	8	3	11
American Indian or Alaska Native	0	0	0
Native Hawaiian or other Pacific Islander	0	0	0
Other	0	3	3
Race/Ethnicity, Customized Units: Subjects			
Hispanic or Latino	1	5	6
Not Hispanic or Latino	14	10	24

End points

End points reporting groups

Reporting group title	Benralizumab Dose 1, Aged 6-14 Years

Reporting group description:

All participants with body weight <35 kilograms (kg) at screening received benralizumab Dose 1 subcutaneous (SC) injection once daily on Day 0 and at Weeks 4, 8, and 16 in Part A, followed by benralizumab Dose 1 at Weeks 24, 32, and 40 in Part B.

Reporting group title	Benralizumab Dose 2, Aged 6-14 Years

Reporting group description:

All participants with body weight >=35 kg or aged 12-14 years (irrespective of body weight) at screening received benralizumab Dose 2 SC injection once daily on Day 0 and at Weeks 4, 8, and 16 in Part A, followed by benralizumab Dose 2 at Weeks 24, 32, and 40 in Part B.

Subject analysis set title	Benralizumab Dose 1, Aged 6-11 Years
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants with body weight <35 kg at screening received benralizumab Dose 1 SC injection once daily on Day 0 and at Weeks 4, 8, and 16 in Part A, followed by benralizumab Dose 1 at Weeks 24, 32, and 40 in Part B.

Subject analysis set title	Benralizumab Dose 2, Aged 6-11 Years
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants with body weight >=35 kg at screening received benralizumab Dose 2 SC injection once daily on Day 0 and at Weeks 4, 8, and 16 in Part A, followed by benralizumab Dose 2 at Weeks 24, 32, and 40 in Part B.

Subject analysis set title	Benralizumab Dose 1, Aged 6-11 Years
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants with body weight <35 kg at screening received benralizumab Dose 1 SC injection once daily on Day 0 and at Weeks 4, 8, and 16 in Part A, followed by benralizumab Dose 1 at Weeks 24, 32, and 40 in Part B.

Subject analysis set title	Benralizumab Dose 2, Aged 6-11 Years
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants with body weight >=35 kg at screening received benralizumab Dose 2 SC injection once daily on Day 0 and at Weeks 4, 8, and 16 in Part A, followed by benralizumab Dose 2 at Weeks 24, 32, and 40 in Part B.

Subject analysis set title	All participants
Subject analysis set type	Full analysis

Subject analysis set description:

All participants aged 6-14 years enrolled in this study irrespective of study treatment received were included in this arm.

Primary: Clearance of Benralizumab

End point title	Clearance of Benralizumab[1]

End point description:

Blood samples were collected to determine the clearance of benralizumab. This was an empirical Bayesian estimate (EBE) derived posthoc using population PK analysis. The PK analysis set consisted of all participants who received at least 1 dose of benralizumab for whom PK blood samples were not assumed to be affected by factors such as protocol violations and who had at least 1 post dose quantifiable serum PK observation.

End point type	Primary

End point timeframe:

Pre-dose on Days 0, 28, 56, 112, 168 and post-dose on Days 1, 7, 14, 84, 336; and at early discontinuation or withdrawal visit

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: No additional statistical analysis was pre-specified for this endpoint.

End point values	All participants			
Subject group type	Subject analysis set			
Number of subjects analysed	30			
Units: liter (L) per day				
arithmetic mean (standard deviation)	0.156 (± 0.0598)			

Statistical analyses

No statistical analyses for this end point

Primary: Area Under the Serum Concentration-Time Curve From Time Zero to Day 28 (AUC0-28) of Benralizumab

End point title	Area Under the Serum Concentration-Time Curve From Time Zero to Day 28 (AUC0-28) of Benralizumab[2]

End point description:

Blood samples were collected to determine the AUC0-28 of benralizumab and it was calculated by linear up/log down trapezoidal summation. The PK parameters were estimated using non-compartmental analysis method. The Non-compartmental analysis (NCA) set consisted of all participants who received the first dose of benralizumab for whom PK blood samples were not assumed to be affected by factors such as protocol violations and who had at least 3 quantifiable serum PK observations post-dose on Days 1, 7, 14, and 28. Only those participants with data available were analyzed.

End point type	Primary

End point timeframe:

Pre-dose on Days 0, 28 and post-dose on Days 1, 7, 14

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: No additional statistical analysis was pre-specified for this endpoint.

End point values	Benralizumab Dose 1, Aged 6-14 Years	Benralizumab Dose 2, Aged 6-14 Years	Benralizumab Dose 1, Aged 6-11 Years	Benralizumab Dose 2, Aged 6-11 Years
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	10	11	10	10
Units: nanogram*day per milliliter (ng*day/mL)				
geometric mean (geometric coefficient of variation)	36918.01 (± 24.61)	73670.51 (± 38.86)	36918.01 (± 24.61)	75593.37 (± 39.96)

Statistical analyses

No statistical analyses for this end point

Primary: Maximum Observed Serum Concentration (Cmax) of Benralizumab

End point title	Maximum Observed Serum Concentration (Cmax) of

	Benralizumab[3]

End point description:

Blood samples were collected to determine Cmax of benralizumab and it was directly calculated from the individual concentration-time curve. The PK parameters were estimated using non-compartmental analysis method. The NCA set consisted of all participants who received the first dose of benralizumab for whom PK blood samples were not assumed to be affected by factors such as protocol violations and who had at least 3 quantifiable serum PK observations post-dose on Days 1, 7, 14, and 28.

End point type	Primary

End point timeframe:

Pre-dose on Days 0, 28, 56, 112, 168 and post-dose on Days 1, 7, 14, 84, 336; and at early discontinuation or withdrawal visit

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: No additional statistical analysis was pre-specified for this endpoint.

End point values	Benralizumab Dose 1, Aged 6-14 Years	Benralizumab Dose 2, Aged 6-14 Years	Benralizumab Dose 1, Aged 6-11 Years	Benralizumab Dose 2, Aged 6-11 Years
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	15	15	15	13
Units: ng/mL				
geometric mean (geometric coefficient of variation)	1901.18 (± 28.42)	3090.85 (± 43.66)	1901.18 (± 28.42)	3118.69 (± 47.35)

Statistical analyses

No statistical analyses for this end point

Primary: Time to Achieve Maximum Observed Serum Concentration (tmax) of Benralizumab

End point title	Time to Achieve Maximum Observed Serum Concentration (tmax) of Benralizumab[4]

End point description:

Blood samples were collected to determine the tmax of benralizumab and it was directly calculated from the individual concentration-time curve. The PK parameters were estimated using non-compartmental analysis method. The NCA set consisted of all participants who received the first dose of benralizumab for whom PK blood samples were not assumed to be affected by factors such as protocol violations and who had at least 3 quantifiable serum PK observations post-dose on Days 1, 7, 14, and 28.

End point type	Primary

End point timeframe:

Pre-dose on Days 0, 28, 56, 112, 168 and post-dose on Days 1, 7, 14, 84, 336; and at early discontinuation or withdrawal visit

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: No additional statistical analysis was pre-specified for this endpoint.

End point values	Benralizumab Dose 1, Aged 6-14 Years	Benralizumab Dose 2, Aged 6-14 Years	Benralizumab Dose 1, Aged 6-11 Years	Benralizumab Dose 2, Aged 6-11 Years
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	15	15	15	13
Units: day				
median (full range (min-max))	6.91 (0.93 to 14.95)	7.94 (1.10 to 14.01)	6.91 (0.93 to 14.95)	7.26 (1.10 to 14.01)

Statistical analyses

No statistical analyses for this end point

Primary: Terminal Phase Elimination Half-Life (t1/2) of Benralizumab

End point title	Terminal Phase Elimination Half-Life (t1/2) of Benralizumab[5]

End point description:

Blood samples were collected to determine the t1/2 of benralizumab and it was calculated as natural logarithm of 2 [ln(2)]/terminal rate constant (λZ). This was an EBE derived posthoc using population PK analysis. The PK analysis set consisted of all participants who received at least 1 dose of benralizumab for whom PK blood samples were not assumed to be affected by factors such as protocol violations and who had at least 1 post dose quantifiable serum PK observation.

End point type	Primary

End point timeframe:

Pre-dose on Days 0, 28, 56, 112, 168 and post-dose on Days 1, 7, 14, 84, 336; and at early discontinuation or withdrawal visit

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: No additional statistical analysis was pre-specified for this endpoint.

End point values	All participants			
Subject group type	Subject analysis set			
Number of subjects analysed	30			
Units: day				
median (full range (min-max))	14.4 (6.94 to 23.4)			

Statistical analyses

No statistical analyses for this end point

Primary: Trough Concentration of Benralizumab at Week 16 (Ctrough16)

End point title	Trough Concentration of Benralizumab at Week 16

End point description:

Blood samples were collected to determine the trough concentration at Week 16, the lowest concentration reached by benralizumab before the next dose was administered. The PK parameters were estimated using non-compartmental analysis method. The NCA set consisted of all participants who received the first dose of benralizumab for whom PK blood samples were not assumed to be affected by factors such as protocol violations and who had at least 3 quantifiable serum PK observations post-dose on Days 1, 7, 14, and 28. Only those participants with data available were analyzed.

End point type	Primary

End point timeframe:

Pre-dose on Day 112

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: No additional statistical analysis was pre-specified for this endpoint.

End point values	Benralizumab Dose 1, Aged 6-14 Years	Benralizumab Dose 2, Aged 6-14 Years	Benralizumab Dose 1, Aged 6-11 Years	Benralizumab Dose 2, Aged 6-11 Years
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	15	14	15	13
Units: ng/mL				
geometric mean (geometric coefficient of variation)	142.42 (± 256.34)	340.46 (± 363.69)	142.42 (± 256.34)	339.35 (± 409.24)

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline in Peripheral Blood Eosinophil Count up to Week 48

End point title	Change From Baseline in Peripheral Blood Eosinophil Count up to Week 48[7]

End point description:

Blood samples were collected for determination of eosinophil count levels and were assessed in a central laboratory. Baseline is the last non-missing measurement prior to the first dose of study treatment. The Safety Analysis set consisted of all participants who received at least 1 dose of benralizumab. Only those participants with data available were analyzed. Here, n= number of participants analyzed at specific timepoint.

End point type	Primary

End point timeframe:

Baseline (Day 0) and at Weeks 4, 8, 12, 16, 24 and 48

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: No additional statistical analysis was pre-specified for this endpoint.

End point values	Benralizumab Dose 1, Aged 6-14 Years	Benralizumab Dose 2, Aged 6-14 Years	Benralizumab Dose 1, Aged 6-11 Years	Benralizumab Dose 2, Aged 6-11 Years
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	15	15	15	13
Units: cells/microliters				
arithmetic mean (standard deviation)				
Week 4 (n=15, 15, 15, 13)	-447.3 (± 283.76)	-455.3 (± 385.58)	-447.3 (± 283.76)	-436.9 (± 408.28)
Week 8 (n=15, 15, 15, 13)	-445.3 (± 276.20)	-470.7 (± 374.25)	-445.3 (± 276.20)	-453.8 (± 396.03)
Week 12 (n=15, 14, 15, 12)	-443.3 (± 286.85)	-472.9 (± 393.49)	-443.3 (± 286.85)	-455.8 (± 419.32)
Week 16 (n=15, 12, 15, 11)	-446.7 (± 279.12)	-430.0 (± 378.68)	-446.7 (± 279.12)	-402.7 (± 384.61)

Week 24 (n=12, 14, 12, 13)	-354.2 (± 323.99)	-457.9 (± 397.77)	-354.2 (± 323.99)	-436.9 (± 405.90)
Week 48 (n=15, 14, 15, 13)	-434.0 (± 286.15)	-474.3 (± 385.04)	-434.0 (± 286.15)	-453.8 (± 392.78)

Statistical analyses

No statistical analyses for this end point

Secondary: Body Weight-Adjusted Clearance of Benralizumab

End point title	Body Weight-Adjusted Clearance of Benralizumab

End point description:

Blood samples were collected to determine the clearance of benralizumab. This was an EBE derived posthoc using population PK analysis. The PK analysis set consisted of all participants who received at least 1 dose of benralizumab for whom PK blood samples were not assumed to be affected by factors such as protocol violations and who had at least 1 post dose quantifiable serum PK observation.

End point type	Secondary

End point timeframe:

Pre-dose on Days 0, 28, 56, 112, 168 and post-dose on Days 1, 7, 14, 84, 336; and at early discontinuation or withdrawal visit

End point values	All participants			
Subject group type	Subject analysis set			
Number of subjects analysed	30			
Units: L/day/kilogram				
arithmetic mean (standard deviation)	0.00408 (± 0.000764)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Anti-Drug Antibodies (ADA) Response to Benralizumab

End point title	Number of Participants With Anti-Drug Antibodies (ADA) Response to Benralizumab

End point description:

ADA prevalence:ADA positive (+ve) at any time point including baseline and/or post baseline(PB). Treatment (Rx) induced ADA+ve:ADA negative (-ve) at baseline and PB ADA+ve. Rx-boosted ADA+ve:baseline +ve ADA titer boosted by >4-fold or higher following study drug administration. Rx-emergent ADA+ve:Rx-induced ADA+ve/treatment-boosted ADA+ve. Persistently +ve ADA:having at least 2 PB ADA+ve assessments with at least 16 weeks (112 days) between first and last +ve assessments/ADA+ve result at last available assessment. Transiently +ve ADA:having at least 1 PB ADA+ve assessment(s) & not persistently ADA+ve. Neutralizing antibodies (nAb) prevalence:nAb+ve at baseline and/or PB. nAb incidence: nAb-ve at baseline (or ADA-ve at baseline) and nAb+ve at any PB visit. The Safety Analysis set consisted of all participants who received at least 1 dose of benralizumab. Only those participants with data available were analyzed.n=number of participants analyzed for specified ADA category.

End point type	Secondary

End point timeframe:

Pre-dose at Baseline (Day 0), Weeks 8, 16 and 24 and post-dose at Week 48; and at early discontinuation or withdrawal visit

End point values	Benralizumab Dose 1, Aged 6-14 Years	Benralizumab Dose 2, Aged 6-14 Years	Benralizumab Dose 1, Aged 6-11 Years	Benralizumab Dose 2, Aged 6-11 Years
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	15	15	15	13
Units: participants				
ADA prevalence (n=15, 15, 15, 13)	3	1	3	1
Treatment-emergent ADA+ve (n=15, 15, 15, 13)	3	1	3	1
Post-baseline (PB) ADA+ve (n=15, 15, 15, 13)	3	1	3	1
Baseline and at least 1 PB ADA+ve (n=13,15,13,13)	0	0	0	0
Only baseline ADA+ve (n=13, 15, 13, 13)	0	0	0	0
Persistently ADA+ve (n=15, 15, 15, 13)	1	0	1	0
Transiently ADA +ve (n=15, 15, 15, 13)	2	1	2	1
nAb prevalence (n=15, 15, 15, 13)	3	1	3	1
nAb incidence (n=15, 15, 15, 13)	3	1	3	1

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Pre-Bronchodilator Forced Expiratory Volume in 1 Second (FEV1) up to Week 48

End point title	Change From Baseline in Pre-Bronchodilator Forced Expiratory Volume in 1 Second (FEV1) up to Week 48

End point description:

The FEV1 was defined as the volume of air exhaled from the lungs in the first second of a forced expiration and was measured by spirometry. Baseline is the last non-missing measurement with acceptable quality prior to the first dose of study treatment. The Safety Analysis set consisted of all participants who received at least 1 dose of benralizumab. Only those participants with data available were analyzed. Here, n= number of participants analyzed at specific timepoint.

End point type	Secondary

End point timeframe:

Baseline (Day 0) and at Weeks 16 and 48

End point values	Benralizumab Dose 1, Aged 6-14 Years	Benralizumab Dose 2, Aged 6-14 Years	Benralizumab Dose 1, Aged 6-11 Years	Benralizumab Dose 2, Aged 6-11 Years
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	15	15	15	13
Units: liters				
arithmetic mean (standard deviation)				
Week 16 (n=11, 8, 11, 7)	-0.001 (± 0.2434)	-0.165 (± 0.2609)	-0.001 (± 0.2434)	-0.119 (± 0.2435)
Week 48 (n=15, 13, 15, 12)	0.003 (± 0.3412)	0.428 (± 0.4209)	0.003 (± 0.3412)	0.425 (± 0.4395)

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Interviewer-Administered Asthma Control Questionnaire (ACQ-IA) Score up to Week 48

End point title	Change From Baseline in Interviewer-Administered Asthma Control Questionnaire (ACQ-IA) Score up to Week 48

End point description:

The ACQ-IA was a 6-item assessment comprised of 6 patient-reported items. Participants were asked to record their experience with 5 symptoms (night-time waking, symptoms on waking, activity limitation, shortness of breath, and wheezing) and use of short-acting beta-2 agonist (SABA) over the previous week using a 7-point scale (0 = no impairment and 6 = maximum impairment). The ACQ-IA score was calculated by taking the mean of the 7 equally weighted items. The score ranged from 0 (well controlled) to 6 (extremely poorly controlled). Higher scores indicated poor asthma control. Baseline is the last non-missing measurement prior to the first dose of study treatment. The Safety Analysis set consisted of all participants who received at least 1 dose of benralizumab. Only those participants with data available were analyzed. Here, n= number of participants analyzed at specific timepoint.

End point type	Secondary

End point timeframe:

Baseline (Day 0), at Weeks 16 and 48; and at early discontinuation or withdrawal visit

End point values	Benralizumab Dose 1, Aged 6-14 Years	Benralizumab Dose 2, Aged 6-14 Years	Benralizumab Dose 1, Aged 6-11 Years	Benralizumab Dose 2, Aged 6-11 Years
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	15	15	15	13
Units: scores on a scale				
arithmetic mean (standard deviation)				
Week 16 (n=15, 13, 15, 12)	-0.62 (± 0.890)	-1.06 (± 1.696)	-0.62 (± 0.890)	-1.18 (± 1.717)
Week 48 (n=14, 13, 14, 12)	-0.56 (± 1.252)	-1.31 (± 1.324)	-0.56 (± 1.252)	-1.36 (± 1.369)

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Responders in Interviewer-Administered Patient Global Impression of Change (PGIC)-IA and Clinician Global Impression of Change (CGIC) Responder Status Questionnaires

End point title	Number of Responders in Interviewer-Administered Patient Global Impression of Change (PGIC)-IA and Clinician Global Impression of Change (CGIC) Responder Status Questionnaires

End point description:

The PGIC-IA and CGIC instruments were used for an overall evaluation of response to Rx, conducted separately by Investigator and by participant (administered by trained individuals to help the child understand the question and response options), using a 7-point scale:1=very much improved;2=much improved;3=minimally improved;4=no change;5=minimally worse;6=much worse;7=very much worse. The clinician and participant rated degree of change in overall asthma status compared to start of study Rx visit. Participants were defined as responders based on categorized responses for PGIC-IA and CGIC. Responder status categories included: Improved=Very much improved, Much improved, Minimally improved, Much improved=Much improved, Very much improved, Very much improved=Very much improved. CGIC=PGIC-IA indicates agreement between CGIC and PGIC-IA assessments of response to treatment at the same visit. The Safety Analysis set included all participants who received at least 1 dose of benralizumab.

End point type	Secondary

End point timeframe:

At Weeks 16 and 48; and at early discontinuation or withdrawal visit

End point values	Benralizumab Dose 1, Aged 6-14 Years	Benralizumab Dose 2, Aged 6-14 Years	Benralizumab Dose 1, Aged 6-11 Years	Benralizumab Dose 2, Aged 6-11 Years
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	15	15	15	13
Units: scores on a scale				
PGIC-IA, Week 16, improved	13	13	13	12
PGIC-IA, Week 16, much improved	10	11	10	10
PGIC-IA, Week 16, very much improved	4	9	4	8
PGIC-IA, Week 48, improved	13	13	13	12
PGIC-IA, Week 48, much improved	9	11	9	10
PGIC-IA, Week 48, very much improved	9	10	9	9
CGIC, Week 16, improved	13	12	13	11
CGIC, Week 16, much improved	8	9	8	9
CGIC, Week 16, very much improved	3	5	3	5
CGIC, Week 48, improved	15	14	15	13
CGIC, Week 48, much improved	8	12	8	11
CGIC, Week 48, very much improved	5	6	5	6
CGIC = PGIC-IA, Week 16, improved	10	6	10	6
CGIC = PGIC-IA, Week 16, much improved	7	5	7	5
CGIC = PGIC-IA, Week 16, very much improved	3	4	3	4
CGIC = PGIC-IA, Week 48, improved	9	8	9	8
CGIC = PGIC-IA, Week 48, much improved	5	7	5	7
CGIC = PGIC-IA, Week 48, very much improved	5	6	5	6

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Treatment-emergent adverse events were collected from the start of study drug administration (Day 1) until end of follow-up, approximately up to Week 53

Adverse event reporting additional description:

The Safety Analysis set consisted of all participants who received at least 1 dose of benralizumab.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	25.0

Reporting groups

Reporting group title	Benralizumab Dose 1, Aged 6-11 Years

Reporting group description:

Participants with body weight <35 kg at screening received benralizumab Dose 1 SC injection once daily on Day 0 and at Weeks 4, 8, and 16 in Part A, followed by benralizumab Dose 1 at Weeks 24, 32, and 40 in Part B.

Reporting group title	Benralizumab Dose 2, Aged 6-14 Years

Reporting group description:

All participants with a body weight >=35 kg or aged 12-14 years (irrespective of body weight) at screening received benralizumab Dose 2 SC injection once daily on Day 0 and at Weeks 4, 8, and 16 in Part A, followed by benralizumab Dose 2 at Weeks 24, 32, and 40 in Part B.

Reporting group title	Benralizumab Dose 1, Aged 6-14 Years

Reporting group description:

All participants with a body weight <35 kg at screening received benralizumab Dose 1 SC injection once daily on Day 0 and at Weeks 4, 8, and 16 in Part A, followed by benralizumab Dose 1 at Weeks 24, 32, and 40 in Part B.

Reporting group title	Benralizumab Dose 2, Aged 6-11 Years

Reporting group description:

Participants with body weight >=35 kg at screening received benralizumab Dose 2 SC injection once daily on Day 0 and at Weeks 4, 8, and 16 in Part A, followed by benralizumab Dose 2 at Weeks 24, 32, and 40 in Part B.

Serious adverse events	Benralizumab Dose 1, Aged 6-11 Years	Benralizumab Dose 2, Aged 6-14 Years	Benralizumab Dose 1, Aged 6-14 Years
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 15 (6.67%)	4 / 15 (26.67%)	1 / 15 (6.67%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	1 / 15 (6.67%)	4 / 15 (26.67%)	1 / 15 (6.67%)
occurrences causally related to treatment / all	0 / 1	0 / 4	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			

Somatic symptom disorder			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Benralizumab Dose 2, Aged 6-11 Years		
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 13 (15.38%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	2 / 13 (15.38%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Somatic symptom disorder			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Benralizumab Dose 1, Aged 6-11 Years	Benralizumab Dose 2, Aged 6-14 Years	Benralizumab Dose 1, Aged 6-14 Years
Total subjects affected by non-serious adverse events			
subjects affected / exposed	13 / 15 (86.67%)	11 / 15 (73.33%)	13 / 15 (86.67%)
General disorders and administration site conditions			
Vaccination site pain			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	1 / 15 (6.67%)
occurrences (all)	1	0	1
Pyrexia			
subjects affected / exposed	3 / 15 (20.00%)	1 / 15 (6.67%)	3 / 15 (20.00%)
occurrences (all)	4	1	4
Injection site reaction			

subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	1 / 15 (6.67%)
occurrences (all)	2	0	2
Fatigue			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	1 / 15 (6.67%)
occurrences (all)	1	0	1
Chills			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	1 / 15 (6.67%)
occurrences (all)	1	0	1
Immune system disorders			
Allergy to animal			
subjects affected / exposed	1 / 15 (6.67%)	1 / 15 (6.67%)	1 / 15 (6.67%)
occurrences (all)	1	1	1
Immunisation reaction			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	1 / 15 (6.67%)
occurrences (all)	1	0	1
Respiratory, thoracic and mediastinal disorders			
Atelectasis			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Cough			
subjects affected / exposed	0 / 15 (0.00%)	3 / 15 (20.00%)	0 / 15 (0.00%)
occurrences (all)	0	3	0
Bronchitis chronic			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Rhinorrhoea			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Oropharyngeal pain			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Nasal congestion			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Hyperventilation			

subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Upper-airway cough syndrome			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	1 / 15 (6.67%)
occurrences (all)	1	0	1
Wheezing			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Psychiatric disorders			
Depression			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Panic attack			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Investigations			
Occult blood positive			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Blood thyroid stimulating hormone decreased			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Injury, poisoning and procedural complications			
Road traffic accident			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	1 / 15 (6.67%)
occurrences (all)	1	0	1
Ligament rupture			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Hand fracture			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	1 / 15 (6.67%)
occurrences (all)	1	0	1
Contusion			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	1 / 15 (6.67%)
occurrences (all)	1	0	1
Cardiac disorders			

Palpitations			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	0 / 15 (0.00%)
occurrences (all)	0	2	0
Nervous system disorders			
Headache			
subjects affected / exposed	2 / 15 (13.33%)	1 / 15 (6.67%)	2 / 15 (13.33%)
occurrences (all)	4	1	4
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Gastrointestinal disorders			
Dental caries			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	1 / 15 (6.67%)
occurrences (all)	3	0	3
Constipation			
subjects affected / exposed	2 / 15 (13.33%)	1 / 15 (6.67%)	2 / 15 (13.33%)
occurrences (all)	2	1	2
Abdominal pain upper			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Abdominal pain			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Diarrhoea			
subjects affected / exposed	0 / 15 (0.00%)	2 / 15 (13.33%)	0 / 15 (0.00%)
occurrences (all)	0	2	0
Vomiting			
subjects affected / exposed	2 / 15 (13.33%)	0 / 15 (0.00%)	2 / 15 (13.33%)
occurrences (all)	2	0	2
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Gastritis			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Dyspepsia			

subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	0 / 15 (0.00%)
occurrences (all)	0	2	0
Skin and subcutaneous tissue disorders			
Haemorrhage subcutaneous			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Eczema			
subjects affected / exposed	1 / 15 (6.67%)	1 / 15 (6.67%)	1 / 15 (6.67%)
occurrences (all)	1	1	1
Dermatitis atopic			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Asteatosis			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	1 / 15 (6.67%)
occurrences (all)	1	0	1
Urticaria			
subjects affected / exposed	1 / 15 (6.67%)	2 / 15 (13.33%)	1 / 15 (6.67%)
occurrences (all)	1	2	1
Musculoskeletal and connective tissue disorders			
Pain in extremity			
subjects affected / exposed	2 / 15 (13.33%)	0 / 15 (0.00%)	2 / 15 (13.33%)
occurrences (all)	2	0	2
Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Asymptomatic COVID-19			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	1 / 15 (6.67%)
occurrences (all)	1	0	1
Viral upper respiratory tract infection			
subjects affected / exposed	2 / 15 (13.33%)	2 / 15 (13.33%)	2 / 15 (13.33%)
occurrences (all)	2	3	2
Streptococcal infection			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	1 / 15 (6.67%)
occurrences (all)	1	0	1
Skin candida			

subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Sinusitis			
subjects affected / exposed	2 / 15 (13.33%)	0 / 15 (0.00%)	2 / 15 (13.33%)
occurrences (all)	2	0	2
Pneumonia			
subjects affected / exposed	0 / 15 (0.00%)	2 / 15 (13.33%)	0 / 15 (0.00%)
occurrences (all)	0	2	0
Bronchitis bacterial			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Pharyngitis			
subjects affected / exposed	1 / 15 (6.67%)	1 / 15 (6.67%)	1 / 15 (6.67%)
occurrences (all)	1	2	1
Oral herpes			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	1 / 15 (6.67%)
occurrences (all)	1	0	1
Nasopharyngitis			
subjects affected / exposed	4 / 15 (26.67%)	2 / 15 (13.33%)	4 / 15 (26.67%)
occurrences (all)	5	3	5
Gastroenteritis			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	1 / 15 (6.67%)
occurrences (all)	1	0	1
COVID-19			
subjects affected / exposed	1 / 15 (6.67%)	2 / 15 (13.33%)	1 / 15 (6.67%)
occurrences (all)	1	2	1
Pharyngitis streptococcal			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	0 / 15 (0.00%)
occurrences (all)	0	1	0

Non-serious adverse events	Benralizumab Dose 2, Aged 6-11 Years		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	9 / 13 (69.23%)		
General disorders and administration site conditions			

Vaccination site pain			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences (all)	0		
Pyrexia			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		
Injection site reaction			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences (all)	0		
Fatigue			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences (all)	0		
Chills			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences (all)	0		
Immune system disorders			
Allergy to animal			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		
Immunisation reaction			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences (all)	0		
Respiratory, thoracic and mediastinal disorders			
Atelectasis			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences (all)	0		
Cough			
subjects affected / exposed	3 / 13 (23.08%)		
occurrences (all)	3		
Bronchitis chronic			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences (all)	0		
Rhinorrhoea			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		
Oropharyngeal pain			

subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		
Nasal congestion			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		
Hyperventilation			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences (all)	0		
Upper-airway cough syndrome			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences (all)	0		
Wheezing			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		
Psychiatric disorders			
Depression			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences (all)	0		
Panic attack			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences (all)	0		
Investigations			
Occult blood positive			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences (all)	0		
Blood thyroid stimulating hormone decreased			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences (all)	0		
Injury, poisoning and procedural complications			
Road traffic accident			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences (all)	0		
Ligament rupture			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences (all)	0		
Hand fracture			

subjects affected / exposed occurrences (all) Contusion subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0 0 / 13 (0.00%) 0		
Cardiac disorders Palpitations subjects affected / exposed occurrences (all)	 0 / 13 (0.00%) 0		
Nervous system disorders Headache subjects affected / exposed occurrences (all)	 1 / 13 (7.69%) 1		
Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all)	 0 / 13 (0.00%) 0		
Gastrointestinal disorders Dental caries subjects affected / exposed occurrences (all) Constipation subjects affected / exposed occurrences (all) Abdominal pain upper subjects affected / exposed occurrences (all) Abdominal pain subjects affected / exposed occurrences (all) Diarrhoea subjects affected / exposed occurrences (all) Vomiting subjects affected / exposed occurrences (all) Gastrooesophageal reflux disease	 0 / 13 (0.00%) 0 0 / 13 (0.00%) 0 1 / 13 (7.69%) 1 0 / 13 (0.00%) 0 1 / 13 (7.69%) 1 0 / 13 (0.00%) 0 		

subjects affected / exposed	0 / 13 (0.00%)		
occurrences (all)	0		
Gastritis			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences (all)	0		
Dyspepsia			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	2		
Skin and subcutaneous tissue disorders			
Haemorrhage subcutaneous			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences (all)	0		
Eczema			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		
Dermatitis atopic			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		
Asteatosis			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences (all)	0		
Urticaria			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		
Musculoskeletal and connective tissue disorders			
Pain in extremity			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences (all)	0		
Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences (all)	0		
Asymptomatic COVID-19			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences (all)	0		
Viral upper respiratory tract infection			

subjects affected / exposed	2 / 13 (15.38%)		
occurrences (all)	3		
Streptococcal infection			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences (all)	0		
Skin candida			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		
Sinusitis			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences (all)	0		
Pneumonia			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		
Bronchitis bacterial			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		
Pharyngitis			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences (all)	0		
Oral herpes			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences (all)	0		
Nasopharyngitis			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		
Gastroenteritis			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences (all)	0		
COVID-19			
subjects affected / exposed	2 / 13 (15.38%)		
occurrences (all)	2		
Pharyngitis streptococcal			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
22 July 2019	Amended to change table of assessments and synopsis. A cohort was added as per requirement by Japanese Regulatory Authority. Information regarding questionnaire assessments, body weight stratification, dosing, investigational product (IP) storage and packaging, time and date of blood sampling was updated. Information regarding the presence of nAb was deleted from the secondary objectives. Annualized asthma exacerbation rate was included as an exploratory objective. Information was added to clarify the risk related to hypersensitivity reactions; the requirements for participants in Part A and to describe the analysis of asthma exacerbation. Japanese Guidelines and definition of inhaled corticosteroid was implemented in the inclusion criteria. A prohibited medication was deleted as per team's decision. Information on the Safety Review Committee was updated. A recommended sequence for the completion of assessments at each visit was added. A rationale was added for the completion of the ACQ-IA at all visits during the treatment and post-treatment periods. A description of the PGIC-IA and CGIC was added. References to liver enzyme elevations and to Hy's Law were deleted. Reference to participants older than 9 years of age was deleted. The definition of participant evaluability was updated.
22 August 2019	Amended to change the synopsis. Clarification was added for the third cohort. Minor changes were added to clarify and improve text.
01 July 2020	Clarification was added on how the study could continue in the event of a serious disruption, including details of mitigations that could be employed to ensure study continuity. Updated inclusion criteria. The minimum observation time following IP administration was updated. The study period during which the use of live attenuated vaccines was prohibited was updated. Criteria for discontinuation was updated. The procedure for performing a forced expiratory maneuver in children aged <10 years was clarified. Procedures for hepatitis B surface antigen screening were updated.
22 February 2022	Estimated date of last participant completed was changed from May 2022 to September 2022. The minimum observation period at the clinical site following IP administration was changed to 1 hour from 2 hours. Aligned information presented with current protocol template. Clarification that electrocardiogram readings could be stored as physical copies in participant's source files. New sections were added to discuss device constituent deficiencies in line with new European Union/United States regulations.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported