Clinical trial results:
A Multinational, Randomized, Double-blind, Parallel-group, Placebo-controlled Study to Investigate the Use of Benralizumab as a Treatment Option for Patients with Bullous Pemphigoid (FJORD)

Summary

EudraCT number	2020-000287-32
Trial protocol	BG DE FR IT GR
Global end of trial date	26 October 2023

Results information

Result version number	v1 (current)
This version publication date	13 October 2024
First version publication date	13 October 2024

Trial information

Trial identification

Sponsor protocol code	D325AC00002

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04612790
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	AstraZeneca AB
Sponsor organisation address	Forskargatan 18, Södertälje, Sweden, 151 85
Public contact	Global Clinical Lead, AstraZeneca AB, +1 877-240-9479, information.center@astrazeneca.com
Scientific contact	Global Clinical Lead, AstraZeneca AB, +1 877-240-9479, information.center@astrazeneca.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	26 October 2023
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	26 October 2023
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To compare the clinical efficacy of benralizumab with placebo in participants with symptomatic bullous pemphigoid (BP).

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	31 March 2021
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	Australia: 2
Country: Number of subjects enrolled	Bulgaria: 7
Country: Number of subjects enrolled	China: 13
Country: Number of subjects enrolled	France: 3
Country: Number of subjects enrolled	Germany: 8
Country: Number of subjects enrolled	Greece: 1
Country: Number of subjects enrolled	Israel: 4
Country: Number of subjects enrolled	Italy: 10
Country: Number of subjects enrolled	Japan: 13
Country: Number of subjects enrolled	Spain: 1
Country: Number of subjects enrolled	United States: 5
Worldwide total number of subjects	67
EEA total number of subjects	30

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37	0

wk	
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)	16
From 65 to 84 years	49
85 years and over	2

Subject disposition

Recruitment

Recruitment details:

This study was conducted in adult participants with symptomatic BP at 32 sites in 11 countries. Study consisted of screening period, double-blind (DB) period for 36 weeks followed by optional open-label extension (OLE) period (who completed the DB period), in which all participants received benralizumab for at least 1 year.

Pre-assignment

Screening details:

Study was terminated following a pre-planned futility analysis as efficacy results did not pass pre-defined futility hurdle. AstraZeneca created protocol#5 and SAP#3 to modify sample size and futility stopping guidelines. Updated protocol was not submitted to health authorities as study was terminating. Results align with protocol#5 and SAP#3.

Period 1

Period 1 title	DB period (Up to 36 weeks)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Carer

Arms

Are arms mutually exclusive?	Yes
Arm title	DB period: Benralizumab

Arm description:

Participants received benralizumab with an initial loading dose of 60 milligrams (mg) followed by a maintenance dose of 30 mg every 4 weeks (Q4W) as a subcutaneous (SC) injection for 36 weeks.

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

Dosage and administration details:

Benralizumab was provided in an accessorized prefilled syringe (APFS). Participants received benralizumab with an initial loading dose of 60 mg followed by a maintenance dose of 30 mg Q4W as a SC injection for 36 weeks.

Arm title	DB period: Placebo

Arm description:

Participants received volume-matched placebo as a SC injection on the same dosing schedule as benralizumab Q4W for 36 weeks.

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

Dosage and administration details:

Matching placebo was provided in an APFS. Participants received volume-matched placebo as a SC injection on the same dosing schedule as benralizumab Q4W for 36 weeks.

Number of subjects in period 1	DB period: Benralizumab	DB period: Placebo
Started	34	33
Completed	16	19
Not completed	18	14
Consent withdrawn by subject	2	4
Physician decision	4	3
Adverse event, non-fatal	2	-
Death	1	1
Study terminated by sponsor	8	6
Unspecified	1	-

Period 2

Period 2 title	OLE period (Up to 1 year)
Is this the baseline period?	No
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	OLE period: Benralizumab (DB)/ Benralizumab (OLE)

Arm description:

Participants who received benralizumab in DB period received benralizumab 30 mg Q4W in OLE period for at least 1 year.

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

Dosage and administration details:

Benralizumab was provided in an APFS. Participants who received benralizumab in DB period received benralizumab 30 mg Q4W in OLE period for at least 1 year.

Arm title	OLE period: Placebo (DB) / Benralizumab (OLE)

Arm description:

Participants who received matched placebo in DB period received benralizumab 30 mg Q4W in OLE period for at least 1 year.

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

Dosage and administration details:

Benralizumab was provided in an APFS. Participants who received matched placebo in DB period received benralizumab 30 mg Q4W in OLE period for at least 1 year.

Number of subjects in period 2[1]	OLE period: Benralizumab (DB)/ Benralizumab (OLE)	OLE period: Placebo (DB) / Benralizumab (OLE)
Started	16	18
Did not receive treatment in OLE period	0	1
Completed	0	0
Not completed	16	18
Consent withdrawn by subject	-	1
Study terminated by sponsor	14	15
Investigator decision	2	1
Unspecified	-	1

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.
Justification: 1 participant did not enter OLE period and hence did not receive treatment in OLE period.

Baseline characteristics

Reporting groups	
Reporting group title	DB period: Benralizumab
Reporting group description:	
Participants received benralizumab with an initial loading dose of 60 milligrams (mg) followed by a maintenance dose of 30 mg every 4 weeks (Q4W) as a subcutaneous (SC) injection for 36 weeks.	
Reporting group title	DB period: Placebo
Reporting group description:	
Participants received volume-matched placebo as a SC injection on the same dosing schedule as benralizumab Q4W for 36 weeks.	

Reporting group values	DB period: Benralizumab	DB period: Placebo	Total
Number of subjects	34	33	67
Age categorical Units: Subjects			
Adults (18-64 years)	10	6	16
From 65-84 years	24	25	49
Elderly 85 years and over	0	2	2
Age Continuous Units: Years			
arithmetic mean	68.0	72.5	
standard deviation	± 10.4	± 11.4	-
Sex: Female, Male Units: Participants			
Female	20	22	42
Male	14	11	25
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	14	13	27
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	2	0	2
White	16	20	36
More than one race	0	0	0
Unknown or Not Reported	2	0	2
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	0	1	1
Not Hispanic or Latino	34	32	66
Unknown or Not Reported	0	0	0

End points

End points reporting groups

Reporting group title	DB period: Benralizumab
Reporting group description:	
Participants received benralizumab with an initial loading dose of 60 milligrams (mg) followed by a maintenance dose of 30 mg every 4 weeks (Q4W) as a subcutaneous (SC) injection for 36 weeks.	
Reporting group title	DB period: Placebo
Reporting group description:	
Participants received volume-matched placebo as a SC injection on the same dosing schedule as benralizumab Q4W for 36 weeks.	
Reporting group title	OLE period: Benralizumab (DB)/ Benralizumab (OLE)
Reporting group description:	
Participants who received benralizumab in DB period received benralizumab 30 mg Q4W in OLE period for at least 1 year.	
Reporting group title	OLE period: Placebo (DB) / Benralizumab (OLE)
Reporting group description:	
Participants who received matched placebo in DB period received benralizumab 30 mg Q4W in OLE period for at least 1 year.	

Primary: Percentage of Responders at Week 36

End point title	Percentage of Responders at Week 36
End point description:	
A responder was defined as a participant who was in complete remission while off OCS for ≥2 months at Week 36. Participants who received restricted medications or withdrew from the study were considered as non-responders from the time such events occurred up to Week 36. Full analysis set (FAS) included all randomized participants who received at least 1 dose of IP, irrespective of their protocol adherence and continued participation in the study. Only those participants with data collected at Week 36 are reported.	
End point type	Primary
End point timeframe:	
At Week 36	

End point values	DB period: Benralizumab	DB period: Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	18	19		
Units: Percentage of participants				
number (confidence interval 95%)	11.1 (-2.70 to 26.11)	5.26 (-5.06 to 15.07)		

Statistical analyses

Statistical analysis title	DB period: Benralizumab vs DB period: Placebo
Statistical analysis description:	
Estimates were from a logistic regression model using the Firth adjustment (adj) that included treatment group, baseline disease severity (moderate, severe) and time of BP diagnosis (participants	

with newly diagnosed BP, participants with a previous diagnosis of BP who have relapsed) as categorical covariates.

Comparison groups	DB period: Benralizumab v DB period: Placebo
Number of subjects included in analysis	37
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.509
Method	Logistic regression model with Firth adj
Parameter estimate	Difference in percentage of responders
Point estimate	6.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-10.9
upper limit	24.29

Secondary: Percentage of Participants who Remained Relapse-Free up to Week 36

End point title	Percentage of Participants who Remained Relapse-Free up to Week 36

End point description:

Relapse was defined as the appearance of 3 or more new lesions per month (blisters, eczematous lesions, or urticarial plaques); or at least 1 large (>10 centimeter [cm] diameter) eczematous lesion or urticarial plaques that did not heal within 1 week; or the extension of established lesions or daily pruritus in participants who had achieved disease control. FAS included all randomized participants who received at least 1 dose of IP, irrespective of their protocol adherence and continued participation in the study. Only those participants with data collected at specified timepoints are reported.

End point type	Secondary

End point timeframe:

Up to Week 36

End point values	DB period: Benralizumab	DB period: Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	18	19		
Units: Percentage of participants				
number (confidence interval 95%)	23.78 (5.95 to 41.61)	19.79 (1.43 to 38.15)		

Statistical analyses

No statistical analyses for this end point

Secondary: Cumulative OCS Exposure from Baseline to Week 36

End point title	Cumulative OCS Exposure from Baseline to Week 36

End point description:

The cumulative OCS exposure was estimated as the sum over the relevant 4-week periods from the mixed-effect model for repeated measures (MMRM) model. Baseline was defined as the last recorded

value on or prior to the date of randomization. Equivalents were prednisone equivalents (converted from mg). FAS included all randomized participants who received at least 1 dose of IP, irrespective of their protocol adherence and continued participation in the study. Only those participants with data collected at specified timepoints are reported.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and Week 36

End point values	DB period: Benralizumab	DB period: Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	18	19		
Units: mg per kilogram (mg/kg)				
arithmetic mean (standard deviation)	71.37 (± 63.19)	62.71 (± 46.90)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Bullous Pemphigoid Disease Area Index (BPDAI) Activity Score at Week 36

End point title	Change From Baseline in Bullous Pemphigoid Disease Area Index (BPDAI) Activity Score at Week 36

End point description:

BPDAI is a clinician completed tool that is used for independent disease severity assessment to measure disease extent in BP. The total BPDAI activity score is calculated as the arithmetic sum of the 3 subcomponents – cutaneous blisters/erosions, cutaneous urticaria/erythema, and mucosal blisters/erosions. The BPDAI total activity gives an indication of disease activity, with score range from 0 (no disease activity) to 360 (severe disease activity). Higher scores indicating greater disease activity. Baseline was defined as the last recorded value on or prior to the date of randomization. FAS included all randomized participants who received at least 1 dose of IP, irrespective of their protocol adherence and continued participation in the study. Only those participants with data collected at specified timepoints are reported.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and Week 36

End point values	DB period: Benralizumab	DB period: Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	14	12		
Units: Score on a scale				
arithmetic mean (standard deviation)	-53.29 (± 46.33)	-52.75 (± 17.36)		

Statistical analyses

No statistical analyses for this end point

Secondary: Cumulative OCS Exposure From Baseline to Week 16

End point title	Cumulative OCS Exposure From Baseline to Week 16

End point description:

The cumulative OCS exposure was estimated as the sum over the relevant 4-week periods from the MMRM model. Baseline was defined as the last recorded value on or prior to the date of randomization. Equivalents were prednisone equivalents (converted from mg). FAS included all randomized participants who received at least 1 dose of IP, irrespective of their protocol adherence and continued participation in the study. Only those participants with data collected at specified timepoints are reported.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and Week 16

End point values	DB period: Benralizumab	DB period: Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	24	24		
Units: mg/kg				
arithmetic mean (standard deviation)	46.90 (± 27.19)	42.15 (± 33.33)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in BPDAI-Pruritus Score at Week 36

End point title	Change From Baseline in BPDAI-Pruritus Score at Week 36

End point description:

The BPDAI-Pruritus is a separate component of the BPDAI that asks the participant to grade the severity of pruritus over the past 24 hours, the past week, and the past month. For each recall period, severity of pruritus is rated on a numeric rating scale (NRS) ranging from 0 for no itch to 10 for maximal itching. The BPDAI-Pruritus score was computed as the sum of 3 components ranging from 0 to 30. Higher scores indicated worse condition. Baseline was defined as the last recorded value on or prior to the date of randomization. FAS included all randomized participants who received at least 1 dose of IP, irrespective of their protocol adherence and continued participation in the study. Only those participants with data collected at specified timepoints are reported.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and Week 36

End point values	DB period: Benralizumab	DB period: Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	14	12		
Units: Score on a scale				
arithmetic mean (standard deviation)	-5.57 (± 7.23)	-16.58 (± 9.21)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Treatment emergent Adverse events(TEAEs) and all-cause mortality: Start of study treatment(Day 1) up to the follow up visit(4 weeks after the last dose of study treatment), or up until the study withdrawal date if earlier,up to approximately 133 weeks.

Adverse event reporting additional description:

The safety analysis set consists of all participants who had received at least 1 dose of IP.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	25.1

Reporting groups

Reporting group title	DB period: Benralizumab

Reporting group description:

Participants received benralizumab with an initial loading dose of 60 mg followed by a maintenance dose of 30 mg Q4W by SC injection for 36 weeks.

Reporting group title	OLE period: Benralizumab (DB)/Benralizumab (OLE)

Reporting group description:

Participants who received benralizumab in DB period received benralizumab 30 mg Q4W in OLE period for at least 1 year.

Reporting group title	OLE period: Placebo (DB)/Benralizumab (OLE)

Reporting group description:

Participants who received matched placebo in DB period benralizumab 30 mg Q4W in OLE period for at least 1 year.

Reporting group title	DB period: Placebo

Reporting group description:

Participants received matched placebo by SC injection Q4W for 36 weeks.

Serious adverse events	DB period: Benralizumab	OLE period: Benralizumab (DB)/Benralizumab	OLE period: Placebo (DB)/Benralizumab (OLE)
Total subjects affected by serious adverse events			
subjects affected / exposed	9 / 34 (26.47%)	4 / 16 (25.00%)	2 / 18 (11.11%)
number of deaths (all causes)	1	0	0
number of deaths resulting from adverse events	1	0	0
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 34 (0.00%)	0 / 16 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lumbar vertebral fracture			

subjects affected / exposed	1 / 34 (2.94%)	0 / 16 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal fracture			
subjects affected / exposed	0 / 34 (0.00%)	0 / 16 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thoracic vertebral fracture			
subjects affected / exposed	1 / 34 (2.94%)	0 / 16 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wound dehiscence			
subjects affected / exposed	1 / 34 (2.94%)	0 / 16 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Hypotension			
subjects affected / exposed	0 / 34 (0.00%)	0 / 16 (0.00%)	1 / 18 (5.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Cardiac failure acute			
subjects affected / exposed	0 / 34 (0.00%)	0 / 16 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Pulmonary oedema			
subjects affected / exposed	0 / 34 (0.00%)	0 / 16 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute respiratory failure			
subjects affected / exposed	1 / 34 (2.94%)	0 / 16 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Skin and subcutaneous tissue disorders			
Pemphigoid			
subjects affected / exposed	4 / 34 (11.76%)	0 / 16 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	1 / 4	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Henoch-schonlein purpura			
subjects affected / exposed	0 / 34 (0.00%)	0 / 16 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Osteoarthritis			
subjects affected / exposed	0 / 34 (0.00%)	2 / 16 (12.50%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteonecrosis			
subjects affected / exposed	0 / 34 (0.00%)	0 / 16 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Pneumocystis jirovecii pneumonia			
subjects affected / exposed	0 / 34 (0.00%)	0 / 16 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	0 / 34 (0.00%)	0 / 16 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bacterial infection			
subjects affected / exposed	1 / 34 (2.94%)	0 / 16 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			

subjects affected / exposed	1 / 34 (2.94%)	0 / 16 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
Staphylococcal sepsis			
subjects affected / exposed	0 / 34 (0.00%)	0 / 16 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	0 / 34 (0.00%)	0 / 16 (0.00%)	1 / 18 (5.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia aspiration			
subjects affected / exposed	0 / 34 (0.00%)	0 / 16 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Covid-19 pneumonia			
subjects affected / exposed	1 / 34 (2.94%)	0 / 16 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Covid-19			
subjects affected / exposed	0 / 34 (0.00%)	2 / 16 (12.50%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Diabetes mellitus			
subjects affected / exposed	0 / 34 (0.00%)	0 / 16 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gout			
subjects affected / exposed	1 / 34 (2.94%)	0 / 16 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	DB period: Placebo		

Total subjects affected by serious adverse events			
subjects affected / exposed	8 / 33 (24.24%)		
number of deaths (all causes)	1		
number of deaths resulting from adverse events	1		
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	1 / 33 (3.03%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Lumbar vertebral fracture			
subjects affected / exposed	0 / 33 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Spinal fracture			
subjects affected / exposed	1 / 33 (3.03%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Thoracic vertebral fracture			
subjects affected / exposed	0 / 33 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Wound dehiscence			
subjects affected / exposed	0 / 33 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Hypotension			
subjects affected / exposed	0 / 33 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Cardiac failure acute			
subjects affected / exposed	1 / 33 (3.03%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Respiratory, thoracic and mediastinal disorders			
Pulmonary oedema			
subjects affected / exposed	1 / 33 (3.03%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Acute respiratory failure			
subjects affected / exposed	0 / 33 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Pemphigoid			
subjects affected / exposed	1 / 33 (3.03%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Henoch-schonlein purpura			
subjects affected / exposed	1 / 33 (3.03%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Osteoarthritis			
subjects affected / exposed	0 / 33 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Osteonecrosis			
subjects affected / exposed	1 / 33 (3.03%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Pneumocystis jirovecii pneumonia			
subjects affected / exposed	1 / 33 (3.03%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cellulitis			

subjects affected / exposed	1 / 33 (3.03%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Bacterial infection				
subjects affected / exposed	0 / 33 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumonia				
subjects affected / exposed	0 / 33 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Staphylococcal sepsis				
subjects affected / exposed	1 / 33 (3.03%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Sepsis				
subjects affected / exposed	1 / 33 (3.03%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumonia aspiration				
subjects affected / exposed	1 / 33 (3.03%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Covid-19 pneumonia				
subjects affected / exposed	0 / 33 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Covid-19				
subjects affected / exposed	0 / 33 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Metabolism and nutrition disorders				
Diabetes mellitus				

subjects affected / exposed	1 / 33 (3.03%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gout			
subjects affected / exposed	0 / 33 (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	DB period: Benralizumab	OLE period: Benralizumab (DB)/Benralizumab	OLE period: Placebo (DB)/Benralizumab (OLE)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	22 / 34 (64.71%)	8 / 16 (50.00%)	8 / 18 (44.44%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Skin papilloma			
subjects affected / exposed	0 / 34 (0.00%)	1 / 16 (6.25%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Vascular disorders			
Hypertension			
subjects affected / exposed	3 / 34 (8.82%)	1 / 16 (6.25%)	1 / 18 (5.56%)
occurrences (all)	5	1	1
Flushing			
subjects affected / exposed	0 / 34 (0.00%)	0 / 16 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	1 / 34 (2.94%)	0 / 16 (0.00%)	1 / 18 (5.56%)
occurrences (all)	1	0	1
Oedema peripheral			
subjects affected / exposed	4 / 34 (11.76%)	0 / 16 (0.00%)	0 / 18 (0.00%)
occurrences (all)	5	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			

subjects affected / exposed	1 / 34 (2.94%)	0 / 16 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Dyspnoea			
subjects affected / exposed	1 / 34 (2.94%)	1 / 16 (6.25%)	0 / 18 (0.00%)
occurrences (all)	1	1	0
Psychiatric disorders			
Delirium			
subjects affected / exposed	1 / 34 (2.94%)	0 / 16 (0.00%)	1 / 18 (5.56%)
occurrences (all)	1	0	1
Insomnia			
subjects affected / exposed	0 / 34 (0.00%)	1 / 16 (6.25%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Investigations			
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 34 (0.00%)	0 / 16 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Weight increased			
subjects affected / exposed	2 / 34 (5.88%)	0 / 16 (0.00%)	0 / 18 (0.00%)
occurrences (all)	2	0	0
Lymphocyte count decreased			
subjects affected / exposed	0 / 34 (0.00%)	0 / 16 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Heart rate increased			
subjects affected / exposed	0 / 34 (0.00%)	1 / 16 (6.25%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Gamma-glutamyltransferase increased			
subjects affected / exposed	2 / 34 (5.88%)	0 / 16 (0.00%)	0 / 18 (0.00%)
occurrences (all)	2	0	0
Injury, poisoning and procedural complications			
Fracture			
subjects affected / exposed	0 / 34 (0.00%)	1 / 16 (6.25%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Contusion			
subjects affected / exposed	0 / 34 (0.00%)	0 / 16 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0

Arthropod bite			
subjects affected / exposed	0 / 34 (0.00%)	0 / 16 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 34 (0.00%)	0 / 16 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Ventricular hypokinesia			
subjects affected / exposed	0 / 34 (0.00%)	0 / 16 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Coronary artery occlusion			
subjects affected / exposed	0 / 34 (0.00%)	1 / 16 (6.25%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 34 (2.94%)	0 / 16 (0.00%)	1 / 18 (5.56%)
occurrences (all)	1	0	1
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 34 (0.00%)	0 / 16 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Ocular hypertension			
subjects affected / exposed	0 / 34 (0.00%)	0 / 16 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Cataract			
subjects affected / exposed	1 / 34 (2.94%)	0 / 16 (0.00%)	1 / 18 (5.56%)
occurrences (all)	1	0	1
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	1 / 34 (2.94%)	0 / 16 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal disorder			
subjects affected / exposed	0 / 34 (0.00%)	0 / 16 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Haemorrhoids			

subjects affected / exposed	0 / 34 (0.00%)	0 / 16 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Hiatus hernia			
subjects affected / exposed	0 / 34 (0.00%)	1 / 16 (6.25%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Nausea			
subjects affected / exposed	0 / 34 (0.00%)	0 / 16 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Hepatobiliary disorders			
Hepatic function abnormal			
subjects affected / exposed	0 / 34 (0.00%)	0 / 16 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Skin and subcutaneous tissue disorders			
Skin ulcer			
subjects affected / exposed	0 / 34 (0.00%)	0 / 16 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Dermatitis contact			
subjects affected / exposed	2 / 34 (5.88%)	1 / 16 (6.25%)	0 / 18 (0.00%)
occurrences (all)	2	1	0
Eczema			
subjects affected / exposed	0 / 34 (0.00%)	1 / 16 (6.25%)	1 / 18 (5.56%)
occurrences (all)	0	4	1
Lichenoid keratosis			
subjects affected / exposed	0 / 34 (0.00%)	1 / 16 (6.25%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Miliaria			
subjects affected / exposed	1 / 34 (2.94%)	0 / 16 (0.00%)	1 / 18 (5.56%)
occurrences (all)	1	0	1
Urticaria			
subjects affected / exposed	2 / 34 (5.88%)	0 / 16 (0.00%)	1 / 18 (5.56%)
occurrences (all)	2	0	1
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 34 (0.00%)	0 / 16 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Renal impairment			

subjects affected / exposed	0 / 34 (0.00%)	0 / 16 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Haematuria			
subjects affected / exposed	0 / 34 (0.00%)	0 / 16 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 34 (0.00%)	2 / 16 (12.50%)	2 / 18 (11.11%)
occurrences (all)	0	2	2
Osteoarthritis			
subjects affected / exposed	0 / 34 (0.00%)	2 / 16 (12.50%)	0 / 18 (0.00%)
occurrences (all)	0	2	0
Back pain			
subjects affected / exposed	2 / 34 (5.88%)	0 / 16 (0.00%)	0 / 18 (0.00%)
occurrences (all)	2	0	0
Infections and infestations			
Oral candidiasis			
subjects affected / exposed	2 / 34 (5.88%)	0 / 16 (0.00%)	1 / 18 (5.56%)
occurrences (all)	2	0	1
Onychomycosis			
subjects affected / exposed	0 / 34 (0.00%)	0 / 16 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Nasopharyngitis			
subjects affected / exposed	2 / 34 (5.88%)	1 / 16 (6.25%)	1 / 18 (5.56%)
occurrences (all)	3	1	2
Herpes zoster			
subjects affected / exposed	4 / 34 (11.76%)	0 / 16 (0.00%)	0 / 18 (0.00%)
occurrences (all)	4	0	0
Coronavirus infection			
subjects affected / exposed	0 / 34 (0.00%)	0 / 16 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Bronchitis			
subjects affected / exposed	0 / 34 (0.00%)	0 / 16 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Body tinea			

subjects affected / exposed	0 / 34 (0.00%)	1 / 16 (6.25%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Covid-19			
subjects affected / exposed	6 / 34 (17.65%)	0 / 16 (0.00%)	1 / 18 (5.56%)
occurrences (all)	6	0	1
Urinary tract infection			
subjects affected / exposed	0 / 34 (0.00%)	0 / 16 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Tinea pedis			
subjects affected / exposed	0 / 34 (0.00%)	0 / 16 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Type 2 diabetes mellitus			
subjects affected / exposed	0 / 34 (0.00%)	1 / 16 (6.25%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Obesity			
subjects affected / exposed	0 / 34 (0.00%)	1 / 16 (6.25%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Hypoglycaemia			
subjects affected / exposed	0 / 34 (0.00%)	0 / 16 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Hypercholesterolaemia			
subjects affected / exposed	0 / 34 (0.00%)	1 / 16 (6.25%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Dehydration			
subjects affected / exposed	0 / 34 (0.00%)	1 / 16 (6.25%)	1 / 18 (5.56%)
occurrences (all)	0	1	1

Non-serious adverse events	DB period: Placebo		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	23 / 33 (69.70%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Skin papilloma			
subjects affected / exposed	0 / 33 (0.00%)		
occurrences (all)	0		
Vascular disorders			

Hypertension			
subjects affected / exposed	2 / 33 (6.06%)		
occurrences (all)	2		
Flushing			
subjects affected / exposed	0 / 33 (0.00%)		
occurrences (all)	0		
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	2 / 33 (6.06%)		
occurrences (all)	3		
Oedema peripheral			
subjects affected / exposed	2 / 33 (6.06%)		
occurrences (all)	2		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	2 / 33 (6.06%)		
occurrences (all)	2		
Dyspnoea			
subjects affected / exposed	0 / 33 (0.00%)		
occurrences (all)	0		
Psychiatric disorders			
Delirium			
subjects affected / exposed	0 / 33 (0.00%)		
occurrences (all)	0		
Insomnia			
subjects affected / exposed	1 / 33 (3.03%)		
occurrences (all)	1		
Investigations			
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 33 (0.00%)		
occurrences (all)	0		
Weight increased			
subjects affected / exposed	1 / 33 (3.03%)		
occurrences (all)	1		
Lymphocyte count decreased			

subjects affected / exposed	2 / 33 (6.06%)		
occurrences (all)	2		
Heart rate increased			
subjects affected / exposed	0 / 33 (0.00%)		
occurrences (all)	0		
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 33 (0.00%)		
occurrences (all)	0		
Injury, poisoning and procedural complications			
Fracture			
subjects affected / exposed	0 / 33 (0.00%)		
occurrences (all)	0		
Contusion			
subjects affected / exposed	3 / 33 (9.09%)		
occurrences (all)	4		
Arthropod bite			
subjects affected / exposed	0 / 33 (0.00%)		
occurrences (all)	0		
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 33 (0.00%)		
occurrences (all)	0		
Ventricular hypokinesia			
subjects affected / exposed	0 / 33 (0.00%)		
occurrences (all)	0		
Coronary artery occlusion			
subjects affected / exposed	0 / 33 (0.00%)		
occurrences (all)	0		
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 33 (0.00%)		
occurrences (all)	0		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	2 / 33 (6.06%)		
occurrences (all)	2		

Eye disorders			
Ocular hypertension			
subjects affected / exposed	0 / 33 (0.00%)		
occurrences (all)	0		
Cataract			
subjects affected / exposed	1 / 33 (3.03%)		
occurrences (all)	1		
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	2 / 33 (6.06%)		
occurrences (all)	2		
Gastrointestinal disorder			
subjects affected / exposed	0 / 33 (0.00%)		
occurrences (all)	0		
Haemorrhoids			
subjects affected / exposed	0 / 33 (0.00%)		
occurrences (all)	0		
Hiatus hernia			
subjects affected / exposed	0 / 33 (0.00%)		
occurrences (all)	0		
Nausea			
subjects affected / exposed	1 / 33 (3.03%)		
occurrences (all)	1		
Hepatobiliary disorders			
Hepatic function abnormal			
subjects affected / exposed	0 / 33 (0.00%)		
occurrences (all)	0		
Skin and subcutaneous tissue disorders			
Skin ulcer			
subjects affected / exposed	2 / 33 (6.06%)		
occurrences (all)	2		
Dermatitis contact			
subjects affected / exposed	0 / 33 (0.00%)		
occurrences (all)	0		
Eczema			
subjects affected / exposed	1 / 33 (3.03%)		
occurrences (all)	1		

Lichenoid keratosis subjects affected / exposed occurrences (all)	0 / 33 (0.00%) 0		
Miliaria subjects affected / exposed occurrences (all)	0 / 33 (0.00%) 0		
Urticaria subjects affected / exposed occurrences (all)	1 / 33 (3.03%) 1		
Renal and urinary disorders Acute kidney injury subjects affected / exposed occurrences (all)	2 / 33 (6.06%) 3		
Renal impairment subjects affected / exposed occurrences (all)	2 / 33 (6.06%) 2		
Haematuria subjects affected / exposed occurrences (all)	2 / 33 (6.06%) 2		
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all)	2 / 33 (6.06%) 2		
Osteoarthritis subjects affected / exposed occurrences (all)	0 / 33 (0.00%) 0		
Back pain subjects affected / exposed occurrences (all)	2 / 33 (6.06%) 2		
Infections and infestations Oral candidiasis subjects affected / exposed occurrences (all)	1 / 33 (3.03%) 1		
Onychomycosis subjects affected / exposed occurrences (all)	0 / 33 (0.00%) 0		

Nasopharyngitis subjects affected / exposed occurrences (all)	0 / 33 (0.00%) 0		
Herpes zoster subjects affected / exposed occurrences (all)	2 / 33 (6.06%) 2		
Coronavirus infection subjects affected / exposed occurrences (all)	0 / 33 (0.00%) 0		
Bronchitis subjects affected / exposed occurrences (all)	1 / 33 (3.03%) 1		
Body tinea subjects affected / exposed occurrences (all)	0 / 33 (0.00%) 0		
Covid-19 subjects affected / exposed occurrences (all)	4 / 33 (12.12%) 4		
Urinary tract infection subjects affected / exposed occurrences (all)	2 / 33 (6.06%) 2		
Tinea pedis subjects affected / exposed occurrences (all)	2 / 33 (6.06%) 2		
Metabolism and nutrition disorders Type 2 diabetes mellitus subjects affected / exposed occurrences (all)	0 / 33 (0.00%) 0		
Obesity subjects affected / exposed occurrences (all)	0 / 33 (0.00%) 0		
Hypoglycaemia subjects affected / exposed occurrences (all)	2 / 33 (6.06%) 2		
Hypercholesterolaemia			

subjects affected / exposed	0 / 33 (0.00%)		
occurrences (all)	0		
Dehydration			
subjects affected / exposed	0 / 33 (0.00%)		
occurrences (all)	0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
30 November 2020	The primary reason for this amendment was to take regulatory feedback into account. Primary endpoint text changed to 'a responder is defined as a participant who is in complete remission while off OCS for ≥ 2 months at Week 36' instead of 'a responder is defined as a participant who is in partial or complete remission off OCS for ≥ 2 months at Week 36'.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

The study was terminated following a pre-planned futility analysis as the efficacy results did not pass the pre-defined futility hurdle with no new safety concerns.

Notes: