Clinical trial results:
A Multicentre, Double-blind, Randomized, Parallel Group, Phase 3 Safety Extension Study to Evaluate the Safety and Tolerability of Benralizumab (MEDI-563) in Asthmatic Adults and Adolescents on Inhaled Corticosteroid Plus Long-acting 2 Agonist (BORA)

Summary

EudraCT number	2014-001086-27
Trial protocol	GB CZ PL DE SE BG ES FR
Global end of trial date	14 August 2018

Results information

Result version number	v2 (current)
This version publication date	25 July 2019
First version publication date	27 December 2018
Version creation reason	

Trial information

Trial identification

Sponsor protocol code	D3250C00021

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02258542
WHO universal trial number (UTN)	U1111-1162-2422

Notes:

Sponsors

Sponsor organisation name	AstraZeneca AB
Sponsor organisation address	Vastra Malarehamnen 9, Sodertalje, Sweden, 151 85
Public contact	Ubaldo Martin, Global Clinical Lead Benralizumab, AstraZeneca AB, Ubaldo.Martin@astrazeneca.com
Scientific contact	AZ Clinical Study Information, AstraZeneca AB, 46 855 326000, 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	Interim
Date of interim/final analysis	31 January 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	18 October 2017
Global end of trial reached?	Yes
Global end of trial date	14 August 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

1. To assess the safety and tolerability of 2 dosing regimens of benralizumab for adult patients during the 56-week treatment period and through the follow-up period (16 weeks from day of last dose) 2. To assess the safety and tolerability of 2 dosing regimens of benralizumab for adolescent patients during the 108-week treatment period and through the follow-up period (16 weeks from day of last dose)

Protection of trial subjects:

Data safety monitoring board (DSMB) evaluates cumulative safety and other clinical trial data at regular intervals and making appropriate recommendations based on the available data. The DSMB functions independently of all other individuals associated with the conduct of the studies, including the study sponsor, AstraZeneca. The committee operates in accordance with a DSMB charter.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	19 November 2014
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	Argentina: 220
Country: Number of subjects enrolled	Australia: 36
Country: Number of subjects enrolled	Brazil: 31
Country: Number of subjects enrolled	Bulgaria: 93
Country: Number of subjects enrolled	Canada: 74
Country: Number of subjects enrolled	Chile: 30
Country: Number of subjects enrolled	Czech Republic: 42
Country: Number of subjects enrolled	France: 83
Country: Number of subjects enrolled	Germany: 178
Country: Number of subjects enrolled	Japan: 73
Country: Number of subjects enrolled	Peru: 50
Country: Number of subjects enrolled	Philippines: 60
Country: Number of subjects enrolled	Poland: 355
Country: Number of subjects enrolled	Romania: 41
Country: Number of subjects enrolled	Russian Federation: 130
Country: Number of subjects enrolled	South Africa: 17
Country: Number of subjects enrolled	Korea, Republic of: 124
Country: Number of subjects enrolled	Spain: 35

Country: Number of subjects enrolled	Sweden: 8
Country: Number of subjects enrolled	Turkey: 42
Country: Number of subjects enrolled	Ukraine: 114
Country: Number of subjects enrolled	United Kingdom: 35
Country: Number of subjects enrolled	United States: 254
Country: Number of subjects enrolled	Vietnam: 8
Worldwide total number of subjects	2133
EEA total number of subjects	870

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)	0
Adolescents (12-17 years)	72
Adults (18-64 years)	1742
From 65 to 84 years	319
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

2133 patients entered BORA. 10 were excluded due to a GCP breach. Of remaining 2123 patients, 1926 entered from SIROCCO/CALIMA and 197 from ZONDA. 2 patients were not treated, and a total of 447 patients (348 SIROCCO/CALIMA and 99 ZONDA) were later enrolled into MELTEMI without completing the follow-up in BORA, so not in the main analyses.

Pre-assignment

Screening details:

953 participants from SIROCCO/CALIMA receive benralizumab 30 mg at every 4 weeks during BORA. 971 participants from SIROCCO/CALIMA receive treatment at every 8 weeks during BORA. 100 participants from ZONDA receive treatment at every 4 weeks during BORA. 97 participants from study ZONDA receive treatment at every 8 weeks during BORA.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	SIROCCO/CALIMA - Benralizumab 30 mg q.4 weeks

Arm description:

Benralizumab administered subcutaneously every 4 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:

30 mg

Arm title	SIROCCO/CALIMA - Benralizumab 30 mg q.8 weeks

Arm description:

Benralizumab administered subcutaneously every 8 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:

30 mg

Arm title	ZONDA - Benralizumab 30 mg q.4 weeks

Arm description:

Benralizumab administered subcutaneously every 4 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:

30 mg

Arm title	ZONDA - Benralizumab 30 mg q.8 weeks

Arm description:

Benralizumab administered subcutaneously every 8 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:

30 mg

Number of subjects in period 1[1]	SIROCCO/CALIMA - Benralizumab 30 mg q.4 weeks	SIROCCO/CALIMA - Benralizumab 30 mg q.8 weeks	ZONDA - Benralizumab 30 mg q.4 weeks
Started	953	973	100
Treated	953	971	100
Completed	911	924	92
Not completed	42	49	8
Adverse event, serious fatal	5	4	-
Consent withdrawn by subject	20	20	7
Eligibility criteria not fulfilled	-	2	-
Adverse event, non-fatal	3	4	-
study specific discount. criteria	1	1	-
Lost to follow-up	5	12	1
eg. not made to the visit	7	4	-
Protocol deviation	1	2	-

Number of subjects in period 1[1]	ZONDA - Benralizumab 30 mg q.8 weeks
Started	97
Treated	97
Completed	92
Not completed	5
Adverse event, serious fatal	1
Consent withdrawn by subject	1
Eligibility criteria not fulfilled	-

Adverse event, non-fatal	-
study specific discount. criteria	-
Lost to follow-up	2
eg. not made to the visit	1
Protocol deviation	-

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: 10 patients in total were excluded from all analyses due to GCP breach.

Baseline characteristics

Reporting groups	
Reporting group title	SIROCCO/CALIMA - Benralizumab 30 mg q.4 weeks
Reporting group description: Benralizumab administered subcutaneously every 4 weeks	
Reporting group title	SIROCCO/CALIMA - Benralizumab 30 mg q.8 weeks
Reporting group description: Benralizumab administered subcutaneously every 8 weeks	
Reporting group title	ZONDA - Benralizumab 30 mg q.4 weeks
Reporting group description: Benralizumab administered subcutaneously every 4 weeks	
Reporting group title	ZONDA - Benralizumab 30 mg q.8 weeks
Reporting group description: Benralizumab administered subcutaneously every 8 weeks	

Reporting group values	SIROCCO/CALIMA - Benralizumab 30 mg q.4 weeks	SIROCCO/CALIMA - Benralizumab 30 mg q.8 weeks	ZONDA - Benralizumab 30 mg q.4 weeks
Number of subjects	953	973	100
Age categorical Units: Subjects			
Adolescents (12-17 years)	21	51	0
Adults (18-64 years)	773	790	86
From 65-84 years	159	132	14
Age Continuous Units: Years			
arithmetic mean	51.1	48.9	49.7
standard deviation	± 13.79	± 15.53	± 10.35
Sex: Female, Male Units: Subjects			
Female	612	584	58
Male	341	389	42
Race/Ethnicity, Customized Units: Subjects			
White	753	774	96
Black and African American	25	30	0
Asian	143	139	4
Other	32	30	0

Reporting group values	ZONDA - Benralizumab 30 mg q.8 weeks	Total	
Number of subjects	97	2123	
Age categorical Units: Subjects			
Adolescents (12-17 years)	0	72	
Adults (18-64 years)	83	1732	
From 65-84 years	14	319	

Age Continuous Units: Years			
arithmetic mean	52.7		
standard deviation	± 8.90	-	
Sex: Female, Male Units: Subjects			
Female	61	1315	
Male	36	808	
Race/Ethnicity, Customized Units: Subjects			
White	88	1711	
Black and African American	2	57	
Asian	7	293	
Other	0	62	

Subject analysis sets

Subject analysis set title	SIROCCO/CALIMA - Benralizumab 30 mg q.4 - Pre Benra q.4
Subject analysis set type	Full analysis
Subject analysis set description: Benralizumab administered subcutaneously every 4 weeks, predecessor study with benralizumab treatment	
Subject analysis set title	SIROCCO/CALIMA - Benralizumab 30 mg q.4 - Predecessor Placebo
Subject analysis set type	Full analysis
Subject analysis set description: Benralizumab administered subcutaneously every 4 weeks, predecessor study with placebo treatment	
Subject analysis set title	SIROCCO/CALIMA - Benralizumab 30 mg q.8 - Pre Benra q.8
Subject analysis set type	Full analysis
Subject analysis set description: Benralizumab administered subcutaneously every 8 weeks, predecessor study with benralizumab treatment	
Subject analysis set title	SIROCCO/CALIMA - Benralizumab 30 mg q.8 - Predecessor Placebo
Subject analysis set type	Full analysis
Subject analysis set description: Benralizumab administered subcutaneously every 8 weeks, predecessor study with placebo treatment	
Subject analysis set title	ZONDA - Benralizumab 30 mg q.4 - Pre Benra q.4
Subject analysis set type	Full analysis
Subject analysis set description: Benralizumab administered subcutaneously every 4 weeks, predecessor study with benralizumab treatment	
Subject analysis set title	ZONDA - Benralizumab 30 mg q.4 - Predecessor Placebo
Subject analysis set type	Full analysis
Subject analysis set description: Benralizumab administered subcutaneously every 4 weeks, predecessor study with placebo treatment	
Subject analysis set title	ZONDA - Benralizumab 30 mg q.8 - Pre Benra q.8
Subject analysis set type	Full analysis
Subject analysis set description: Benralizumab administered subcutaneously every 8 weeks, predecessor study with benralizumab treatment	
Subject analysis set title	ZONDA - Benralizumab 30 mg q.8 - Predecessor Placebo
Subject analysis set type	Full analysis

Subject analysis set description:

Benralizumab administered subcutaneously every 8 weeks, predecessor study with placebo treatment

Subject analysis set title	SIROCCO/CALIMA - Benra 30 mg q.4 - Pre Benra q.4-adolescents
Subject analysis set type	Full analysis

Subject analysis set description:

Benralizumab administered subcutaneously every 4 weeks, predecessor study with benralizumab treatment-adolescents only

Subject analysis set title	SIROCCO/CALIMA - Benra 30 mg q.4 - Predecessor Pbo-adolescents
Subject analysis set type	Full analysis

Subject analysis set description:

Benralizumab administered subcutaneously every 4 weeks, predecessor study with placebo treatment-adolescents only

Subject analysis set title	SIROCCO/CALIMA - Benra 30 mg q.8 - Pre Benra q.8-adolescents
Subject analysis set type	Full analysis

Subject analysis set description:

Benralizumab administered subcutaneously every 8 weeks, predecessor study with benralizumab treatment- adolescents only

Subject analysis set title	SIROCCO/CALIMA - Benra 30 mg q.8 - Predecessor Pbo-adolescents
Subject analysis set type	Full analysis

Subject analysis set description:

Benralizumab administered subcutaneously every 8 weeks, predecessor study with placebo treatment

Reporting group values	SIROCCO/CALIMA - Benralizumab 30 mg q.4 - Pre Benra q.4	SIROCCO/CALIMA - Benralizumab 30 mg q.4 - Predecessor Placebo	SIROCCO/CALIMA - Benralizumab 30 mg q.8 - Pre Benra q.8
Number of subjects	518	265	512
Age categorical Units: Subjects			
Adolescents (12-17 years)	12	9	25
Adults (18-64 years)	421	213	421
From 65-84 years	85	43	66
Age Continuous Units: Years			
arithmetic mean	51.7	49.9	49.3
standard deviation	± 13.26	± 14.73	± 14.81
Sex: Female, Male Units: Subjects			
Female	339	164	307
Male	179	101	205
Race/Ethnicity, Customized Units: Subjects			
White	398	201	388
Black and African American	6	10	12
Asian	94	44	92
Other	20	10	20

Reporting group values	SIROCCO/CALIMA - Benralizumab 30 mg q.8 - Predecessor Placebo	ZONDA - Benralizumab 30 mg q.4 - Pre Benra q.4	ZONDA - Benralizumab 30 mg q.4 - Predecessor Placebo
Number of subjects	281	31	18

Age categorical Units: Subjects			
Adolescents (12-17 years)	26	0	0
Adults (18-64 years)	211	30	16
From 65-84 years	44	1	2
Age Continuous Units: Years			
arithmetic mean	48.2	47.9	52.7
standard deviation	± 16.77	± 10.42	± 9.77
Sex: Female, Male Units: Subjects			
Female	163	13	14
Male	118	18	4
Race/Ethnicity, Customized Units: Subjects			
White	224	28	17
Black and African American	7	0	0
Asian	44	3	1
Other	6	0	0

Reporting group values	ZONDA - Benralizumab 30 mg q.8 - Pre Benra q.8	ZONDA - Benralizumab 30 mg q.8 - Predecessor Placebo	SIROCCO/CALIMA - Benra 30 mg q.4 - Pre Benra q.4-adolescents
Number of subjects	31	18	14
Age categorical Units: Subjects			
Adolescents (12-17 years)	0	0	14
Adults (18-64 years)	11	17	0
From 65-84 years	20	1	0
Age Continuous Units: Years			
arithmetic mean	54.3	49.9	14.6
standard deviation	± 8.39	± 9.30	± 1.39
Sex: Female, Male Units: Subjects			
Female	20	9	6
Male	11	9	8
Race/Ethnicity, Customized Units: Subjects			
White	26	16	10
Black and African American	0	1	1
Asian	5	1	0
Other	0	0	3

Reporting group values	SIROCCO/CALIMA - Benra 30 mg q.4 - Predecessor Pbo-adolescents	SIROCCO/CALIMA - Benra 30 mg q.8 - Pre Benra q.8-adolescents	SIROCCO/CALIMA - Benra 30 mg q.8 - Predecessor Pbo-adolescents
Number of subjects	11	32	29
Age categorical Units: Subjects			
Adolescents (12-17 years)	11	32	29
Adults (18-64 years)	0	0	0

From 65-84 years	0	0	0

Age Continuous Units: Years			
arithmetic mean	14.5	14.4	13.9
standard deviation	± 1.51	± 1.85	± 1.77
Sex: Female, Male Units: Subjects			
Female	4	13	12
Male	7	19	17
Race/Ethnicity, Customized Units: Subjects			
White	8	27	28
Black and African American	2	1	0
Asian	0	0	1
Other	1	4	0

End points

End points reporting groups

Reporting group title	SIROCCO/CALIMA - Benralizumab 30 mg q.4 weeks
Reporting group description: Benralizumab administered subcutaneously every 4 weeks	
Reporting group title	SIROCCO/CALIMA - Benralizumab 30 mg q.8 weeks
Reporting group description: Benralizumab administered subcutaneously every 8 weeks	
Reporting group title	ZONDA - Benralizumab 30 mg q.4 weeks
Reporting group description: Benralizumab administered subcutaneously every 4 weeks	
Reporting group title	ZONDA - Benralizumab 30 mg q.8 weeks
Reporting group description: Benralizumab administered subcutaneously every 8 weeks	
Subject analysis set title	SIROCCO/CALIMA - Benralizumab 30 mg q.4 - Pre Benra q.4
Subject analysis set type	Full analysis
Subject analysis set description: Benralizumab administered subcutaneously every 4 weeks, predecessor study with benralizumab treatment	
Subject analysis set title	SIROCCO/CALIMA - Benralizumab 30 mg q.4 - Predecessor Placebo
Subject analysis set type	Full analysis
Subject analysis set description: Benralizumab administered subcutaneously every 4 weeks, predecessor study with placebo treatment	
Subject analysis set title	SIROCCO/CALIMA - Benralizumab 30 mg q.8 - Pre Benra q.8
Subject analysis set type	Full analysis
Subject analysis set description: Benralizumab administered subcutaneously every 8 weeks, predecessor study with benralizumab treatment	
Subject analysis set title	SIROCCO/CALIMA - Benralizumab 30 mg q.8 - Predecessor Placebo
Subject analysis set type	Full analysis
Subject analysis set description: Benralizumab administered subcutaneously every 8 weeks, predecessor study with placebo treatment	
Subject analysis set title	ZONDA - Benralizumab 30 mg q.4 - Pre Benra q.4
Subject analysis set type	Full analysis
Subject analysis set description: Benralizumab administered subcutaneously every 4 weeks, predecessor study with benralizumab treatment	
Subject analysis set title	ZONDA - Benralizumab 30 mg q.4 - Predecessor Placebo
Subject analysis set type	Full analysis
Subject analysis set description: Benralizumab administered subcutaneously every 4 weeks, predecessor study with placebo treatment	
Subject analysis set title	ZONDA - Benralizumab 30 mg q.8 - Pre Benra q.8
Subject analysis set type	Full analysis
Subject analysis set description: Benralizumab administered subcutaneously every 8 weeks, predecessor study with benralizumab treatment	
Subject analysis set title	ZONDA - Benralizumab 30 mg q.8 - Predecessor Placebo
Subject analysis set type	Full analysis

Subject analysis set description:

Benralizumab administered subcutaneously every 8 weeks, predecessor study with placebo treatment

Subject analysis set title	SIROCCO/CALIMA - Benra 30 mg q.4 - Pre Benra q.4-adolescents
Subject analysis set type	Full analysis

Subject analysis set description:

Benralizumab administered subcutaneously every 4 weeks, predecessor study with benralizumab treatment-adolescents only

Subject analysis set title	SIROCCO/CALIMA - Benra 30 mg q.4 - Predecessor Pbo-adolescents
Subject analysis set type	Full analysis

Subject analysis set description:

Benralizumab administered subcutaneously every 4 weeks, predecessor study with placebo treatment-adolescents only

Subject analysis set title	SIROCCO/CALIMA - Benra 30 mg q.8 - Pre Benra q.8-adolescents
Subject analysis set type	Full analysis

Subject analysis set description:

Benralizumab administered subcutaneously every 8 weeks, predecessor study with benralizumab treatment- adolescents only

Subject analysis set title	SIROCCO/CALIMA - Benra 30 mg q.8 - Predecessor Pbo-adolescents
Subject analysis set type	Full analysis

Subject analysis set description:

Benralizumab administered subcutaneously every 8 weeks, predecessor study with placebo treatment

Primary: Change from baseline in Basophils, Full analysis set, Excluding MELTEMI patients

End point title	Change from baseline in Basophils, Full analysis set, Excluding MELTEMI patients[1]

End point description:

Change from baseline in hematologic lab parameter of Basophils.

End point type	Primary

End point timeframe:

Week 56

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: This is safety study and use safety endpoints as primary, only descriptive summary is planned. No statistical power or hypothesis testing is planned.

End point values	SIROCCO/CALIMA - Benralizumab 30 mg q.4 weeks	SIROCCO/CALIMA - Benralizumab 30 mg q.8 weeks	ZONDA - Benralizumab 30 mg q.4 weeks	ZONDA - Benralizumab 30 mg q.8 weeks
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	691	703	39	42
Units: 10^9 cells/L				
arithmetic mean (standard deviation)	-0.005 (± 0.0223)	-0.005 (± 0.0239)	-0.007 (± 0.0283)	-0.005 (± 0.0244)

Statistical analyses

No statistical analyses for this end point

Primary: Change from baseline in Basophils, Full analysis set, adolescents only

End point title	Change from baseline in Basophils, Full analysis set, adolescents only[2][3]

End point description:

Change from baseline in hematologic lab parameter of Basophils.

End point type	Primary

End point timeframe:

Week 108

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: This is safety study and use safety endpoints as primary, only descriptive summary is planned. No statistical power or hypothesis testing is planned.
[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This is safety study and use safety endpoints as primary, only descriptive summary is planned. No statistical power or hypothesis testing is planned.

End point values	SIROCCO/CALIMA - Benralizumab 30 mg q.4 weeks	SIROCCO/CALIMA - Benralizumab 30 mg q.8 weeks		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16	45		
Units: 10^9 cells/L				
arithmetic mean (standard deviation)	-0.006 (± 0.0145)	0.001 (± 0.0208)		

Statistical analyses

No statistical analyses for this end point

Primary: Change from baseline in Leukocytes, Full analysis set, Excluding MELTEMI patients

End point title	Change from baseline in Leukocytes, Full analysis set, Excluding MELTEMI patients[4]

End point description:

Change from baseline in hematologic lab parameter of Leukocytes.

End point type	Primary

End point timeframe:

Week 56

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: This is safety study and use safety endpoints as primary, only descriptive summary is planned. No statistical power or hypothesis testing is planned.

End point values	SIROCCO/CALIMA - Benralizumab 30 mg q.4 weeks	SIROCCO/CALIMA - Benralizumab 30 mg q.8 weeks	ZONDA - Benralizumab 30 mg q.4 weeks	ZONDA - Benralizumab 30 mg q.8 weeks
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	695	710	39	42
Units: 10^9 cells/L				
arithmetic mean (standard deviation)	-0.344 (± 2.0412)	-0.128 (± 1.8614)	-0.808 (± 1.8177)	-0.507 (± 3.3612)

Statistical analyses

No statistical analyses for this end point

Primary: Change from baseline in Leukocytes, Full analysis set, adolescents only

End point title	Change from baseline in Leukocytes, Full analysis set, adolescents only[5][6]

End point description:

Change from baseline in hematologic lab parameter of Leukocytes.

End point type	Primary

End point timeframe:

Week 108

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: This is safety study and use safety endpoints as primary, only descriptive summary is planned. No statistical power or hypothesis testing is planned.
[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This is safety study and use safety endpoints as primary, only descriptive summary is planned. No statistical power or hypothesis testing is planned.

End point values	SIROCCO/CALIMA - Benralizumab 30 mg q.4 weeks	SIROCCO/CALIMA - Benralizumab 30 mg q.8 weeks		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16	47		
Units: 10^9 cells/L				
arithmetic mean (standard deviation)	-0.487 (± 1.7289)	-0.079 (± 1.8432)		

Statistical analyses

No statistical analyses for this end point

Primary: Change from baseline in Lymphocytes, Full analysis set, Excluding MELTEMI patients

End point title	Change from baseline in Lymphocytes, Full analysis set, Excluding MELTEMI patients[7]

End point description:

Change from baseline in hematologic lab parameter of Lymphocytes.

End point type	Primary

End point timeframe:

Week 56

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: This is safety study and use safety endpoints as primary, only descriptive summary is planned. No statistical power or hypothesis testing is planned.

End point values	SIROCCO/CALIMA - Benralizumab 30 mg q.4 weeks	SIROCCO/CALIMA - Benralizumab 30 mg q.8 weeks	ZONDA - Benralizumab 30 mg q.4 weeks	ZONDA - Benralizumab 30 mg q.8 weeks
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	691	703	39	42
Units: 10^9 cells/L				
arithmetic mean (standard deviation)	-0.032 (± 0.6242)	0.003 (± 0.5402)	-0.093 (± 0.6403)	0.007 (± 0.6864)

Statistical analyses

No statistical analyses for this end point

Primary: Change from baseline in Lymphocytes, Full analysis set, adolescents only

End point title	Change from baseline in Lymphocytes, Full analysis set, adolescents only[8][9]

End point description:

Change from baseline in hematologic lab parameter of Lymphocytes.

End point type	Primary

End point timeframe:

Week 108

Notes:

[8] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: This is safety study and use safety endpoints as primary, only descriptive summary is planned. No statistical power or hypothesis testing is planned.
[9] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This is safety study and use safety endpoints as primary, only descriptive summary is planned. No statistical power or hypothesis testing is planned.

End point values	SIROCCO/CALIMA - Benralizumab 30 mg q.4 weeks	SIROCCO/CALIMA - Benralizumab 30 mg q.8 weeks		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16	45		
Units: 10^9 cells/L				
arithmetic mean (standard deviation)	-0.180 (± 0.6946)	-0.070 (± 0.6671)		

Statistical analyses

No statistical analyses for this end point

Primary: Change from baseline in Neutrophils, Full analysis set, Excluding MELTEMI patients

End point title	Change from baseline in Neutrophils, Full analysis set, Excluding MELTEMI patients[10]

End point description:

Change from baseline in hematologic lab parameter of Neutrophils.

End point type	Primary

End point timeframe:

Week 56

Notes:

[10] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: This is safety study and use safety endpoints as primary, only descriptive summary is planned. No statistical power or hypothesis testing is planned.

End point values	SIROCCO/CALIMA - Benralizumab 30 mg q.4 weeks	SIROCCO/CALIMA - Benralizumab 30 mg q.8 weeks	ZONDA - Benralizumab 30 mg q.4 weeks	ZONDA - Benralizumab 30 mg q.8 weeks
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	691	703	39	42
Units: 10^9 cells/L				
arithmetic mean (standard deviation)	-0.171 (± 1.8746)	0.013 (± 1.7024)	-0.501 (± 1.7096)	-0.368 (± 3.2057)

Statistical analyses

No statistical analyses for this end point

Primary: Change from baseline in Neutrophils, Full analysis set, adolescents only

End point title	Change from baseline in Neutrophils, Full analysis set, adolescents only[11][12]

End point description:

Change from baseline in hematologic lab parameter of Neutrophils.

End point type	Primary

End point timeframe:

Week 108

Notes:

[11] - 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: This is safety study and use safety endpoints as primary, only descriptive summary is

planned. No statistical power or hypothesis testing is planned.

[12] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This is safety study and use safety endpoints as primary, only descriptive summary is planned. No statistical power or hypothesis testing is planned.

End point values	SIROCCO/CALIMA - Benralizumab 30 mg q.4 weeks	SIROCCO/CALIMA - Benralizumab 30 mg q.8 weeks		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16	45		
Units: 10^9 cells/L				
arithmetic mean (standard deviation)	-0.451 (± 1.7645)	0.242 (± 1.8469)		

Statistical analyses

No statistical analyses for this end point

Primary: Change from baseline in Eosinophils, Full analysis set, Excluding MELTEMI patients

End point title	Change from baseline in Eosinophils, Full analysis set, Excluding MELTEMI patients[13]

End point description:

Change from baseline in hematologic lab parameter of Eosinophils.

End point type	Primary

End point timeframe:

Week 56

Notes:

[13] - 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: This is safety study and use safety endpoints as primary, only descriptive summary is planned. No statistical power or hypothesis testing is planned.

End point values	SIROCCO/CALIMA - Benralizumab 30 mg q.4 weeks	SIROCCO/CALIMA - Benralizumab 30 mg q.8 weeks	ZONDA - Benralizumab 30 mg q.4 weeks	ZONDA - Benralizumab 30 mg q.8 weeks
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	691	703	39	42
Units: 10^9 cells/L				
arithmetic mean (standard deviation)	-0.1220 (± 0.30599)	-0.1271 (± 0.26161)	-0.1451 (± 0.30766)	-0.1664 (± 0.35139)

Statistical analyses

No statistical analyses for this end point

Primary: Change from baseline in Eosinophils, Full analysis set, adolescents only

End point title	Change from baseline in Eosinophils, Full analysis set, adolescents only[14][15]

End point description:

Change from baseline in hematologic lab parameter of Eosinophils.

End point type	Primary

End point timeframe:

Week 108

Notes:

[14] - 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: This is safety study and use safety endpoints as primary, only descriptive summary is planned. No statistical power or hypothesis testing is planned.
[15] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This is safety study and use safety endpoints as primary, only descriptive summary is planned. No statistical power or hypothesis testing is planned.

End point values	SIROCCO/CALIMA - Benralizumab 30 mg q.4 weeks	SIROCCO/CALIMA - Benralizumab 30 mg q.8 weeks		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16	45		
Units: 10^9 cells/L				
arithmetic mean (standard deviation)	-0.1294 (± 0.27973)	-0.1838 (± 0.3381)		

Statistical analyses

No statistical analyses for this end point

Primary: Change from baseline in ALT, Full analysis set, Excluding MELTEMI patients

End point title	Change from baseline in ALT, Full analysis set, Excluding MELTEMI patients[16]

End point description:

Change from baseline in chemistry tests ALT.

End point type	Primary

End point timeframe:

Week 56

Notes:

[16] - 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: This is safety study and use safety endpoints as primary, only descriptive summary is planned. No statistical power or hypothesis testing is planned.

End point values	SIROCCO/CALIMA - Benralizumab 30 mg q.4 weeks	SIROCCO/CALIMA - Benralizumab 30 mg q.8 weeks	ZONDA - Benralizumab 30 mg q.4 weeks	ZONDA - Benralizumab 30 mg q.8 weeks
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	684	712	37	43
Units: ukat/L				
arithmetic mean (standard deviation)	-0.007 (± 0.2102)	0.017 (± 0.4651)	-0.064 (± 0.3547)	-0.023 (± 0.1940)

Statistical analyses

No statistical analyses for this end point

Primary: Change from baseline in ALT, Full analysis set, adolescents only

End point title	Change from baseline in ALT, Full analysis set, adolescents

End point description:

Change from baseline in hematologic lab parameter of ALT.

End point type	Primary

End point timeframe:

Week 108

Notes:

[17] - 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: This is safety study and use safety endpoints as primary, only descriptive summary is planned. No statistical power or hypothesis testing is planned.
[18] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This is safety study and use safety endpoints as primary, only descriptive summary is planned. No statistical power or hypothesis testing is planned.

End point values	SIROCCO/CALIMA - Benralizumab 30 mg q.4 weeks	SIROCCO/CALIMA - Benralizumab 30 mg q.8 weeks		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	17	51		
Units: ukat/L				
arithmetic mean (standard deviation)	0.048 (± 0.2195)	0.034 (± 0.2312)		

Statistical analyses

No statistical analyses for this end point

Primary: Change from baseline in AST, Full analysis set, Excluding MELTEMI patients

End point title	Change from baseline in AST, Full analysis set, Excluding MELTEMI patients[19]

End point description:

Change from baseline in chemistry tests AST.

End point type	Primary

End point timeframe:

Week 56

Notes:

[19] - 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: This is safety study and use safety endpoints as primary, only descriptive summary is planned. No statistical power or hypothesis testing is planned.

End point values	SIROCCO/CALIMA - Benralizumab 30 mg q.4 weeks	SIROCCO/CALIMA - Benralizumab 30 mg q.8 weeks	ZONDA - Benralizumab 30 mg q.4 weeks	ZONDA - Benralizumab 30 mg q.8 weeks
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	684	712	37	43
Units: ukat/L				
arithmetic mean (standard deviation)	-0.005 (± 0.1431)	0.004 (± 0.3303)	-0.027 (± 0.2291)	-0.026 (± 0.1178)

Statistical analyses

No statistical analyses for this end point

Primary: Change from baseline in AST, Full analysis set, adolescents only

End point title	Change from baseline in AST, Full analysis set, adolescents only[20][21]

End point description:

Change from baseline in hematologic lab parameter of AST.

End point type	Primary

End point timeframe:

Week 108

Notes:

[20] - 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: This is safety study and use safety endpoints as primary, only descriptive summary is planned. No statistical power or hypothesis testing is planned.
[21] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This is safety study and use safety endpoints as primary, only descriptive summary is planned. No statistical power or hypothesis testing is planned.

End point values	SIROCCO/CALIMA - Benralizumab 30 mg q.4 weeks	SIROCCO/CALIMA - Benralizumab 30 mg q.8 weeks		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	17	50		
Units: ukat/L				
arithmetic mean (standard deviation)	-0.006 (± 0.1196)	-0.013 (± 0.1297)		

Statistical analyses

No statistical analyses for this end point

Primary: Change from baseline in Bilirubin, Full analysis set, Excluding MELTEMI patients

End point title	Change from baseline in Bilirubin, Full analysis set, Excluding MELTEMI patients[22]

End point description:

Change from baseline in chemistry test Bilirubin.

End point type	Primary

End point timeframe:

Week 56

Notes:

[22] - 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: This is safety study and use safety endpoints as primary, only descriptive summary is planned. No statistical power or hypothesis testing is planned.

End point values	SIROCCO/CALIMA - Benralizumab 30 mg q.4 weeks	SIROCCO/CALIMA - Benralizumab 30 mg q.8 weeks	ZONDA - Benralizumab 30 mg q.4 weeks	ZONDA - Benralizumab 30 mg q.8 weeks
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	685	712	37	43
Units: umol/L				
arithmetic mean (standard deviation)	0.187 (± 3.6261)	0.391 (± 3.9945)	0.146 (± 2.8094)	0.279 (± 3.8765)

Statistical analyses

No statistical analyses for this end point

Primary: Change from baseline in Bilirubin, Full analysis set, adolescents only

End point title	Change from baseline in Bilirubin, Full analysis set, adolescents only[23][24]

End point description:

Change from baseline in hematologic lab parameter of Bilirubin.

End point type	Primary

End point timeframe:

Week 108

Notes:

[23] - 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: This is safety study and use safety endpoints as primary, only descriptive summary is

planned. No statistical power or hypothesis testing is planned.

[24] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This is safety study and use safety endpoints as primary, only descriptive summary is planned. No statistical power or hypothesis testing is planned.

End point values	SIROCCO/CALIMA - Benralizumab 30 mg q.4 weeks	SIROCCO/CALIMA - Benralizumab 30 mg q.8 weeks		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	17	51		
Units: umol/L				
arithmetic mean (standard deviation)	2.221 (± 8.3453)	0.202 (± 3.6575)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of overall patients with asthma exacerbations during study period

End point title	Number of overall patients with asthma exacerbations during study period

End point description:

Annual asthma exacerbation rate, where an asthma exacerbation is defined by a worsening of asthma requiring the use of systemic corticosteroids for at least 3 days, and/or an in patient hospitalization, and/or an emergency department or urgent care visit

End point type	Secondary

End point timeframe:

From week 0 to week 56 in study treatment period and through the follow up period (16 weeks from day of last dose)

End point values	SIROCCO/CALIMA - Benralizumab 30 mg q.4 weeks	SIROCCO/CALIMA - Benralizumab 30 mg q.8 weeks	ZONDA - Benralizumab 30 mg q.4 weeks	ZONDA - Benralizumab 30 mg q.8 weeks
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	783	793	49	49
Units: participants				
Sirocco/Calima eos>=300/µL|# exacerb.	159	170	0	0
Sirocco/Calima eos<300/µL|# exacerb.	113	97	0	0
Zonda|# exacerb.	0	0	17	24

End point values	SIROCCO/CALI	SIROCCO/CALI	SIROCCO/CALI	SIROCCO/CALI

	MA - Benralizumab 30 mg q.4 - Pre Benra q.4	MA - Benralizumab 30 mg q.4 - Predecessor Placebo	MA - Benralizumab 30 mg q.8 - Pre Benra q.8	MA - Benralizumab 30 mg q.8 - Predecessor Placebo
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	518	265	512	281
Units: participants				
Sirocco/Calima eos>=300/µL|# exacerb.	99	60	104	66
Sirocco/Calima eos<300/µL|# exacerb.	69	44	65	32
Zonda|# exacerb.	0	0	0	0

End point values	ZONDA - Benralizumab 30 mg q.4 - Pre Benra q.4	ZONDA - Benralizumab 30 mg q.4 - Predecessor Placebo	ZONDA - Benralizumab 30 mg q.8 - Pre Benra q.8	ZONDA - Benralizumab 30 mg q.8 - Predecessor Placebo
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	31	18	31	18
Units: participants				
Sirocco/Calima eos>=300/µL|# exacerb.	0	0	0	0
Sirocco/Calima eos<300/µL|# exacerb.	0	0	0	0
Zonda|# exacerb.	12	5	13	11

Statistical analyses

No statistical analyses for this end point

Secondary: Number of overall patients with asthma exacerbations during study period, adolescents only

End point title	Number of overall patients with asthma exacerbations during study period, adolescents only[25]

End point description:

Annual asthma exacerbation rate, where an asthma exacerbation is defined by a worsening of asthma requiring the use of systemic corticosteroids for at least 3 days, and/or an in patient hospitalization, and/or an emergency department or urgent care visit

End point type	Secondary

End point timeframe:

From week 0 to week 108 in study treatment period and through the follow up period (16 weeks from day of last dose)

Notes:

[25] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This is safety study and use safety endpoints as primary, only descriptive summary is planned. No statistical power or hypothesis testing is planned.

End point values	SIROCCO/CALIMA - Benralizumab 30 mg q.4 weeks	SIROCCO/CALIMA - Benralizumab 30 mg q.8 weeks	SIROCCO/CALIMA - Benra 30 mg q.4 - Pre Benra q.4-adolescents	SIROCCO/CALIMA - Benra 30 mg q.4 - Predecessor Pbo-adolescents
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	25	61	14	11
Units: participants				
Sirocco/Calima eos>=300/µL|# exacerb.	8	8	2	6
Sirocco/Calima eos<300/µL|# exacerb.	0	11	0	0

End point values	SIROCCO/CALIMA - Benra 30 mg q.8 - Pre Benra q.8-adolescents	SIROCCO/CALIMA - Benra 30 mg q.8 - Predecessor Pbo-adolescents		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	32	29		
Units: participants				
Sirocco/Calima eos>=300/µL|# exacerb.	3	5		
Sirocco/Calima eos<300/µL|# exacerb.	5	6		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in pre-brochodilator FEV1 (L)

End point title	Change from baseline in pre-brochodilator FEV1 (L)
End point description:	
Change from baseline to Week 56 in Pre-bronchodilator Forced expiratory volume in 1 second (FEV1).	
End point type	Secondary
End point timeframe:	
Week 56	

End point values	SIROCCO/CALIMA - Benralizumab 30 mg q.4 weeks	SIROCCO/CALIMA - Benralizumab 30 mg q.8 weeks	ZONDA - Benralizumab 30 mg q.4 weeks	ZONDA - Benralizumab 30 mg q.8 weeks
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	665[26]	660[27]	38[28]	43[29]
Units: Liter				
arithmetic mean (standard deviation)				
Sirocco/Calima patients with eos>=300/µL|	0.038 (± 0.346)	0.040 (± 0.356)	0 (± 0)	0 (± 0)

Sirocco/Calima patients with eos<300/µL|	-0.017 (± 0.345)	-0.001 (± 0.312)	0 (± 0)	0 (± 0)
Number of Zonda Patients|	0 (± 0)	0 (± 0)	0.057 (± 0.412)	-0.012 (± 0.314)

Notes:

[26] - 439 for EOS>=300 226 for EOS<300

[27] - 442 for EOS>=300 218 for EOS<300

[28] - Over all EOS

[29] - Over all EOS

End point values	SIROCCO/CALIMA - Benralizumab 30 mg q.4 - Pre Benra q.4	SIROCCO/CALIMA - Benralizumab 30 mg q.4 - Predecessor Placebo	SIROCCO/CALIMA - Benralizumab 30 mg q.8 - Pre Benra q.8	SIROCCO/CALIMA - Benralizumab 30 mg q.8 - Predecessor Placebo
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	444[30]	221[31]	440[32]	220[33]
Units: Liter				
arithmetic mean (standard deviation)				
Sirocco/Calima patients with eos>=300/µL|	-0.006 (± 0.295)	0.131 (± 0.422)	0.019 (± 0.317)	0.081 (± 0.419)
Sirocco/Calima patients with eos<300/µL|	-0.021 (± 0.376)	-0.011 (± 0.280)	-0.015 (± 0.293)	0.030 (± 0.350)
Number of Zonda Patients|	0 (± 0)	0 (± 0)	0 (± 0)	0 (± 0)

Notes:

[30] - 297 for EOS>=300 147 for EOS<300

[31] - 142 for EOS>=300 79 for EOS<300

[32] - 291 for EOS>=300 149 for EOS<300

[33] - 151 for EOS>=300 69 for EOS<300

End point values	ZONDA - Benralizumab 30 mg q.4 - Pre Benra q.4	ZONDA - Benralizumab 30 mg q.4 - Predecessor Placebo	ZONDA - Benralizumab 30 mg q.8 - Pre Benra q.8	ZONDA - Benralizumab 30 mg q.8 - Predecessor Placebo
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	27[34]	11[35]	28[36]	15[37]
Units: Liter				
arithmetic mean (standard deviation)				
Sirocco/Calima patients with eos>=300/µL|	0 (± 0)	0 (± 0)	0 (± 0)	0 (± 0)
Sirocco/Calima patients with eos<300/µL|	0 (± 0)	0 (± 0)	0 (± 0)	0 (± 0)
Number of Zonda Patients|	0.013 (± 0.354)	0.167 (± 0.533)	-0.093 (± 0.280)	0.138 (± 0.329)

Notes:

[34] - Over all EOS

[35] - Over all EOS

[36] - Over all EOS

[37] - Over all EOS

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in pre-brochodilator FEV1 (L), adolescents only

End point title	Change from baseline in pre-brochodilator FEV1 (L), adolescents only[38]

End point description:

Change from baseline to Week 108 in Pre-bronchodilator Forced expiratory volume in 1 second (FEV1).

End point type	Secondary

End point timeframe:

Week 108

Notes:

[38] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This is safety study and use safety endpoints as primary, only descriptive summary is planned. No statistical power or hypothesis testing is planned.

End point values	SIROCCO/CALIMA - Benralizumab 30 mg q.4 weeks	SIROCCO/CALIMA - Benralizumab 30 mg q.8 weeks	SIROCCO/CALIMA - Benra 30 mg q.4 - Pre Benra q.4-adolescents	SIROCCO/CALIMA - Benra 30 mg q.4 - Predecessor Pbo-adolescents
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	17	51	8[39]	9[40]
Units: Liter				
arithmetic mean (standard deviation)				
Sirocco/Calima patients with eos>=300/µL|	-0.020 (± 0.375)	0.496 (± 0.502)	0.205 (± 0.289)	-0.189 (± 0.354)
Sirocco/Calima patients with eos<300/µL|	0.597 (± 0.561)	0.147 (± 0.444)	0.325 (± 0.431)	1.140 (± 0)

Notes:

[39] - 6 for EOS>=300 2 for EOS<300

[40] - 8 for EOS>=300 1 for EOS<300

End point values	SIROCCO/CALIMA - Benra 30 mg q.8 - Pre Benra q.8-adolescents	SIROCCO/CALIMA - Benra 30 mg q.8 - Predecessor Pbo-adolescents		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	25[41]	26[42]		
Units: Liter				
arithmetic mean (standard deviation)				
Sirocco/Calima patients with eos>=300/µL|	0.578 (± 0.608)	0.413 (± 0.375)		
Sirocco/Calima patients with eos<300/µL|	0.047 (± 0.340)	0.240 (± 0.519)		

Notes:

[41] - 13 for EOS>=300 12 for EOS<300

[42] - 13 for EOS>=300 13 for EOS<300

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in post-brochodilator FEV1 (L)

End point title	Change from baseline in post-brochodilator FEV1 (L)[43]

End point description:

Change from baseline to Week 56 in Post-bronchodilator Forced expiratory volume in 1 second (FEV1).

End point type	Secondary

End point timeframe:

Week 56

Notes:

[43] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This is safety study and use safety endpoints as primary, only descriptive summary is planned. No statistical power or hypothesis testing is planned.

End point values	SIROCCO/CALIMA - Benralizumab 30 mg q.4 weeks	SIROCCO/CALIMA - Benralizumab 30 mg q.8 weeks	SIROCCO/CALIMA - Benralizumab 30 mg q.4 - Pre Benra q.4	SIROCCO/CALIMA - Benralizumab 30 mg q.4 - Predecessor Placebo
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	659[44]	652[45]	439[46]	220[47]
Units: Liter				
arithmetic mean (standard deviation)				
Sirocco/Calima patients with eos>=300/µL|	-0.015 (± 0.354)	-0.004 (± 0.329)	-0.066 (± 0.280)	0.089 (± 0.455)
Sirocco/Calima patients with eos<300/µL|	-0.046 (± 0.350)	-0.015 (± 0.316)	-0.058 (± 0.379)	-0.024 (± 0.289)

Notes:

[44] - 440 for EOS>=300 219 for EOS<300

[45] - 443 for EOS>=300 209 for EOS<300

[46] - 296 for EOS >=300 143 for EOS<300

[47] - 144 for EOS>=300 76 for EOS<300

End point values	SIROCCO/CALIMA - Benralizumab 30 mg q.8 - Pre Benra q.8	SIROCCO/CALIMA - Benralizumab 30 mg q.8 - Predecessor Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	438[48]	214[49]		
Units: Liter				
arithmetic mean (standard deviation)				
Sirocco/Calima patients with eos>=300/µL|	-0.029 (± 0.281)	0.045 (± 0.401)		
Sirocco/Calima patients with eos<300/µL|	-0.043 (± 0.273)	0.049 (± 0.394)		

Notes:

[48] - 292 for EOS>=300 146 for EOS<300

[49] - 151 for EOS>=300 63 for EOS<300

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in Post-bronchodilator FEV1 (L), adolescents only

End point title	Change from baseline in Post-bronchodilator FEV1 (L), adolescents only[50]

End point description:

Change from baseline to Week 108 in Post-bronchodilator Forced expiratory volume in 1 second (FEV1).

End point type	Secondary

End point timeframe:

Week 108

Notes:

[50] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This is safety study and use safety endpoints as primary, only descriptive summary is planned. No statistical power or hypothesis testing is planned.

End point values	SIROCCO/CALIMA - Benralizumab 30 mg q.4 weeks	SIROCCO/CALIMA - Benralizumab 30 mg q.8 weeks	SIROCCO/CALIMA - Benra 30 mg q.4 - Pre Benra q.4-adolescents	SIROCCO/CALIMA - Benra 30 mg q.4 - Predecessor Pbo-adolescents
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	17	51	8[51]	9[52]
Units: Liter				
arithmetic mean (standard deviation)				
Sirocco/Calima patients with eos>=300/µL|	-0.201 (± 0.458)	0.448 (± 0.712)	-0.062 (± 0.537)	-0.305 (± 0.394)
Sirocco/Calima patients with eos<300/µL|	0.543 (± 0.444)	0.111 (± 0.454)	0.375 (± 0.474)	0.880 (± 0)

Notes:

[51] - 6 for EOS>=300 2 for EOS<300

[52] - 8 for EOS>=300 1 for EOS<300

End point values	SIROCCO/CALIMA - Benra 30 mg q.8 - Pre Benra q.8-adolescents	SIROCCO/CALIMA - Benra 30 mg q.8 - Predecessor Pbo-adolescents		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	25[53]	26[54]		
Units: Liter				
arithmetic mean (standard deviation)				
Sirocco/Calima patients with eos>=300/µL|	0.603 (± 0.749)	0.279 (± 0.659)		
Sirocco/Calima patients with eos<300/µL|	-0.006 (± 0.327)	0.218 (± 0.536)		

Notes:

[53] - 13 for EOS>=300 12 for EOS<300

[54] - 13 for EOS>=300 13 for EOS<300

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in Asthma Control Questionnaire (ACQ) as a measure of asthma control in overall patients

End point title	Change from baseline in Asthma Control Questionnaire (ACQ) as a measure of asthma control in overall patients

End point description:

Asthma Control Questionnaire 6 (ACQ-6) contains 1 bronchodilator use question and 5 symptom

questions. Questions were weighted equally and scored from 0 (totally controlled) to 6 (severely uncontrolled). The mean ACQ-6 score was the mean of the responses.

End point type	Secondary

End point timeframe:

Week 56

End point values	SIROCCO/CALIMA - Benralizumab 30 mg q.4 weeks	SIROCCO/CALIMA - Benralizumab 30 mg q.8 weeks	ZONDA - Benralizumab 30 mg q.4 weeks	ZONDA - Benralizumab 30 mg q.8 weeks
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	671[55]	664[56]	39[57]	43[58]
Units: Score on a scale				
arithmetic mean (standard deviation)				
Sirocco/Calima patients with eos>=300/µL|	-0.09 (± 0.91)	-0.12 (± 0.91)	0 (± 0)	0 (± 0)
Sirocco/Calima patients with eos<300/µL|	-0.15 (± 0.86)	-0.10 (± 0.90)	0 (± 0)	0 (± 0)
Number of Zonda Patients|	0 (± 0)	0 (± 0)	-0.21 (± 0.87)	-0.05 (± 1.04)

Notes:

[55] - 444 for EOS>=300 227 for EOS<300

[56] - 447 for EOS>=300 217 for EOS<300

[57] - Over all EOS

[58] - Over all EOS

End point values	SIROCCO/CALIMA - Benralizumab 30 mg q.4 - Pre Benra q.4	SIROCCO/CALIMA - Benralizumab 30 mg q.4 - Predecessor Placebo	SIROCCO/CALIMA - Benralizumab 30 mg q.8 - Pre Benra q.8	SIROCCO/CALIMA - Benralizumab 30 mg q.8 - Predecessor Placebo
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	447[59]	224[60]	444[61]	220[62]
Units: Score on a scale				
arithmetic mean (standard deviation)				
Sirocco/Calima patients with eos>=300/µL|	-0.04 (± 0.83)	-0.20 (± 1.04)	-0.06 (± 0.82)	-0.25 (± 1.06)
Sirocco/Calima patients with eos<300/µL|	-0.16 (± 0.90)	-0.12 (± 0.80)	-0.10 (± 0.83)	-0.09 (± 1.06)
Number of Zonda Patients|	0 (± 0)	0 (± 0)	0 (± 0)	0 (± 0)

Notes:

[59] - 298 for EOS >=300 149 for EOS<300

[60] - 146 for EOS>=300 78 for EOS<300

[61] - 294 for EOS>=300 150 for EOS<300

[62] - 153 for EOS>=300 67 for EOS<300

End point values	ZONDA - Benralizumab 30 mg q.4 - Pre Benra q.4	ZONDA - Benralizumab 30 mg q.4 - Predecessor Placebo	ZONDA - Benralizumab 30 mg q.8 - Pre Benra q.8	ZONDA - Benralizumab 30 mg q.8 - Predecessor Placebo
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	28[63]	11[64]	28[65]	15[66]

Units: Score on a scale				
arithmetic mean (standard deviation)				
Sirocco/Calima patients with eos>=300/µL|	0 (± 0)	0 (± 0)	0 (± 0)	0 (± 0)
Sirocco/Calima patients with eos<300/µL|	0 (± 0)	0 (± 0)	0 (± 0)	0 (± 0)
Number of Zonda Patients|	-0.05 (± 0.89)	-0.61 (± 0.74)	0.15 (± 1.02)	-0.43 (± 1.00)

Notes:

[63] - Over all EOS

[64] - Over all EOS

[65] - Over all EOS

[66] - Over all EOS

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in Asthma Control Questionnaire (ACQ) as a measure of asthma control in overall patients, adolescents only

End point title	Change from baseline in Asthma Control Questionnaire (ACQ) as a measure of asthma control in overall patients, adolescents only[67]

End point description:

Asthma Control Questionnaire 6 (ACQ-6) contains 1 bronchodilator use question and 5 symptom questions. Questions were weighted equally and scored from 0 (totally controlled) to 6 (severely uncontrolled). The mean ACQ-6 score was the mean of the responses.

End point type	Secondary

End point timeframe:

Week 108

Notes:

[67] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This is safety study and use safety endpoints as primary, only descriptive summary is planned. No statistical power or hypothesis testing is planned.

End point values	SIROCCO/CALIMA - Benralizumab 30 mg q.4 weeks	SIROCCO/CALIMA - Benralizumab 30 mg q.8 weeks	SIROCCO/CALIMA - Benra 30 mg q.4 - Pre Benra q.4-adolescents	SIROCCO/CALIMA - Benra 30 mg q.4 - Predecessor Pbo-adolescents
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	18	51	9[68]	9[69]
Units: Score on a scale				
arithmetic mean (standard deviation)				
Sirocco/Calima patients with eos>=300/µL|	0.16 (± 0.50)	-0.12 (± 1.02)	0.26 (± 0.53)	0.06 (± 0.49)
Sirocco/Calima patients with eos<300/µL|	0.94 (± 0.79)	-0.21 (± 0.76)	-0.50 (± 0.24)	-1.83 (± 0)

Notes:

[68] - 7 for EOS>=300 2 for EOS<300

[69] - 8 for EOS>=300 1 for EOS<300

End point values	SIROCCO/CALIMA - Benra 30 mg q.8 - Pre Benra q.8-	SIROCCO/CALIMA - Benra 30 mg q.8 - Predecessor		

	adolescents	Pbo-adolescents		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	25[70]	26[71]		
Units: Score on a scale				
arithmetic mean (standard deviation)				
Sirocco/Calima patients with eos>=300/µL|	-0.14 (± 0.51)	-0.10 (± 1.38)		
Sirocco/Calima patients with eos<300/µL|	-0.21 (± 0.78)	-0.21 (± 0.77)		

Notes:

[70] - 13 for EOS>=300 12 for EOS<300

[71] - 13 for EOS>=300 13 for EOS<300

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in total score of asthma related and general health-related quality of life questionnaire (AQLQ(S)+12)

End point title	Change from baseline in total score of asthma related and general health-related quality of life questionnaire (AQLQ(S)+12)

End point description:

Standardised Asthma Quality of Life Questionnaire for 12 Years and Older (AQLQ(S)+12) comprises 4 separate domains (symptoms, activity limitations, emotional function, and environmental stimuli). It contains 32 questions on a 7 point scale ranging from 7 (no impairment) to 1 (severe impairment); total score is an average of all questions. An increase in score indicates improvement.

End point type	Secondary

End point timeframe:

Week 56

End point values	SIROCCO/CALIMA - Benralizumab 30 mg q.4 weeks	SIROCCO/CALIMA - Benralizumab 30 mg q.8 weeks	ZONDA - Benralizumab 30 mg q.4 weeks	ZONDA - Benralizumab 30 mg q.8 weeks
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	668[72]	662[73]	37[74]	43[75]
Units: Score on a scale				
arithmetic mean (standard deviation)				
Sirocco/Calima patients with eos>=300/µL|	0.08 (± 0.87)	0.15 (± 0.94)	0 (± 0)	0 (± 0)
Sirocco/Calima patients with eos<300/µL|	0.09 (± 0.85)	0.11 (± 0.95)	0 (± 0)	0 (± 0)
Number of Zonda Patients|	0 (± 0)	0 (± 0)	0.22 (± 0.92)	0.11 (± 0.98)

Notes:

[72] - 442 for EOS>=300 226 for EOS<300

[73] - 446 for EOS>=300 216 for EOS<300

[74] - Over all EOS

[75] - Over all EOS

End point values	SIROCCO/CALIMA -	SIROCCO/CALIMA -	SIROCCO/CALIMA -	SIROCCO/CALIMA -

	Benralizumab 30 mg q.4 - Pre Benra q.4	Benralizumab 30 mg q.4 - Predecessor Placebo	Benralizumab 30 mg q.8 - Pre Benra q.8	Benralizumab 30 mg q.8 - Predecessor Placebo
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	444[76]	224[77]	442[78]	220[79]
Units: Score on a scale				
arithmetic mean (standard deviation)				
Sirocco/Calima patients with eos>=300/µL|	0.02 (± 0.80)	0.21 (± 0.98)	0.08 (± 0.91)	0.26 (± 1.00)
Sirocco/Calima patients with eos<300/µL|	0.11 (± 0.84)	0.03 (± 0.89)	0.15 (± 0.90)	0.02 (± 1.06)
Number of Zonda Patients|	0 (± 0)	0 (± 0)	0 (± 0)	0 (± 0)

Notes:

[76] - 296 for EOS>=300 148 for EOS<300

[77] - 146 for EOS>=300 78 for EOS<300

[78] - 293 for EOS>=300 149 for EOS<300

[79] - 153 for EOS>=300 67 for EOS<300

End point values	ZONDA - Benralizumab 30 mg q.4 - Pre Benra q.4	ZONDA - Benralizumab 30 mg q.4 - Predecessor Placebo	ZONDA - Benralizumab 30 mg q.8 - Pre Benra q.8	ZONDA - Benralizumab 30 mg q.8 - Predecessor Placebo
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	26[80]	11[81]	28[82]	15[83]
Units: Score on a scale				
arithmetic mean (standard deviation)				
Sirocco/Calima patients with eos>=300/µL|	0 (± 0)	0 (± 0)	0 (± 0)	0 (± 0)
Sirocco/Calima patients with eos<300/µL|	0 (± 0)	0 (± 0)	0 (± 0)	0 (± 0)
Number of Zonda Patients|	0.13 (± 0.93)	0.43 (± 0.91)	-0.04 (± 0.94)	0.40 (± 1.03)

Notes:

[80] - Over all EOS

[81] - Over all EOS

[82] - Over all EOS

[83] - Over all EOS

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in total score of asthma related and general health-related quality of life questionnaire (AQLQ(S)+12), adolescents only

End point title	Change from baseline in total score of asthma related and general health-related quality of life questionnaire (AQLQ(S)+12), adolescents only[84]

End point description:

Standardised Asthma Quality of Life Questionnaire for 12 Years and Older (AQLQ(S)+12) comprises 4 separate domains (symptoms, activity limitations, emotional function, and environmental stimuli). It contains 32 questions on a 7 point scale ranging from 7 (no impairment) to 1 (severe impairment); total score is an average of all questions. An increase in score indicates improvement.

End point type	Secondary

End point timeframe:

Week 108

Notes:

[84] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This is safety study and use safety endpoints as primary, only descriptive summary is planned. No statistical power or hypothesis testing is planned.

End point values	SIROCCO/CALIMA - Benralizumab 30 mg q.4 weeks	SIROCCO/CALIMA - Benralizumab 30 mg q.8 weeks	SIROCCO/CALIMA - Benra 30 mg q.4 - Pre Benra q.4-adolescents	SIROCCO/CALIMA - Benra 30 mg q.4 - Predecessor Pbo-adolescents
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	17	51	9[85]	8[86]
Units: Score on a scale				
arithmetic mean (standard deviation)				
Sirocco/Calima patients with eos>=300/µL|	0.25 (± 0.92)	0.29 (± 0.54)	0.60 (± 1.22)	-0.11 (± 0.21)
Sirocco/Calima patients with eos<300/µL|	0.94 (± 0.65)	0.42 (± 0.89)	0.64 (± 0.55)	1.53 (± 0)

Notes:

[85] - 7 for EOS>=300 2 for EOS<300

[86] - 7 for EOS>=300 1 for EOS<300

End point values	SIROCCO/CALIMA - Benra 30 mg q.8 - Pre Benra q.8-adolescents	SIROCCO/CALIMA - Benra 30 mg q.8 - Predecessor Pbo-adolescents		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	25[87]	26[88]		
Units: Score on a scale				
arithmetic mean (standard deviation)				
Sirocco/Calima patients with eos>=300/µL|	0.52 (± 0.37)	0.06 (± 0.59)		
Sirocco/Calima patients with eos<300/µL|	0.58 (± 1.01)	0.27 (± 0.77)		

Notes:

[87] - 13 for EOS>=300 12 for EOS<300

[88] - 13 for EOS>=300 13 for EOS>=300

Statistical analyses

No statistical analyses for this end point

Secondary: Change of blood eosinophil levels measurement in overall patients

End point title	Change of blood eosinophil levels measurement in overall patients

End point description:

Change from baseline to Week 56 in Blood eosinophils

End point type	Secondary

End point timeframe:

Week 56

End point values	SIROCCO/CALIMA - Benralizumab 30 mg q.4 weeks	SIROCCO/CALIMA - Benralizumab 30 mg q.8 weeks	ZONDA - Benralizumab 30 mg q.4 weeks	ZONDA - Benralizumab 30 mg q.8 weeks
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	691[89]	703[90]	39[91]	42[92]
Units: cell/uL				
arithmetic mean (standard deviation)				
Sirocco/Calima patients with eos>=300/µL|	-148.6 (± 332.91)	-154.1 (± 297.34)	0 (± 0)	0 (± 0)
Sirocco/Calima patients with eos<300/µL|	-68.4 (± 234.40)	-74.7 (± 160.29)	0 (± 0)	0 (± 0)
Number of Zonda Patients|	0 (± 0)	0 (± 0)	-145.1 (± 307.66)	-166.4 (± 351.39)

Notes:

[89] - 462 for EOS>=300 229 for EOS<300

[90] - 464 for EOS>=300 239 for EOS<300

[91] - Over all EOS

[92] - Over all EOS

End point values	SIROCCO/CALIMA - Benralizumab 30 mg q.4 - Pre Benra q.4	SIROCCO/CALIMA - Benralizumab 30 mg q.4 - Predecessor Placebo	SIROCCO/CALIMA - Benralizumab 30 mg q.8 - Pre Benra q.8	SIROCCO/CALIMA - Benralizumab 30 mg q.8 - Predecessor Placebo
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	454[93]	237[94]	461[95]	242[96]
Units: cell/uL				
arithmetic mean (standard deviation)				
Sirocco/Calima patients with eos>=300/µL|	4.9 (± 177.42)	-449.6 (± 360.6)	-10.1 (± 134.7)	-422.5 (± 330.01)
Sirocco/Calima patients with eos<300/µL|	15.7 (± 87.04)	-222.1 (± 325.03)	-2.9 (± 59.11)	-217.4 (± 198.56)
Number of Zonda Patients|	0 (± 0)	0 (± 0)	0 (± 0)	0 (± 0)

Notes:

[93] - 306 for EOS>=300 148 for EOS<300

[94] - 156 for EOS>=300 81 for EOS<300

[95] - 302 for EOS>=300 159 for EOS<300

[96] - 162 for EOS>300 80 for EOS<300

End point values	ZONDA - Benralizumab 30 mg q.4 - Pre Benra q.4	ZONDA - Benralizumab 30 mg q.4 - Predecessor Placebo	ZONDA - Benralizumab 30 mg q.8 - Pre Benra q.8	ZONDA - Benralizumab 30 mg q.8 - Predecessor Placebo
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	28[97]	11[98]	27[99]	15[100]
Units: cell/uL				
arithmetic mean (standard deviation)				
Sirocco/Calima patients with eos>=300/µL|	0 (± 0)	0 (± 0)	0 (± 0)	0 (± 0)

Sirocco/Calima patients with eos<300/µL|	0 (± 0)	0 (± 0)	0 (± 0)	0 (± 0)
Number of Zonda Patients|	2.5 (± 69.85)	-520.9 (± 360.79)	-17.0 (± 107.48)	-435.3 (± 468.64)

Notes:

[97] - Over all EOS

[98] - Over all EOS

[99] - Over all EOS

[100] - Over all EOS

Statistical analyses

No statistical analyses for this end point

Secondary: Change of blood eosinophil levels measurement in adolescents patients.

End point title	Change of blood eosinophil levels measurement in adolescents patients.[101]

End point description:

Change from baseline to Week 108 in Blood eosinophils.

End point type	Secondary

End point timeframe:

Week 108

Notes:

[101] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This is safety study and use safety endpoints as primary, only descriptive summary is planned. No statistical power or hypothesis testing is planned.

End point values	SIROCCO/CALIMA - Benralizumab 30 mg q.4 weeks	SIROCCO/CALIMA - Benralizumab 30 mg q.8 weeks	SIROCCO/CALIMA - Benra 30 mg q.4 - Pre Benra q.4-adolescents	SIROCCO/CALIMA - Benra 30 mg q.4 - Predecessor Pbo-adolescents
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	14	37	7[102]	7[103]
Units: cell/uL				
arithmetic mean (standard deviation)				
Sirocco/Calima patients with eos>=300/µL|	-139.2 (± 299.16)	-229.4 (± 446.21)	78.3 (± 192.19)	-356.7 (± 215.47)
Sirocco/Calima patients with eos<300/µL|	5.0 (± 219.20)	-97.9 (± 145.40)	160.0 (± 0)	-150.0 (± 0)

Notes:

[102] - 6 for EOS>=300 1 for EOS<300

[103] - 6 for EOS>=300 1 for EOS<300

End point values	SIROCCO/CALIMA - Benra 30 mg q.8 - Pre Benra q.8-adolescents	SIROCCO/CALIMA - Benra 30 mg q.8 - Predecessor Pbo-adolescents		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	21[104]	16[105]		
Units: cell/uL				
arithmetic mean (standard deviation)				

Sirocco/Calima patients with eos>=300/µL|	-163.6 (± 502.76)	-332.9 (± 349.89)		
Sirocco/Calima patients with eos<300/µL|	-2.0 (± 9.19)	-204.4 (± 152.32)		

Notes:

[104] - 11 for EOS>=300 10 for EOS<300

[105] - 7 for EOS>=300 9 for EOS<300

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in EQ-5D-5L visual analog scale

End point title	Change from baseline in EQ-5D-5L visual analog scale

End point description:

The questionnaire included a VAS, where the patient was asked to rate current health status on a scale of 0 to 100, with 0 being the worst imaginable health state; thus, an increase in VAS score indicated improvement.

End point type	Secondary

End point timeframe:

Week 56

End point values	SIROCCO/CALIMA - Benralizumab 30 mg q.4 weeks	SIROCCO/CALIMA - Benralizumab 30 mg q.8 weeks	ZONDA - Benralizumab 30 mg q.4 weeks	ZONDA - Benralizumab 30 mg q.8 weeks
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	682[106]	709[107]	21[108]	28[109]
Units: Score on a scale				
arithmetic mean (standard deviation)				
Sirocco/Calima patients with eos>=300/µL|	6.08 (± 15.68)	6.02 (± 17.68)	0 (± 0)	0 (± 0)
Sirocco/Calima patients with eos<300/µL|	4.38 (± 14.99)	6.69 (± 15.96)	0 (± 0)	0 (± 0)
Number of Zonda Patients|	0 (± 0)	0 (± 0)	5.00 (± 10.35)	1.36 (± 13.58)

Notes:

[106] - 454 for EOS>=300 228 for EOS<300

[107] - 468 for EOS>=300 241 for EOS<300

[108] - Over all EOS

[109] - Over all EOS

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in EQ-5D-5L visual analog scale, adolescents only

End point title	Change from baseline in EQ-5D-5L visual analog scale, adolescents only[110]

End point description:

The questionnaire included a VAS, where the patient was asked to rate current health status on a scale of 0 to 100, with 0 being the worst imaginable health state; thus, an increase in VAS score indicated improvement.

End point type	Secondary

End point timeframe:

Week 108

Notes:

[110] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This is safety study and use safety endpoints as primary, only descriptive summary is planned. No statistical power or hypothesis testing is planned.

End point values	SIROCCO/CALIMA - Benralizumab 30 mg q.4 weeks	SIROCCO/CALIMA - Benralizumab 30 mg q.8 weeks	SIROCCO/CALIMA - Benra 30 mg q.4 - Pre Benra q.4-adolescents	SIROCCO/CALIMA - Benra 30 mg q.4 - Predecessor Pbo-adolescents
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	18	48	9[111]	9[112]
Units: Score on a scale				
arithmetic mean (standard deviation)				
Sirocco/Calima patients with eos>=300/µL|	6.07 (± 12.71)	10.72 (± 21.26)	5.43 (± 9.73)	6.63 (± 15.53)
Sirocco/Calima patients with eos<300/µL|	13.33 (± 17.50)	7.52 (± 23.39)	22.00 (± 12.73)	-4.00 (± 0)

Notes:

[111] - 7 for EOS>=300 2 for EOS<300

[112] - 8 for EOS>=300 1 for EOS<300

End point values	SIROCCO/CALIMA - Benra 30 mg q.8 - Pre Benra q.8-adolescents	SIROCCO/CALIMA - Benra 30 mg q.8 - Predecessor Pbo-adolescents		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	24[113]	24[114]		
Units: Score on a scale				
arithmetic mean (standard deviation)				
Sirocco/Calima patients with eos>=300/µL|	11.54 (± 26.95)	9.83 (± 13.87)		
Sirocco/Calima patients with eos<300/µL|	10.18 (± 32.69)	5.08 (± 10.45)		

Notes:

[113] - 13 for EOS>=300 11 for EOS<300

[114] - 12 for EOS>=300 12 for EOS<300

Statistical analyses

No statistical analyses for this end point

Secondary: Work Productivity loss in adults, using Work Productivity and Activity Impairment Questionnaire (WPAI)

End point title	Work Productivity loss in adults, using Work Productivity and Activity Impairment Questionnaire (WPAI)

End point description:

The WPAI+CIQ is a 10-item questionnaire that assesses productivity and activity impairment over the previous week. The questionnaire includes hours missed from work/school due to asthma, degree health affected productivity while at work/school, as well as the degree to which health affected regular activities other than work or school. The questionnaire related to the previous 7 days. Work productivity

loss is calculated with sum of hours missed at work due to health problem and hours that affected due to health problem at work, divided by sum of hours missed due to health problem and hours actually worked, presented by percentage.

End point type	Secondary

End point timeframe:

Baseline and Week 68

End point values	SIROCCO/CALIMA - Benralizumab 30 mg q.4 weeks	SIROCCO/CALIMA - Benralizumab 30 mg q.8 weeks	ZONDA - Benralizumab 30 mg q.4 weeks	ZONDA - Benralizumab 30 mg q.8 weeks
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	783[115]	793[116]	49[117]	49[118]
Units: percentage				
arithmetic mean (standard deviation)				
Sirocco/Calima patients with eos>=300/µL-baseline|	25.3 (± 24.70)	25.0 (± 24.15)	0 (± 0)	0 (± 0)
Sirocco/Calima patients with eos>=300/µL-wk 68|	23.3 (± 26.18)	21.0 (± 25.54)	0 (± 0)	0 (± 0)
Sirocco/Calima patients with eos<300/µL-baseline|	31.0 (± 27.06)	32.6 (± 26.29)	0 (± 0)	0 (± 0)
Sirocco/Calima patients with eos<300/µL-wk 68|	32.7 (± 27.55)	25.8 (± 24.05)	0 (± 0)	0 (± 0)
Zonda Patients-baseline|	0 (± 0)	0 (± 0)	23.5 (± 25.13)	7.1 (± 10.47)
Zonda Patients-wk 68|	0 (± 0)	0 (± 0)	18.9 (± 24.94)	21.0 (± 27.13)

Notes:

[115] - BS: 234 for EOS>=300 WK68: 236 for EOS>=300 BS: 101 for EOS<300 WK68: 97 for EOS<300

[116] - BS: 217 for EOS>=300 WK68: 217 for EOS>=300 BS: 93 for EOS<300 WK68: 96 for EOS<300

[117] - BS: 16 WK68: 19

[118] - BS: 17 WK68: 20

Statistical analyses

No statistical analyses for this end point

Secondary: Work Productivity loss in adults, using Work Productivity and Activity Impairment Questionnaire (WPAI), adolescents only

End point title	Work Productivity loss in adults, using Work Productivity and Activity Impairment Questionnaire (WPAI), adolescents only[119]

End point description:

The WPAI+CIQ is a 10-item questionnaire that assesses productivity and activity impairment over the previous week. The questionnaire includes hours missed from work/school due to asthma, degree health affected productivity while at work/school, as well as the degree to which health affected regular activities other than work or school. The questionnaire related to the previous 7 days. Work productivity loss is calculated with sum of hours missed at work due to health problem and hours that affected due to health problem at work, divided by sum of hours missed due to health problem and hours actually worked, presented by percentage.

End point type	Secondary

End point timeframe:

Baseline and Week 108

Notes:

[119] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This is safety study and use safety endpoints as primary, only descriptive summary is planned. No statistical power or hypothesis testing is planned.

End point values	SIROCCO/CALIMA - Benralizumab 30 mg q.4 weeks	SIROCCO/CALIMA - Benralizumab 30 mg q.8 weeks	SIROCCO/CALIMA - Benra 30 mg q.4 - Pre Benra q.4-adolescents	SIROCCO/CALIMA - Benra 30 mg q.4 - Predecessor Pbo-adolescents
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	25	61	14	11
Units: Percentage				
arithmetic mean (standard deviation)				
Sirocco/Calima patients with eos>=300/µL-baseline|	10.0 (± 0)	77.5 (± 24.75)	10.0 (± 0)	0 (± 0)
Sirocco/Calima patients with eos>=300/µL-wk 108|	3 (± 3.3)	15.0 (± 7.07)	0.0 (± 0.00)	10.0 (± 0)
Sirocco/Calima patients with eos<300/µL-baseline|	0 (± 0)	55.0 (± 0)	0 (± 0)	0 (± 0)
Sirocco/Calima patients with eos<300/µL-wk-108|	0 (± 0)	8.0 (± 8.37)	0 (± 0)	0 (± 0)

End point values	SIROCCO/CALIMA - Benra 30 mg q.8 - Pre Benra q.8-adolescents	SIROCCO/CALIMA - Benra 30 mg q.8 - Predecessor Pbo-adolescents		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	32	29		
Units: Percentage				
arithmetic mean (standard deviation)				
Sirocco/Calima patients with eos>=300/µL-baseline|	60.0 (± 0)	95.0 (± 0)		
Sirocco/Calima patients with eos>=300/µL-wk 108|	20.0 (± 0)	10.0 (± 0)		
Sirocco/Calima patients with eos<300/µL-baseline|	0 (± 0)	55.0 (± 0)		
Sirocco/Calima patients with eos<300/µL-wk-108|	0.0 (± 0.00)	13.3 (± 5.77)		

Statistical analyses

No statistical analyses for this end point

Secondary: Classroom productivity loss using Classroom Impairment Questionnaire (CIQ)

End point title	Classroom productivity loss using Classroom Impairment Questionnaire (CIQ)[120]

End point description:

The WPAI (+CIQ) is a 10-item questionnaire that assesses productivity and activity impairment over the previous week. The questionnaire includes hours missed from work/school due to asthma, degree health affected productivity while at work/school, as well as the degree to which health affected regular activities other than work or school. The questionnaire related to the previous 7 days. Classroom productivity loss is calculated with sum of hours missed for classes due to health problem and hours that affected due to health problem in classes, divided by sum of hours missed due to health problem and hours actually attended classes, presented by percentage.

End point type	Secondary

End point timeframe:

Baseline and Week 56

Notes:

[120] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This is safety study and use safety endpoints as primary, only descriptive summary is planned. No statistical power or hypothesis testing is planned.

End point values	SIROCCO/CALIMA - Benralizumab 30 mg q.4 weeks	SIROCCO/CALIMA - Benralizumab 30 mg q.8 weeks		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	25[121]	61[122]		
Units: Percentage				
arithmetic mean (standard deviation)				
Sirocco/Calima patients with eos>=300/µL-Baseline|	13.0 (± 19.14)	30.7 (± 31.41)		
Sirocco/Calima patients with eos>=300/µL-wk 56|	3.8 (± 7.44)	15.2 (± 20.69)		
Sirocco/Calima patients with eos<300/µL-Baseline|	42.1 (± 32.50)	35.4 (± 23.92)		
Sirocco/Calima patients with eos<300/µL-wk 56|	5.0 (± 7.07)	17.1 (± 20.06)		

Notes:

[121] - BS: 11 for EOS>=300 WK56: 8 for EOS>=300 BS: 4 for EOS<300 WK56: 2 for EOS<300

[122] - BS: 23 for EOS>=300 WK56: 24 for EOS>=300 BS: 19 for EOS<300 WK56: 24 for EOS<300

Statistical analyses

No statistical analyses for this end point

Secondary: Classroom productivity loss using Classroom Impairment Questionnaire (CIQ), adolescents only

End point title	Classroom productivity loss using Classroom Impairment Questionnaire (CIQ), adolescents only[123]

End point description:

The WPAI (+CIQ) is a 10-item questionnaire that assesses productivity and activity impairment over the previous week. The questionnaire includes hours missed from work/school due to asthma, degree health affected productivity while at work/school, as well as the degree to which health affected regular activities other than work or school. The questionnaire related to the previous 7 days. Classroom productivity loss is calculated with sum of hours missed for classes due to health problem and hours that affected due to health problem in classes, divided by sum of hours missed due to health problem and hours actually attended classes, presented by percentage.

End point type	Secondary

End point timeframe:

Baseline and Week 108

Notes:

[123] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This is safety study and use safety endpoints as primary, only descriptive summary is planned. No statistical power or hypothesis testing is planned.

End point values	SIROCCO/CALIMA - Benralizumab 30 mg q.4 weeks	SIROCCO/CALIMA - Benralizumab 30 mg q.8 weeks	SIROCCO/CALIMA - Benra 30 mg q.4 - Pre Benra q.4-adolescents	SIROCCO/CALIMA - Benra 30 mg q.4 - Predecessor Pbo-adolescents
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	25	61	14	11
Units: Percentage				
arithmetic mean (standard deviation)				
Sirocco/Calima patients with eos>=300/µL-baseline|	13.0 (± 19.14)	30.7 (± 31.41)	18.8 (± 24.08)	6.0 (± 8.94)
Sirocco/Calima patients with eos>=300/µL-wk 108|	9.5 (± 12.98)	12.3 (± 21.62)	4.9 (± 6.82)	15.2 (± 17.55)
Sirocco/Calima patients with eos<300/µL-baseline|	42.1 (± 32.50)	35.4 (± 23.92)	25.0 (± 35.36)	59.3 (± 27.27)
Sirocco/Calima patients with eos<300/µL-wk-108|	21.5 (± 30.41)	11.5 (± 14.66)	21.5 (± 30.41)	0 (± 0)

End point values	SIROCCO/CALIMA - Benra 30 mg q.8 - Pre Benra q.8-adolescents	SIROCCO/CALIMA - Benra 30 mg q.8 - Predecessor Pbo-adolescents		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	32	29		
Units: Percentage				
arithmetic mean (standard deviation)				
Sirocco/Calima patients with eos>=300/µL-baseline|	31.9 (± 32.10)	29.3 (± 32.13)		
Sirocco/Calima patients with eos>=300/µL-wk 108|	5.4 (± 8.32)	18.6 (± 27.94)		
Sirocco/Calima patients with eos<300/µL-baseline|	36.5 (± 28.23)	34.4 (± 20.82)		
Sirocco/Calima patients with eos<300/µL-wk-108|	12.5 (± 18.10)	10.6 (± 11.68)		

Statistical analyses

No statistical analyses for this end point

Secondary: Activity impairment (%), using Work Productivity and Activity Impairment Questionnaire (WPAI)

End point title	Activity impairment (%), using Work Productivity and Activity Impairment Questionnaire (WPAI)

End point description:

The WPAI+CIQ is a 10-item questionnaire that assesses productivity and activity impairment over the previous week. The questionnaire includes hours missed from work/school due to asthma, degree health affected productivity while at work/school, as well as the degree to which health affected regular activities other than work or school. The questionnaire related to the previous 7 days. The WPAI+CIQ outcomes are expressed as impairment percentages, with higher numbers indicating greater impairment and less productivity.

End point type	Secondary

End point timeframe:

Baseline and Week 68

End point values	SIROCCO/CALIMA - Benralizumab 30 mg q.4 weeks	SIROCCO/CALIMA - Benralizumab 30 mg q.8 weeks	ZONDA - Benralizumab 30 mg q.4 weeks	ZONDA - Benralizumab 30 mg q.8 weeks
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	783[124]	793[125]	49[126]	49[127]
Units: percentage				
arithmetic mean (standard deviation)				
Sirocco/Calima patients with eos>=300/µL-baseline|	31.3 (± 26.44)	31.2 (± 25.63)	0 (± 0)	0 (± 0)
Sirocco/Calima patients with eos>=300/µL-wk 68|	26.6 (± 26.14)	24.4 (± 25.26)	0 (± 0)	0 (± 0)
Sirocco/Calima patients with eos<300/µL-baseline|	39.6 (± 25.75)	36.3 (± 25.72)	0 (± 0)	0 (± 0)
Sirocco/Calima patients with eos<300/µL-wk 68|	33.6 (± 26.55)	32.7 (± 26.58)	0 (± 0)	0 (± 0)
Zonda Patients-baseline|	0 (± 0)	0 (± 0)	31.5 (± 29.49)	24.5 (± 29.08)
Zonda Patients-wk 68|	0 (± 0)	0 (± 0)	28.4 (± 27.85)	39.0 (± 34.36)

Notes:

[124] - BS: 518 for EOS>=300 WK68: 458 for EOS>=300 BS: 261 for EOS<300 WK68: 239 for EOS<300

[125] - BS: 524 for EOS>=300 WK68: 454 for EOS>=300 BS: 264 for EOS<300 WK68: 220 for EOS<300

[126] - BS: 26 WK68: 38

[127] - BS: 31 WK68: 41

Statistical analyses

No statistical analyses for this end point

Secondary: Activity impairment (%), using Work Productivity and Activity Impairment Questionnaire (WPAI), adolescents only

End point title	Activity impairment (%), using Work Productivity and Activity Impairment Questionnaire (WPAI), adolescents only[128]

End point description:

The WPAI+CIQ is a 10-item questionnaire that assesses productivity and activity impairment over the previous week. The questionnaire includes hours missed from work/school due to asthma, degree health affected productivity while at work/school, as well as the degree to which health affected regular activities other than work or school. The questionnaire related to the previous 7 days. The WPAI+CIQ outcomes are expressed as impairment percentages, with higher numbers indicating greater impairment and less productivity.

End point type	Secondary

End point timeframe:

Baseline and Week 108

Notes:

[128] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This is safety study and use safety endpoints as primary, only descriptive summary is planned. No statistical power or hypothesis testing is planned.

End point values	SIROCCO/CALIMA - Benralizumab 30 mg q.4 weeks	SIROCCO/CALIMA - Benralizumab 30 mg q.8 weeks	SIROCCO/CALIMA - Benra 30 mg q.4 - Pre Benra q.4-adolescents	SIROCCO/CALIMA - Benra 30 mg q.4 - Predecessor Pbo-adolescents
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	25	61	14	11
Units: Percentage				
arithmetic mean (standard deviation)				
Sirocco/Calima patients with eos>=300/µL-baseline|	14.5 (± 22.59)	29.7 (± 29.15)	21.8 (± 27.86)	5.6 (± 8.82)
Sirocco/Calima patients with eos>=300/µL-wk 108|	6.0 (± 9.86)	12.3 (± 19.25)	7.1 (± 11.13)	5.0 (± 9.26)
Sirocco/Calima patients with eos<300/µL-baseline|	36.0 (± 27.02)	31.3 (± 21.29)	23.3 (± 25.17)	55.0 (± 21.21)
Sirocco/Calima patients with eos<300/µL-wk-108|	13.3 (± 11.55)	12.8 (± 14.87)	10.0 (± 14.14)	20.0 (± 0)

End point values	SIROCCO/CALIMA - Benra 30 mg q.8 - Pre Benra q.8-adolescents	SIROCCO/CALIMA - Benra 30 mg q.8 - Predecessor Pbo-adolescents		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	32	29		
Units: Percentage				
arithmetic mean (standard deviation)				
Sirocco/Calima patients with eos>=300/µL-baseline|	25.3 (± 23.75)	35.0 (± 34.81)		
Sirocco/Calima patients with eos>=300/µL-wk 108|	5.4 (± 8.77)	19.2 (± 24.31)		
Sirocco/Calima patients with eos<300/µL-baseline|	30.7 (± 21.20)	32.0 (± 22.10)		
Sirocco/Calima patients with eos<300/µL-wk-108|	14.2 (± 18.81)	11.5 (± 10.68)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of patients who had health care encounter (ie, Hospitalization, Emergency department visits, urgent care visits, and all other outpatient visits due to asthma) during study period

End point title	Number of patients who had health care encounter (ie, Hospitalization, Emergency department visits, urgent care

	visits, and all other outpatient visits due to asthma) during study period

End point description:

Hospitalizations, ED visits, urgent care visits and all other outpatient visits due to asthma

End point type	Secondary

End point timeframe:

From week 0 to week 68 in study treatment period and through the follow up period (16 weeks from day of last dose)

End point values	SIROCCO/CALIMA - Benralizumab 30 mg q.4 weeks	SIROCCO/CALIMA - Benralizumab 30 mg q.8 weeks	ZONDA - Benralizumab 30 mg q.4 weeks	ZONDA - Benralizumab 30 mg q.8 weeks
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	519[129]	527[130]	49[131]	49[132]
Units: Participants				
Sirocco/Calima patients with eos>=300/µL|	193	198	0	0
Sirocco/Calima patients with eos<300/µL|	118	102	0	0
Number of Zonda Patients|	0	0	20	25

Notes:

[129] - 519 for EOS>=300 264 for EOS<300

[130] - 527 for EOS>=300 266 for EOS<300

[131] - Over all EOS

[132] - Over all EOS

Statistical analyses

No statistical analyses for this end point

Secondary: Number of patients who had health care encounter (ie, Hospitalization, Emergency department visits, urgent care visits, and all other outpatient visits due to asthma) during study period, adolescents only

End point title	Number of patients who had health care encounter (ie, Hospitalization, Emergency department visits, urgent care visits, and all other outpatient visits due to asthma) during study period, adolescents only[133]

End point description:

Hospitalizations, ED visits, urgent care visits and all other outpatient visits due to asthma

End point type	Secondary

End point timeframe:

Baseline and Week 108

Notes:

[133] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This is safety study and use safety endpoints as primary, only descriptive summary is planned. No statistical power or hypothesis testing is planned.

End point values	SIROCCO/CALIMA - Benralizumab 30 mg q.4 weeks	SIROCCO/CALIMA - Benralizumab 30 mg q.8 weeks	SIROCCO/CALIMA - Benra 30 mg q.4 - Pre Benra q.4- adolescents	SIROCCO/CALIMA - Benra 30 mg q.4 - Predecessor Pbo- adolescents
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	25	61	14	11
Units: Participants				
Sirocco/Calima patients with eos>=300/µL|	7	14	2	5
Sirocco/Calima patients with eos<300/µL|	1	12	0	1

End point values	SIROCCO/CALIMA - Benra 30 mg q.8 - Pre Benra q.8- adolescents	SIROCCO/CALIMA - Benra 30 mg q.8 - Predecessor Pbo- adolescents		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	32	29		
Units: Participants				
Sirocco/Calima patients with eos>=300/µL|	7	7		
Sirocco/Calima patients with eos<300/µL|	7	5		

Statistical analyses

No statistical analyses for this end point

Secondary: Pre-dose benralizumab concentration in serum during the treatment phase of the safety study

End point title	Pre-dose benralizumab concentration in serum during the treatment phase of the safety study
End point description:	
Endpoint: Pharmacokinetic (PK) parameters	
End point type	Secondary
End point timeframe:	
Week 0 and Week 56	

End point values	SIROCCO/CALIMA - Benralizumab 30 mg q.4 - Pre Benra q.4	SIROCCO/CALIMA - Benralizumab 30 mg q.4 - Predecessor Placebo	SIROCCO/CALIMA - Benralizumab 30 mg q.8 - Pre Benra q.8	SIROCCO/CALIMA - Benralizumab 30 mg q.8 - Predecessor Placebo
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	514[134]	263[135]	511[136]	279[137]

Units: ng/mL				
geometric mean (geometric coefficient of variation)				
Baseline	714.25 (± 311.38)	0 (± 0)	142.92 (± 353.94)	0 (± 0)
Week 56	930.01 (± 200.59)	865.93 (± 242.55)	173.95 (± 269.62)	162.03 (± 295.05)

Notes:

[134] - 507 for Baseline 442 for Week 56

[135] - 260 for Baseline 225 for Week 56

[136] - 503 for Baseline 440 for Week 56

[137] - 275 for Baseline 215 for Week 56

End point values	ZONDA - Benralizumab 30 mg q.4 - Pre Benra q.4	ZONDA - Benralizumab 30 mg q.4 - Predecessor Placebo	ZONDA - Benralizumab 30 mg q.8 - Pre Benra q.8	ZONDA - Benralizumab 30 mg q.8 - Predecessor Placebo
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	31[138]	16[139]	31[140]	17[141]
Units: ng/mL				
geometric mean (geometric coefficient of variation)				
Baseline	964.21 (± 224.01)	0 (± 0)	692.91 (± 205.97)	0 (± 0)
Week 56	823.62 (± 239.39)	1160.58 (± 48.82)	247.26 (± 133.0)	139.35 (± 274.98)

Notes:

[138] - 31 for Baseline 27 for Week 56

[139] - 16 for Baseline 10 for Week 56

[140] - 30 for Baseline 27 for Week 56

[141] - 17 for Baseline 15 for Week 56

Statistical analyses

No statistical analyses for this end point

Secondary: Pre-dose benralizumab concentration in serum during the treatment phase of the safety study, adolescents only

End point title	Pre-dose benralizumab concentration in serum during the treatment phase of the safety study, adolescents only

End point description:

Endpoint: Pharmacokinetic (PK) parameters

End point type	Secondary

End point timeframe:

Baseline and Week 108

End point values	SIROCCO/CALIMA - Benra 30 mg q.4 - Pre Benra q.4-adolescents	SIROCCO/CALIMA - Benra 30 mg q.4 - Predecessor Pbo-adolescents	SIROCCO/CALIMA - Benra 30 mg q.8 - Pre Benra q.8-adolescents	SIROCCO/CALIMA - Benra 30 mg q.8 - Predecessor Pbo-adolescents
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	14	11	32	29
Units: ng/mL				
geometric mean (geometric coefficient of variation)				
Baseline	725.55 (± 589.57)	0 (± 0)	218.53 (± 286.39)	0 (± 0)
Week 108	383.73 (± 9364.83)	853.51 (± 314.40)	436.85 (± 858.56)	524.39 (± 284.63)

Statistical analyses

No statistical analyses for this end point

Secondary: Number of patients with Anti-drug antibodies (ADA) responses during the study

End point title	Number of patients with Anti-drug antibodies (ADA) responses during the study

End point description:

Assessments for the presence of ADA and nAb throughout study

End point type	Secondary

End point timeframe:

From week 0 to week 56 in study treatment period (adults) and plus 16 weeks the follow up period; From week 0 to week 108-week in study treatment period (adolescents) and plus 16 weeks the follow up period

End point values	SIROCCO/CALIMA - Benralizumab 30 mg q.4 weeks	SIROCCO/CALIMA - Benralizumab 30 mg q.8 weeks	ZONDA - Benralizumab 30 mg q.4 weeks	ZONDA - Benralizumab 30 mg q.8 weeks
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	783	793	49	49
Units: Participants				
Positive at any visit|	80	93	4	8
Base- and Post-baseline Positive|	23	41	2	4
Newly Persistently Positive|	28	34	1	3
Stable persistently positive|	21	29	2	2
Newly treatment-induced positive|	38	41	2	2
ADA treatment boosted positive|	6	6	0	1
Decreased in titre|	17	9	2	1
Only post-baseline positive|	48	48	2	1
ADA incidence|	44	47	2	3
Transiently Positive|	22	26	1	3
Only baseline positive|	9	4	0	0

nAb positive|	57	75	3	4

Statistical analyses

No statistical analyses for this end point

Secondary: Number of patients with Anti-drug antibodies (ADA) responses during the study, adolescents only.

End point title	Number of patients with Anti-drug antibodies (ADA) responses during the study, adolescents only.[142]

End point description:

Assessments for the presence of ADA and nAb throughout study

End point type	Secondary

End point timeframe:

From week 0 to week 108 study treatment period (adults) and plus 16 weeks the follow up period; From week 0 to week 108-week in study treatment period (adolescents) and plus 16 weeks the follow up period

Notes:

[142] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This is safety study and use safety endpoints as primary, only descriptive summary is planned. No statistical power or hypothesis testing is planned.

End point values	SIROCCO/CALIMA - Benralizumab 30 mg q.4 weeks	SIROCCO/CALIMA - Benralizumab 30 mg q.8 weeks		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	25	61		
Units: Participants				
Positive at any visit|	1	5		
Base- and Post-baseline Positive|	0	3		
Newly Persistently Positive|	0	2		
Stable persistently positive|	0	3		
Newly treatment-induced positive|	1	1		
ADA treatment boosted positive|	0	2		
Decreased in titre|	0	2		
Only post-baseline positive|	1	2		
ADA incidence|	1	3		
Transiently Positive|	1	0		
Only baseline positive|	0	0		
nAb positive|	57	5		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
From first dose of study drug until last study visit	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	20.0

Reporting groups	
Reporting group title	Sirocco/Calima - Benralizumab 30 mg q.4 weeks
Reporting group description: -	
Reporting group title	Sirocco/Calima - Benralizumab 30 mg q.8 weeks
Reporting group description: -	
Reporting group title	Zonda - Benralizumab 30 mg q.4 weeks
Reporting group description: -	
Reporting group title	Zonda - Benralizumab 30 mg q.8 weeks
Reporting group description: -	

Serious adverse events	Sirocco/Calima - Benralizumab 30 mg q.4 weeks	Sirocco/Calima - Benralizumab 30 mg q.8 weeks	Zonda - Benralizumab 30 mg q.4 weeks
Total subjects affected by serious adverse events			
subjects affected / exposed	102 / 783 (13.03%)	94 / 793 (11.85%)	10 / 49 (20.41%)
number of deaths (all causes)	5	4	0
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma of colon			
subjects affected / exposed	1 / 783 (0.13%)	0 / 793 (0.00%)	0 / 49 (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
Benign neoplasm of thyroid gland			
subjects affected / exposed	1 / 783 (0.13%)	0 / 793 (0.00%)	0 / 49 (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
Chronic myeloid leukaemia			
subjects affected / exposed	1 / 783 (0.13%)	0 / 793 (0.00%)	0 / 49 (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
Diffuse large B-cell lymphoma stage			

II			
subjects affected / exposed	2 / 783 (0.26%)	0 / 793 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nasal cavity cancer			
subjects affected / exposed	0 / 783 (0.00%)	1 / 793 (0.13%)	0 / 49 (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
Ovarian germ cell teratoma benign			
subjects affected / exposed	0 / 783 (0.00%)	0 / 793 (0.00%)	0 / 49 (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
Solid pseudopapillary tumour of the pancreas			
subjects affected / exposed	1 / 783 (0.13%)	0 / 793 (0.00%)	0 / 49 (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
B-cell lymphoma			
subjects affected / exposed	0 / 783 (0.00%)	1 / 793 (0.13%)	0 / 49 (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
Basal cell carcinoma			
subjects affected / exposed	2 / 783 (0.26%)	0 / 793 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Benign neoplasm of eyelid			
subjects affected / exposed	0 / 783 (0.00%)	1 / 793 (0.13%)	0 / 49 (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
Colon cancer stage 0			
subjects affected / exposed	1 / 783 (0.13%)	0 / 793 (0.00%)	0 / 49 (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
Large intestine benign neoplasm			

subjects affected / exposed	0 / 783 (0.00%)	1 / 793 (0.13%)	0 / 49 (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
Lipoma			
subjects affected / exposed	1 / 783 (0.13%)	0 / 793 (0.00%)	0 / 49 (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
Osteochondroma			
subjects affected / exposed	1 / 783 (0.13%)	0 / 793 (0.00%)	0 / 49 (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
Prostate cancer			
subjects affected / exposed	0 / 783 (0.00%)	2 / 793 (0.25%)	0 / 49 (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
Thymoma			
subjects affected / exposed	1 / 783 (0.13%)	0 / 793 (0.00%)	0 / 49 (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
Uterine leiomyoma			
subjects affected / exposed	1 / 783 (0.13%)	2 / 793 (0.25%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Hypertensive emergency			
subjects affected / exposed	0 / 783 (0.00%)	1 / 793 (0.13%)	0 / 49 (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
Phlebitis			
subjects affected / exposed	0 / 783 (0.00%)	1 / 793 (0.13%)	0 / 49 (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
Pregnancy, puerperium and perinatal conditions			

Abortion spontaneous			
subjects affected / exposed	0 / 783 (0.00%)	1 / 793 (0.13%)	0 / 49 (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
General disorders and administration site conditions			
Death			
subjects affected / exposed	2 / 783 (0.26%)	0 / 793 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 2	0 / 0	0 / 0
Multiple organ dysfunction syndrome			
subjects affected / exposed	1 / 783 (0.13%)	0 / 793 (0.00%)	0 / 49 (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
Oedema peripheral			
subjects affected / exposed	1 / 783 (0.13%)	0 / 793 (0.00%)	0 / 49 (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
Immune system disorders			
Anaphylactic reaction			
subjects affected / exposed	1 / 783 (0.13%)	0 / 793 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Food allergy			
subjects affected / exposed	0 / 783 (0.00%)	2 / 793 (0.25%)	0 / 49 (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
Reproductive system and breast disorders			
Cervical polyp			
subjects affected / exposed	1 / 783 (0.13%)	0 / 793 (0.00%)	0 / 49 (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
Ovarian cyst			

subjects affected / exposed	1 / 783 (0.13%)	0 / 793 (0.00%)	0 / 49 (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
Vaginal fistula			
subjects affected / exposed	1 / 783 (0.13%)	0 / 793 (0.00%)	0 / 49 (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
Vaginal haemorrhage			
subjects affected / exposed	0 / 783 (0.00%)	1 / 793 (0.13%)	0 / 49 (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
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	36 / 783 (4.60%)	26 / 793 (3.28%)	3 / 49 (6.12%)
occurrences causally related to treatment / all	0 / 40	1 / 31	0 / 4
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Asthmatic crisis			
subjects affected / exposed	0 / 783 (0.00%)	1 / 793 (0.13%)	0 / 49 (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
Interstitial lung disease			
subjects affected / exposed	1 / 783 (0.13%)	0 / 793 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Middle lobe syndrome			
subjects affected / exposed	1 / 783 (0.13%)	0 / 793 (0.00%)	0 / 49 (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
Nasal polyps			
subjects affected / exposed	2 / 783 (0.26%)	2 / 793 (0.25%)	1 / 49 (2.04%)
occurrences causally related to treatment / all	0 / 3	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleural effusion			

subjects affected / exposed	0 / 783 (0.00%)	1 / 793 (0.13%)	0 / 49 (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
Pulmonary hypertension			
subjects affected / exposed	1 / 783 (0.13%)	0 / 793 (0.00%)	0 / 49 (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
Status asthmaticus			
subjects affected / exposed	1 / 783 (0.13%)	2 / 793 (0.25%)	1 / 49 (2.04%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Investigations			
Endocrine test abnormal			
subjects affected / exposed	1 / 783 (0.13%)	0 / 793 (0.00%)	0 / 49 (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
Injury, poisoning and procedural complications			
Head injury			
subjects affected / exposed	1 / 783 (0.13%)	0 / 793 (0.00%)	0 / 49 (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
Humerus fracture			
subjects affected / exposed	0 / 783 (0.00%)	1 / 793 (0.13%)	0 / 49 (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
Limb injury			
subjects affected / exposed	0 / 783 (0.00%)	1 / 793 (0.13%)	0 / 49 (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
Radius fracture			
subjects affected / exposed	0 / 783 (0.00%)	1 / 793 (0.13%)	0 / 49 (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

Rib fracture			
subjects affected / exposed	1 / 783 (0.13%)	0 / 793 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arthropod bite			
subjects affected / exposed	0 / 783 (0.00%)	1 / 793 (0.13%)	0 / 49 (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
Bone contusion			
subjects affected / exposed	1 / 783 (0.13%)	0 / 793 (0.00%)	0 / 49 (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
Clavicle fracture			
subjects affected / exposed	0 / 783 (0.00%)	0 / 793 (0.00%)	1 / 49 (2.04%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fall			
subjects affected / exposed	1 / 783 (0.13%)	0 / 793 (0.00%)	0 / 49 (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
Femur fracture			
subjects affected / exposed	0 / 783 (0.00%)	1 / 793 (0.13%)	0 / 49 (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
Incisional hernia			
subjects affected / exposed	1 / 783 (0.13%)	0 / 793 (0.00%)	0 / 49 (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
Ligament rupture			
subjects affected / exposed	0 / 783 (0.00%)	1 / 793 (0.13%)	0 / 49 (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
Lower limb fracture			

subjects affected / exposed	1 / 783 (0.13%)	0 / 793 (0.00%)	0 / 49 (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
Multiple fractures			
subjects affected / exposed	1 / 783 (0.13%)	0 / 793 (0.00%)	0 / 49 (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
Patella fracture			
subjects affected / exposed	0 / 783 (0.00%)	1 / 793 (0.13%)	0 / 49 (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
Road traffic accident			
subjects affected / exposed	0 / 783 (0.00%)	1 / 793 (0.13%)	0 / 49 (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
Subdural haemorrhage			
subjects affected / exposed	0 / 783 (0.00%)	1 / 793 (0.13%)	0 / 49 (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
Upper limb fracture			
subjects affected / exposed	1 / 783 (0.13%)	0 / 793 (0.00%)	0 / 49 (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
Cardiac disorders			
Acute coronary syndrome			
subjects affected / exposed	0 / 783 (0.00%)	1 / 793 (0.13%)	0 / 49 (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
Acute myocardial infarction			
subjects affected / exposed	1 / 783 (0.13%)	2 / 793 (0.25%)	1 / 49 (2.04%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Angina unstable			

subjects affected / exposed	1 / 783 (0.13%)	2 / 793 (0.25%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial fibrillation			
subjects affected / exposed	0 / 783 (0.00%)	1 / 793 (0.13%)	0 / 49 (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
Cardiac arrest			
subjects affected / exposed	1 / 783 (0.13%)	0 / 793 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Cardiac failure congestive			
subjects affected / exposed	0 / 783 (0.00%)	1 / 793 (0.13%)	0 / 49 (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
Cardio-respiratory arrest			
subjects affected / exposed	1 / 783 (0.13%)	0 / 793 (0.00%)	0 / 49 (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
Congestive cardiomyopathy			
subjects affected / exposed	0 / 783 (0.00%)	1 / 793 (0.13%)	0 / 49 (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
Coronary artery disease			
subjects affected / exposed	0 / 783 (0.00%)	1 / 793 (0.13%)	0 / 49 (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
Coronary artery insufficiency			
subjects affected / exposed	1 / 783 (0.13%)	0 / 793 (0.00%)	0 / 49 (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
Supraventricular extrasystoles			

subjects affected / exposed	0 / 783 (0.00%)	1 / 793 (0.13%)	0 / 49 (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
Supraventricular tachycardia			
subjects affected / exposed	1 / 783 (0.13%)	0 / 793 (0.00%)	0 / 49 (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
Nervous system disorders			
Syncope			
subjects affected / exposed	1 / 783 (0.13%)	1 / 793 (0.13%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diabetic neuropathy			
subjects affected / exposed	0 / 783 (0.00%)	1 / 793 (0.13%)	0 / 49 (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
Dysarthria			
subjects affected / exposed	0 / 783 (0.00%)	1 / 793 (0.13%)	0 / 49 (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
Ischaemic stroke			
subjects affected / exposed	0 / 783 (0.00%)	2 / 793 (0.25%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Lumbosacral radiculopathy			
subjects affected / exposed	1 / 783 (0.13%)	0 / 793 (0.00%)	0 / 49 (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
Transient ischaemic attack			
subjects affected / exposed	0 / 783 (0.00%)	1 / 793 (0.13%)	0 / 49 (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
Blood and lymphatic system disorders			

Hypochromic anaemia			
subjects affected / exposed	1 / 783 (0.13%)	0 / 793 (0.00%)	0 / 49 (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
Iron deficiency anaemia			
subjects affected / exposed	0 / 783 (0.00%)	0 / 793 (0.00%)	1 / 49 (2.04%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutropenia			
subjects affected / exposed	1 / 783 (0.13%)	0 / 793 (0.00%)	0 / 49 (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
Eye disorders			
Cataract			
subjects affected / exposed	0 / 783 (0.00%)	1 / 793 (0.13%)	0 / 49 (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
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 783 (0.13%)	0 / 793 (0.00%)	0 / 49 (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
Duodenal ulcer			
subjects affected / exposed	0 / 783 (0.00%)	1 / 793 (0.13%)	0 / 49 (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
Inguinal hernia			
subjects affected / exposed	0 / 783 (0.00%)	1 / 793 (0.13%)	0 / 49 (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
Oesophageal ulcer			
subjects affected / exposed	1 / 783 (0.13%)	0 / 793 (0.00%)	0 / 49 (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

Abdominal pain lower			
subjects affected / exposed	0 / 783 (0.00%)	1 / 793 (0.13%)	0 / 49 (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
Abdominal pain upper			
subjects affected / exposed	0 / 783 (0.00%)	1 / 793 (0.13%)	0 / 49 (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
Barrett's oesophagus			
subjects affected / exposed	1 / 783 (0.13%)	0 / 793 (0.00%)	0 / 49 (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
Colitis ulcerative			
subjects affected / exposed	0 / 783 (0.00%)	0 / 793 (0.00%)	0 / 49 (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
Duodenal ulcer haemorrhage			
subjects affected / exposed	0 / 783 (0.00%)	1 / 793 (0.13%)	0 / 49 (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
Femoral hernia strangulated			
subjects affected / exposed	1 / 783 (0.13%)	0 / 793 (0.00%)	0 / 49 (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
Gastritis			
subjects affected / exposed	2 / 783 (0.26%)	0 / 793 (0.00%)	1 / 49 (2.04%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 783 (0.00%)	1 / 793 (0.13%)	0 / 49 (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
Ileus			

subjects affected / exposed	0 / 783 (0.00%)	1 / 793 (0.13%)	0 / 49 (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
Irritable bowel syndrome			
subjects affected / exposed	1 / 783 (0.13%)	1 / 793 (0.13%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oesophagitis			
subjects affected / exposed	0 / 783 (0.00%)	1 / 793 (0.13%)	0 / 49 (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
Pancreatitis acute			
subjects affected / exposed	0 / 783 (0.00%)	1 / 793 (0.13%)	0 / 49 (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
Vomiting			
subjects affected / exposed	1 / 783 (0.13%)	0 / 793 (0.00%)	0 / 49 (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
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	1 / 783 (0.13%)	1 / 793 (0.13%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis acute			
subjects affected / exposed	1 / 783 (0.13%)	0 / 793 (0.00%)	0 / 49 (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
Cholecystitis chronic			
subjects affected / exposed	0 / 783 (0.00%)	1 / 793 (0.13%)	0 / 49 (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
Bile duct stone			

subjects affected / exposed	0 / 783 (0.00%)	1 / 793 (0.13%)	0 / 49 (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
Cholelithiasis			
subjects affected / exposed	2 / 783 (0.26%)	1 / 793 (0.13%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatitis			
subjects affected / exposed	1 / 783 (0.13%)	0 / 793 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Erythema nodosum			
subjects affected / exposed	0 / 783 (0.00%)	1 / 793 (0.13%)	0 / 49 (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
Pemphigoid			
subjects affected / exposed	0 / 783 (0.00%)	0 / 793 (0.00%)	0 / 49 (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
Rosacea			
subjects affected / exposed	1 / 783 (0.13%)	0 / 793 (0.00%)	0 / 49 (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
Urticaria papular			
subjects affected / exposed	0 / 783 (0.00%)	1 / 793 (0.13%)	0 / 49 (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
Renal and urinary disorders			
Calculus urinary			
subjects affected / exposed	1 / 783 (0.13%)	0 / 793 (0.00%)	0 / 49 (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
Chronic kidney disease			

subjects affected / exposed	0 / 783 (0.00%)	1 / 793 (0.13%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nephrolithiasis			
subjects affected / exposed	0 / 783 (0.00%)	1 / 793 (0.13%)	0 / 49 (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
Ureterolithiasis			
subjects affected / exposed	2 / 783 (0.26%)	0 / 793 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocrine disorders			
Goitre			
subjects affected / exposed	1 / 783 (0.13%)	0 / 793 (0.00%)	0 / 49 (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
Hyperparathyroidism			
subjects affected / exposed	1 / 783 (0.13%)	0 / 793 (0.00%)	0 / 49 (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
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 783 (0.00%)	1 / 793 (0.13%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arthritis			
subjects affected / exposed	1 / 783 (0.13%)	0 / 793 (0.00%)	0 / 49 (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
Intervertebral disc protrusion			
subjects affected / exposed	1 / 783 (0.13%)	1 / 793 (0.13%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Jaw cyst			
subjects affected / exposed	0 / 783 (0.00%)	0 / 793 (0.00%)	1 / 49 (2.04%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Muscular weakness			
subjects affected / exposed	1 / 783 (0.13%)	0 / 793 (0.00%)	0 / 49 (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
Osteoarthritis			
subjects affected / exposed	0 / 783 (0.00%)	2 / 793 (0.25%)	0 / 49 (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
Rotator cuff syndrome			
subjects affected / exposed	0 / 783 (0.00%)	0 / 793 (0.00%)	0 / 49 (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			
Lower respiratory tract infection viral			
subjects affected / exposed	1 / 783 (0.13%)	0 / 793 (0.00%)	0 / 49 (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	2 / 783 (0.26%)	4 / 793 (0.50%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Postoperative abscess			
subjects affected / exposed	1 / 783 (0.13%)	0 / 793 (0.00%)	0 / 49 (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
Sinusitis			
subjects affected / exposed	1 / 783 (0.13%)	1 / 793 (0.13%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			

subjects affected / exposed	0 / 783 (0.00%)	1 / 793 (0.13%)	0 / 49 (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
Anal abscess			
subjects affected / exposed	0 / 783 (0.00%)	1 / 793 (0.13%)	0 / 49 (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
Bronchitis			
subjects affected / exposed	2 / 783 (0.26%)	1 / 793 (0.13%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	0 / 783 (0.00%)	1 / 793 (0.13%)	0 / 49 (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
Diverticulitis			
subjects affected / exposed	0 / 783 (0.00%)	0 / 793 (0.00%)	1 / 49 (2.04%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Erysipelas			
subjects affected / exposed	1 / 783 (0.13%)	0 / 793 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis salmonella			
subjects affected / exposed	0 / 783 (0.00%)	1 / 793 (0.13%)	0 / 49 (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
Influenza			
subjects affected / exposed	2 / 783 (0.26%)	2 / 793 (0.25%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower respiratory tract infection			

subjects affected / exposed	0 / 783 (0.00%)	0 / 793 (0.00%)	0 / 49 (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
Lung infection			
subjects affected / exposed	0 / 783 (0.00%)	1 / 793 (0.13%)	0 / 49 (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
Pneumonia bacterial			
subjects affected / exposed	1 / 783 (0.13%)	5 / 793 (0.63%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 1	1 / 6	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary sepsis			
subjects affected / exposed	0 / 783 (0.00%)	1 / 793 (0.13%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Respiratory tract infection viral			
subjects affected / exposed	1 / 783 (0.13%)	1 / 793 (0.13%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	0 / 783 (0.00%)	1 / 793 (0.13%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Sinusitis bacterial			
subjects affected / exposed	1 / 783 (0.13%)	0 / 793 (0.00%)	0 / 49 (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
Urinary tract infection bacterial			
subjects affected / exposed	1 / 783 (0.13%)	0 / 793 (0.00%)	0 / 49 (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
Urosepsis			

subjects affected / exposed	1 / 783 (0.13%)	0 / 793 (0.00%)	0 / 49 (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
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	1 / 783 (0.13%)	0 / 793 (0.00%)	0 / 49 (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
Obesity			
subjects affected / exposed	0 / 783 (0.00%)	0 / 793 (0.00%)	1 / 49 (2.04%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Type 2 diabetes mellitus			
subjects affected / exposed	2 / 783 (0.26%)	0 / 793 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Zonda - Benralizumab 30 mg q.8 weeks		
Total subjects affected by serious adverse events			
subjects affected / exposed	9 / 49 (18.37%)		
number of deaths (all causes)	1		
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma of colon			
subjects affected / exposed	0 / 49 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Benign neoplasm of thyroid gland			
subjects affected / exposed	0 / 49 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Chronic myeloid leukaemia			

subjects affected / exposed	0 / 49 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Diffuse large B-cell lymphoma stage II				
subjects affected / exposed	0 / 49 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Nasal cavity cancer				
subjects affected / exposed	0 / 49 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Ovarian germ cell teratoma benign				
subjects affected / exposed	1 / 49 (2.04%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Solid pseudopapillary tumour of the pancreas				
subjects affected / exposed	0 / 49 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
B-cell lymphoma				
subjects affected / exposed	0 / 49 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Basal cell carcinoma				
subjects affected / exposed	0 / 49 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Benign neoplasm of eyelid				
subjects affected / exposed	0 / 49 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Colon cancer stage 0				

subjects affected / exposed	0 / 49 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Large intestine benign neoplasm				
subjects affected / exposed	0 / 49 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Lipoma				
subjects affected / exposed	0 / 49 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Osteochondroma				
subjects affected / exposed	0 / 49 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Prostate cancer				
subjects affected / exposed	0 / 49 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Thymoma				
subjects affected / exposed	0 / 49 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Uterine leiomyoma				
subjects affected / exposed	0 / 49 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Vascular disorders				
Hypertensive emergency				
subjects affected / exposed	0 / 49 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Phlebitis				

subjects affected / exposed	0 / 49 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pregnancy, puerperium and perinatal conditions			
Abortion spontaneous			
subjects affected / exposed	0 / 49 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Death			
subjects affected / exposed	0 / 49 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Multiple organ dysfunction syndrome			
subjects affected / exposed	0 / 49 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Oedema peripheral			
subjects affected / exposed	0 / 49 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Immune system disorders			
Anaphylactic reaction			
subjects affected / exposed	0 / 49 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Food allergy			
subjects affected / exposed	0 / 49 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Reproductive system and breast disorders			
Cervical polyp			

subjects affected / exposed	0 / 49 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Ovarian cyst				
subjects affected / exposed	0 / 49 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Vaginal fistula				
subjects affected / exposed	0 / 49 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Vaginal haemorrhage				
subjects affected / exposed	0 / 49 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Respiratory, thoracic and mediastinal disorders				
Asthma				
subjects affected / exposed	2 / 49 (4.08%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Asthmatic crisis				
subjects affected / exposed	0 / 49 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Interstitial lung disease				
subjects affected / exposed	0 / 49 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Middle lobe syndrome				
subjects affected / exposed	0 / 49 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Nasal polyps				

subjects affected / exposed	0 / 49 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pleural effusion				
subjects affected / exposed	0 / 49 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pulmonary hypertension				
subjects affected / exposed	0 / 49 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Status asthmaticus				
subjects affected / exposed	0 / 49 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Investigations				
Endocrine test abnormal				
subjects affected / exposed	0 / 49 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Injury, poisoning and procedural complications				
Head injury				
subjects affected / exposed	0 / 49 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Humerus fracture				
subjects affected / exposed	0 / 49 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Limb injury				
subjects affected / exposed	0 / 49 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

Radius fracture				
subjects affected / exposed	0 / 49 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Rib fracture				
subjects affected / exposed	0 / 49 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Arthropod bite				
subjects affected / exposed	0 / 49 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Bone contusion				
subjects affected / exposed	0 / 49 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Clavicle fracture				
subjects affected / exposed	0 / 49 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Fall				
subjects affected / exposed	1 / 49 (2.04%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Femur fracture				
subjects affected / exposed	0 / 49 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Incisional hernia				
subjects affected / exposed	0 / 49 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Ligament rupture				

subjects affected / exposed	0 / 49 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Lower limb fracture				
subjects affected / exposed	0 / 49 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Multiple fractures				
subjects affected / exposed	0 / 49 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Patella fracture				
subjects affected / exposed	0 / 49 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Road traffic accident				
subjects affected / exposed	0 / 49 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Subdural haemorrhage				
subjects affected / exposed	0 / 49 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Upper limb fracture				
subjects affected / exposed	0 / 49 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiac disorders				
Acute coronary syndrome				
subjects affected / exposed	0 / 49 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Acute myocardial infarction				

subjects affected / exposed	0 / 49 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Angina unstable				
subjects affected / exposed	0 / 49 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Atrial fibrillation				
subjects affected / exposed	0 / 49 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiac arrest				
subjects affected / exposed	0 / 49 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiac failure congestive				
subjects affected / exposed	0 / 49 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardio-respiratory arrest				
subjects affected / exposed	0 / 49 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Congestive cardiomyopathy				
subjects affected / exposed	0 / 49 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Coronary artery disease				
subjects affected / exposed	0 / 49 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Coronary artery insufficiency				

subjects affected / exposed	0 / 49 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Supraventricular extrasystoles				
subjects affected / exposed	0 / 49 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Supraventricular tachycardia				
subjects affected / exposed	0 / 49 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Nervous system disorders				
Syncope				
subjects affected / exposed	0 / 49 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Diabetic neuropathy				
subjects affected / exposed	0 / 49 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Dysarthria				
subjects affected / exposed	0 / 49 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Ischaemic stroke				
subjects affected / exposed	0 / 49 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Lumbosacral radiculopathy				
subjects affected / exposed	0 / 49 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Transient ischaemic attack				

subjects affected / exposed	0 / 49 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Hypochromic anaemia			
subjects affected / exposed	0 / 49 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Iron deficiency anaemia			
subjects affected / exposed	0 / 49 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Neutropenia			
subjects affected / exposed	0 / 49 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Eye disorders			
Cataract			
subjects affected / exposed	0 / 49 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 49 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Duodenal ulcer			
subjects affected / exposed	0 / 49 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Inguinal hernia			
subjects affected / exposed	1 / 49 (2.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Oesophageal ulcer				
subjects affected / exposed	0 / 49 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Abdominal pain lower				
subjects affected / exposed	0 / 49 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Abdominal pain upper				
subjects affected / exposed	0 / 49 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Barrett's oesophagus				
subjects affected / exposed	0 / 49 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Colitis ulcerative				
subjects affected / exposed	1 / 49 (2.04%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Duodenal ulcer haemorrhage				
subjects affected / exposed	0 / 49 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Femoral hernia strangulated				
subjects affected / exposed	0 / 49 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastritis				
subjects affected / exposed	0 / 49 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastrooesophageal reflux disease				

subjects affected / exposed	0 / 49 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Ileus				
subjects affected / exposed	0 / 49 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Irritable bowel syndrome				
subjects affected / exposed	0 / 49 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Oesophagitis				
subjects affected / exposed	0 / 49 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pancreatitis acute				
subjects affected / exposed	0 / 49 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Vomiting				
subjects affected / exposed	0 / 49 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hepatobiliary disorders				
Cholecystitis				
subjects affected / exposed	0 / 49 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cholecystitis acute				
subjects affected / exposed	0 / 49 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cholecystitis chronic				

subjects affected / exposed	0 / 49 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Bile duct stone				
subjects affected / exposed	0 / 49 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cholelithiasis				
subjects affected / exposed	0 / 49 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hepatitis				
subjects affected / exposed	0 / 49 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Skin and subcutaneous tissue disorders				
Erythema nodosum				
subjects affected / exposed	0 / 49 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pemphigoid				
subjects affected / exposed	1 / 49 (2.04%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Rosacea				
subjects affected / exposed	0 / 49 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Urticaria papular				
subjects affected / exposed	0 / 49 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Renal and urinary disorders				

Calculus urinary				
subjects affected / exposed	0 / 49 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Chronic kidney disease				
subjects affected / exposed	0 / 49 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Nephrolithiasis				
subjects affected / exposed	0 / 49 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Ureterolithiasis				
subjects affected / exposed	0 / 49 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Endocrine disorders				
Goitre				
subjects affected / exposed	0 / 49 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hyperparathyroidism				
subjects affected / exposed	0 / 49 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Musculoskeletal and connective tissue disorders				
Arthralgia				
subjects affected / exposed	0 / 49 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Arthritis				
subjects affected / exposed	0 / 49 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

Intervertebral disc protrusion				
subjects affected / exposed	0 / 49 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Jaw cyst				
subjects affected / exposed	0 / 49 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Muscular weakness				
subjects affected / exposed	0 / 49 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Osteoarthritis				
subjects affected / exposed	0 / 49 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Rotator cuff syndrome				
subjects affected / exposed	1 / 49 (2.04%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Infections and infestations				
Lower respiratory tract infection viral				
subjects affected / exposed	0 / 49 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumonia				
subjects affected / exposed	1 / 49 (2.04%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Postoperative abscess				
subjects affected / exposed	0 / 49 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Sinusitis				

subjects affected / exposed	0 / 49 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Urinary tract infection				
subjects affected / exposed	0 / 49 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Anal abscess				
subjects affected / exposed	0 / 49 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Bronchitis				
subjects affected / exposed	0 / 49 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cellulitis				
subjects affected / exposed	0 / 49 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Diverticulitis				
subjects affected / exposed	0 / 49 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Erysipelas				
subjects affected / exposed	0 / 49 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastroenteritis salmonella				
subjects affected / exposed	0 / 49 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Influenza				

subjects affected / exposed	0 / 49 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Lower respiratory tract infection				
subjects affected / exposed	1 / 49 (2.04%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Lung infection				
subjects affected / exposed	0 / 49 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumonia bacterial				
subjects affected / exposed	0 / 49 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pulmonary sepsis				
subjects affected / exposed	0 / 49 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Respiratory tract infection viral				
subjects affected / exposed	0 / 49 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Sepsis				
subjects affected / exposed	0 / 49 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Sinusitis bacterial				
subjects affected / exposed	0 / 49 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Urinary tract infection bacterial				

subjects affected / exposed	0 / 49 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Urosepsis			
subjects affected / exposed	0 / 49 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 49 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Obesity			
subjects affected / exposed	0 / 49 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Type 2 diabetes mellitus			
subjects affected / exposed	0 / 49 (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: 3 %

Non-serious adverse events	Sirocco/Calima - Benralizumab 30 mg q.4 weeks	Sirocco/Calima - Benralizumab 30 mg q.8 weeks	Zonda - Benralizumab 30 mg q.4 weeks
Total subjects affected by non-serious adverse events			
subjects affected / exposed	543 / 783 (69.35%)	557 / 793 (70.24%)	36 / 49 (73.47%)
Investigations			
Blood creatinine increased			
subjects affected / exposed	0 / 783 (0.00%)	0 / 793 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Blood pressure increased			
subjects affected / exposed	4 / 783 (0.51%)	3 / 793 (0.38%)	1 / 49 (2.04%)
occurrences (all)	5	3	1
Vascular disorders			

Hypertension			
subjects affected / exposed	31 / 783 (3.96%)	28 / 793 (3.53%)	0 / 49 (0.00%)
occurrences (all)	32	32	0
Peripheral venous disease			
subjects affected / exposed	1 / 783 (0.13%)	3 / 793 (0.38%)	0 / 49 (0.00%)
occurrences (all)	1	3	0
Nervous system disorders			
Headache			
subjects affected / exposed	38 / 783 (4.85%)	40 / 793 (5.04%)	2 / 49 (4.08%)
occurrences (all)	54	55	2
General disorders and administration site conditions			
Influenza like illness			
subjects affected / exposed	27 / 783 (3.45%)	30 / 793 (3.78%)	3 / 49 (6.12%)
occurrences (all)	41	35	3
Injection site bruising			
subjects affected / exposed	0 / 783 (0.00%)	2 / 793 (0.25%)	0 / 49 (0.00%)
occurrences (all)	0	4	0
Non-cardiac chest pain			
subjects affected / exposed	2 / 783 (0.26%)	4 / 793 (0.50%)	0 / 49 (0.00%)
occurrences (all)	2	6	0
Oedema peripheral			
subjects affected / exposed	4 / 783 (0.51%)	6 / 793 (0.76%)	0 / 49 (0.00%)
occurrences (all)	4	7	0
Immune system disorders			
Seasonal allergy			
subjects affected / exposed	13 / 783 (1.66%)	8 / 793 (1.01%)	2 / 49 (4.08%)
occurrences (all)	15	8	2
Eye disorders			
Conjunctivitis allergic			
subjects affected / exposed	4 / 783 (0.51%)	8 / 793 (1.01%)	3 / 49 (6.12%)
occurrences (all)	5	8	3
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	12 / 783 (1.53%)	9 / 793 (1.13%)	1 / 49 (2.04%)
occurrences (all)	14	9	1
Gastritis			

subjects affected / exposed	6 / 783 (0.77%)	7 / 793 (0.88%)	2 / 49 (4.08%)
occurrences (all)	6	8	2
Large intestine polyp			
subjects affected / exposed	1 / 783 (0.13%)	1 / 793 (0.13%)	2 / 49 (4.08%)
occurrences (all)	1	1	2
Nausea			
subjects affected / exposed	10 / 783 (1.28%)	5 / 793 (0.63%)	2 / 49 (4.08%)
occurrences (all)	11	13	2
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	62 / 783 (7.92%)	53 / 793 (6.68%)	4 / 49 (8.16%)
occurrences (all)	100	76	4
Dyspnoea			
subjects affected / exposed	6 / 783 (0.77%)	9 / 793 (1.13%)	3 / 49 (6.12%)
occurrences (all)	6	9	3
Nasal congestion			
subjects affected / exposed	2 / 783 (0.26%)	12 / 793 (1.51%)	0 / 49 (0.00%)
occurrences (all)	2	12	0
Nasal polyps			
subjects affected / exposed	5 / 783 (0.64%)	4 / 793 (0.50%)	2 / 49 (4.08%)
occurrences (all)	6	4	2
Rhinitis allergic			
subjects affected / exposed	38 / 783 (4.85%)	22 / 793 (2.77%)	0 / 49 (0.00%)
occurrences (all)	43	32	0
Psychiatric disorders			
Insomnia			
subjects affected / exposed	12 / 783 (1.53%)	8 / 793 (1.01%)	3 / 49 (6.12%)
occurrences (all)	13	8	3
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	26 / 783 (3.32%)	20 / 793 (2.52%)	5 / 49 (10.20%)
occurrences (all)	32	20	5
Back pain			
subjects affected / exposed	24 / 783 (3.07%)	21 / 793 (2.65%)	2 / 49 (4.08%)
occurrences (all)	25	21	2
Infections and infestations			

Bronchitis			
subjects affected / exposed	50 / 783 (6.39%)	51 / 793 (6.43%)	3 / 49 (6.12%)
occurrences (all)	66	76	7
Upper respiratory tract infection			
subjects affected / exposed	61 / 783 (7.79%)	56 / 793 (7.06%)	0 / 49 (0.00%)
occurrences (all)	95	82	0
Acute sinusitis			
subjects affected / exposed	27 / 783 (3.45%)	44 / 793 (5.55%)	2 / 49 (4.08%)
occurrences (all)	46	61	5
Bronchitis bacterial			
subjects affected / exposed	19 / 783 (2.43%)	16 / 793 (2.02%)	3 / 49 (6.12%)
occurrences (all)	24	22	3
Chronic sinusitis			
subjects affected / exposed	12 / 783 (1.53%)	10 / 793 (1.26%)	1 / 49 (2.04%)
occurrences (all)	13	17	1
Herpes zoster			
subjects affected / exposed	8 / 783 (1.02%)	2 / 793 (0.25%)	2 / 49 (4.08%)
occurrences (all)	8	2	2
Oral candidiasis			
subjects affected / exposed	14 / 783 (1.79%)	13 / 793 (1.64%)	1 / 49 (2.04%)
occurrences (all)	20	16	1
Pharyngitis			
subjects affected / exposed	24 / 783 (3.07%)	26 / 793 (3.28%)	0 / 49 (0.00%)
occurrences (all)	28	37	0
Respiratory tract infection viral			
subjects affected / exposed	8 / 783 (1.02%)	12 / 793 (1.51%)	2 / 49 (4.08%)
occurrences (all)	8	13	2
Sinusitis			
subjects affected / exposed	22 / 783 (2.81%)	18 / 793 (2.27%)	3 / 49 (6.12%)
occurrences (all)	25	22	3
Upper respiratory tract infection bacterial			
subjects affected / exposed	15 / 783 (1.92%)	23 / 793 (2.90%)	1 / 49 (2.04%)
occurrences (all)	17	28	1
Urinary tract infection			

subjects affected / exposed	14 / 783 (1.79%)	8 / 793 (1.01%)	0 / 49 (0.00%)
occurrences (all)	17	8	0
Viral upper respiratory tract infection			
subjects affected / exposed	124 / 783 (15.84%)	130 / 793 (16.39%)	14 / 49 (28.57%)
occurrences (all)	186	196	22

Non-serious adverse events	Zonda - Benralizumab 30 mg q.8 weeks		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	39 / 49 (79.59%)		
Investigations			
Blood creatinine increased			
subjects affected / exposed	2 / 49 (4.08%)		
occurrences (all)	2		
Blood pressure increased			
subjects affected / exposed	2 / 49 (4.08%)		
occurrences (all)	2		
Vascular disorders			
Hypertension			
subjects affected / exposed	2 / 49 (4.08%)		
occurrences (all)	2		
Peripheral venous disease			
subjects affected / exposed	2 / 49 (4.08%)		
occurrences (all)	2		
Nervous system disorders			
Headache			
subjects affected / exposed	4 / 49 (8.16%)		
occurrences (all)	4		
General disorders and administration site conditions			
Influenza like illness			
subjects affected / exposed	1 / 49 (2.04%)		
occurrences (all)	1		
Injection site bruising			
subjects affected / exposed	2 / 49 (4.08%)		
occurrences (all)	2		
Non-cardiac chest pain			

subjects affected / exposed	2 / 49 (4.08%)		
occurrences (all)	3		
Oedema peripheral			
subjects affected / exposed	4 / 49 (8.16%)		
occurrences (all)	6		
Immune system disorders			
Seasonal allergy			
subjects affected / exposed	0 / 49 (0.00%)		
occurrences (all)	0		
Eye disorders			
Conjunctivitis allergic			
subjects affected / exposed	0 / 49 (0.00%)		
occurrences (all)	0		
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	2 / 49 (4.08%)		
occurrences (all)	2		
Gastritis			
subjects affected / exposed	1 / 49 (2.04%)		
occurrences (all)	1		
Large intestine polyp			
subjects affected / exposed	1 / 49 (2.04%)		
occurrences (all)	1		
Nausea			
subjects affected / exposed	0 / 49 (0.00%)		
occurrences (all)	0		
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	7 / 49 (14.29%)		
occurrences (all)	9		
Dyspnoea			
subjects affected / exposed	1 / 49 (2.04%)		
occurrences (all)	1		
Nasal congestion			
subjects affected / exposed	2 / 49 (4.08%)		
occurrences (all)	2		

Nasal polyps			
subjects affected / exposed	2 / 49 (4.08%)		
occurrences (all)	2		
Rhinitis allergic			
subjects affected / exposed	2 / 49 (4.08%)		
occurrences (all)	2		
Psychiatric disorders			
Insomnia			
subjects affected / exposed	0 / 49 (0.00%)		
occurrences (all)	0		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 49 (0.00%)		
occurrences (all)	0		
Back pain			
subjects affected / exposed	4 / 49 (8.16%)		
occurrences (all)	4		
Infections and infestations			
Bronchitis			
subjects affected / exposed	10 / 49 (20.41%)		
occurrences (all)	16		
Upper respiratory tract infection			
subjects affected / exposed	7 / 49 (14.29%)		
occurrences (all)	8		
Acute sinusitis			
subjects affected / exposed	2 / 49 (4.08%)		
occurrences (all)	4		
Bronchitis bacterial			
subjects affected / exposed	2 / 49 (4.08%)		
occurrences (all)	2		
Chronic sinusitis			
subjects affected / exposed	2 / 49 (4.08%)		
occurrences (all)	7		
Herpes zoster			
subjects affected / exposed	0 / 49 (0.00%)		
occurrences (all)	0		

Oral candidiasis			
subjects affected / exposed	2 / 49 (4.08%)		
occurrences (all)	2		
Pharyngitis			
subjects affected / exposed	0 / 49 (0.00%)		
occurrences (all)	0		
Respiratory tract infection viral			
subjects affected / exposed	0 / 49 (0.00%)		
occurrences (all)	0		
Sinusitis			
subjects affected / exposed	4 / 49 (8.16%)		
occurrences (all)	4		
Upper respiratory tract infection bacterial			
subjects affected / exposed	2 / 49 (4.08%)		
occurrences (all)	2		
Urinary tract infection			
subjects affected / exposed	2 / 49 (4.08%)		
occurrences (all)	2		
Viral upper respiratory tract infection			
subjects affected / exposed	13 / 49 (26.53%)		
occurrences (all)	19		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
01 September 2015	Update study objectives; Remove requirement of continuing regular study visits after discontinuation of treatment; and other administrative changes.
13 January 2016	Add MELTEMI study as an extension of treatment study; Adjust unblinding language.
16 December 2016	Add Japanese interim analysis

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.

Patients in this study had to complete treatment in predecessor studies. Therefore selection bias may exist. Baseline is defined for this study’s entry value, not all values are prior to active treatment due to some patients being treated previously.

Notes: