



## 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	v1
This version publication date	27 December 2018
First version publication date	27 December 2018

#### Trial information

##### Trial identification

Sponsor protocol code	D3250C00021
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##### 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:

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### 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 were entered. 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 enrolled into MELTEMI without completing the full follow-up, thus not in the main analyses.

### Pre-assignment

Screening details:

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

### 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, Carer, Data analyst, Assessor, Monitor

### Arms

Are arms mutually exclusive?	Yes
<b>Arm title</b>	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

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

<b>Arm title</b>	ZONDA - Benralizumab 30 mg q.4 weeks
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Arm description:

Benralizumab administered subcutaneously every 4 weeks

Arm type	Experimental
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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	
<b>Arm title</b>	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

<b>Number of subjects in period 1<sup>[1]</sup></b>	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	892	871	92
Not completed	61	102	8
Adverse event, serious fatal	5	4	-
Consent withdrawn by subject	20	17	7
Eligibility criteria not fulfilled	-	2	-
Adverse event, non-fatal	3	4	-
Ongoing	19	58	-
study specific discount. criteria	1	1	-
Lost to follow-up	5	10	1
eg. not made to the visit	7	4	-
Protocol deviation	1	2	-

<b>Number of subjects in period 1<sup>[1]</sup></b>	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	-
Ongoing	-
study specific discount. criteria	-
Lost to follow-up	2
eg. not made to the visit	1
Protocol deviation	-

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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: There are total 2133 enrolled, 10 patients were excluded from all analyses due to GCP breach. Thus there is a 10 patient difference.

## Baseline characteristics

### Reporting groups

Reporting group title	SIROCCO/CALIMA - Benralizumab 30 mg q.4 weeks
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Reporting group description:

Benralizumab administered subcutaneously every 4 weeks

Reporting group title	SIROCCO/CALIMA - Benralizumab 30 mg q.8 weeks
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Reporting group description:

Benralizumab administered subcutaneously every 8 weeks

Reporting group title	ZONDA - Benralizumab 30 mg q.4 weeks
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Reporting group description:

Benralizumab administered subcutaneously every 4 weeks

Reporting group title	ZONDA - Benralizumab 30 mg q.8 weeks
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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			
Two separate summaries presented: Overall all randomized patients (excluding non-GCP compliant patients); Separately for Full analysis set, excluding patients enrolled in MELTEMI.			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	21	51	0
Adults (18-64 years)	773	790	86
From 65-84 years	159	132	14
85 years and over	0	0	0
Age Continuous			
Full analysis set, Excluding patients enrolled in MELTEMI			
Units: years			
arithmetic mean	51.1	48.9	49.7
standard deviation	± 13.79	± 15.53	± 10.35
Sex: Female, Male			
Two separate summaries presented: Overall all randomized patients (excluding non-GCP compliant patients); Separately for Full analysis set, excluding patients enrolled in MELTEMI.			
Units: Subjects			
Female	612	584	58
Male	341	389	42
Race/Ethnicity, Customized			
Two separate summaries presented: Overall all randomized patients (excluding non-GCP compliant patients); Separately for Full analysis set, excluding patients enrolled in MELTEMI.			
Units: Subjects			
White	753	774	96

Black and African American	25	30	0
Asian	143	139	4
Other	32	30	0

<b>Reporting group values</b>	ZONDA - Benralizumab 30 mg q.8 weeks	Total	
Number of subjects	97	2123	
Age categorical			
Two separate summaries presented: Overall all randomized patients (excluding non-GCP compliant patients); Separately for Full analysis set, excluding patients enrolled in MELTEMI.			
Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	72	
Adults (18-64 years)	83	1732	
From 65-84 years	14	319	
85 years and over	0	0	
Age Continuous			
Full analysis set, Excluding patients enrolled in MELTEMI			
Units: years			
arithmetic mean	52.7		
standard deviation	± 8.90	-	
Sex: Female, Male			
Two separate summaries presented: Overall all randomized patients (excluding non-GCP compliant patients); Separately for Full analysis set, excluding patients enrolled in MELTEMI.			
Units: Subjects			
Female	61	1315	
Male	36	808	
Race/Ethnicity, Customized			
Two separate summaries presented: Overall all randomized patients (excluding non-GCP compliant patients); Separately for Full analysis set, excluding patients enrolled in MELTEMI.			
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
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Subject analysis set type	Full analysis
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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
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Subject analysis set type	Full analysis
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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
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Subject analysis set type	Full analysis
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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
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Subject analysis set type	Full analysis
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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
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Subject analysis set type	Full analysis
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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
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Subject analysis set type	Full analysis
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Subject analysis set description:

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

<b>Reporting group values</b>	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			
Two separate summaries presented: Overall all randomized patients (excluding non-GCP compliant patients); Separately for Full analysis set, excluding patients enrolled in MELTEMI.			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	12	9	25
Adults (18-64 years)	421	213	421
From 65-84 years	85	43	66
85 years and over	0	0	0
Age Continuous			
Full analysis set, Excluding patients enrolled in MELTEMI			
Units: years			
arithmetic mean	51.7	49.9	49.3

standard deviation	± 13.26	± 14.73	± 14.81
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Sex: Female, Male			
Two separate summaries presented: Overall all randomized patients (excluding non-GCP compliant patients); Separately for Full analysis set, excluding patients enrolled in MELTEMI.			
Units: Subjects			
Female	339	164	307
Male	179	101	205
Race/Ethnicity, Customized			
Two separate summaries presented: Overall all randomized patients (excluding non-GCP compliant patients); Separately for Full analysis set, excluding patients enrolled in MELTEMI.			
Units: Subjects			
White	398	201	388
Black and African American	6	10	12
Asian	94	44	92
Other	20	10	20

<b>Reporting group values</b>	<b>SIROCCO/CALIMA - Benralizumab 30 mg q.8 - Predecessor Placebo</b>	<b>ZONDA - Benralizumab 30 mg q.4 - Pre Benra q.4</b>	<b>ZONDA - Benralizumab 30 mg q.4 - Predecessor Placebo</b>
Number of subjects	281	31	18
Age categorical			
Two separate summaries presented: Overall all randomized patients (excluding non-GCP compliant patients); Separately for Full analysis set, excluding patients enrolled in MELTEMI.			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	26	0	0
Adults (18-64 years)	211	30	16
From 65-84 years	44	1	2
85 years and over	0	0	0
Age Continuous			
Full analysis set, Excluding patients enrolled in MELTEMI			
Units: years			
arithmetic mean	48.2	47.9	52.7
standard deviation	± 16.77	± 10.42	± 9.77
Sex: Female, Male			
Two separate summaries presented: Overall all randomized patients (excluding non-GCP compliant patients); Separately for Full analysis set, excluding patients enrolled in MELTEMI.			
Units: Subjects			
Female	163	13	14
Male	118	18	4
Race/Ethnicity, Customized			
Two separate summaries presented: Overall all randomized patients (excluding non-GCP compliant patients); Separately for Full analysis set, excluding patients enrolled in MELTEMI.			
Units: Subjects			
White	224	28	17
Black and African American	7	0	0

Asian	44	3	1
Other	6	0	0

<b>Reporting group values</b>	ZONDA - Benralizumab 30 mg q.8 - Pre Benra q.8	ZONDA - Benralizumab 30 mg q.8 - Predecessor Placebo	
Number of subjects	31	18	
Age categorical			
Two separate summaries presented: Overall all randomized patients (excluding non-GCP compliant patients); Separately for Full analysis set, excluding patients enrolled in MELTEMI.			
Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	26	17	
From 65-84 years	5	1	
85 years and over	0	0	
Age Continuous			
Full analysis set, Excluding patients enrolled in MELTEMI			
Units: years			
arithmetic mean	54.3	49.9	
standard deviation	± 8.39	± 9.30	
Sex: Female, Male			
Two separate summaries presented: Overall all randomized patients (excluding non-GCP compliant patients); Separately for Full analysis set, excluding patients enrolled in MELTEMI.			
Units: Subjects			
Female	20	9	
Male	11	9	
Race/Ethnicity, Customized			
Two separate summaries presented: Overall all randomized patients (excluding non-GCP compliant patients); Separately for Full analysis set, excluding patients enrolled in MELTEMI.			
Units: Subjects			
White	26	16	
Black and African American	0	1	
Asian	5	1	
Other	0	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

**Primary: Change from baseline in lab variables, Full analysis set, Excluding MELTEMI patients**

End point title	Change from baseline in lab variables, Full analysis set, Excluding MELTEMI patients <sup>[1]</sup>
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End point description:

Change from baseline in hematologic (Basophils, Leukocytes, Lymphocytes, Neutrophils, Eosinophils) and chemistry tests (ALT, AST, Bilirubin).

End point type	Primary
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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 study is safety follow-up study. All analyses are descriptive and no hypothesis testing was intended or planned.

End point values	SIROCCO/CALI MA - Benralizumab 30 mg q.4 weeks	SIROCCO/CALI MA - 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: SI unit				
arithmetic mean (standard deviation)				
Basophils (10**9/L)	-0.005 (± 0.0223)	-0.005 (± 0.0239)	-0.007 (± 0.0283)	-0.005 (± 0.0244)
Leukocytes (10**9/L)	-0.344 (± 2.0412)	-0.128 (± 1.8614)	-0.808 (± 1.8177)	-0.507 (± 3.3612)
Lymphocytes (10**9/L)	-0.032 (± 0.6242)	0.003 (± 0.5402)	-0.093 (± 0.6403)	0.007 (± 0.6864)
Neutrophils (10**9/L)	-0.171 (± 1.8746)	0.013 (± 1.7024)	-0.501 (± 1.7096)	-0.368 (± 3.2057)
Eosinophils (10**9/L)	-0.1220 (± 0.30599)	-0.1271 (± 0.26161)	-0.1451 (± 0.30766)	-0.1664 (± 0.35139)
Alanine Aminotransferase (ukat/L)	-0.007 (± 0.2102)	0.017 (± 0.4651)	-0.064 (± 0.3547)	-0.023 (± 0.1940)
Aspartate Aminotransferase (ukat/L)	-0.005 (± 0.1431)	0.004 (± 0.3303)	-0.027 (± 0.2291)	-0.026 (± 0.1178)
Bilirubin (umol/L)	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

**Secondary: Number of overall patients with asthma exacerbations during study period, Full analysis set, Excluding MELTEMI patients**

End point title	Number of overall patients with asthma exacerbations during study period, Full analysis set, Excluding MELTEMI patients
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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
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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 $\geq$ 300/ $\mu$ L # exacerb.	159	170	0	0
Sirocco/Calima eos $<$ 300/ $\mu$ L # exacerb.	113	97	0	0
Zonda # of exacerbation	0	0	17	24

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	518	265	512	281
Units: participants				
Sirocco/Calima eos $\geq$ 300/ $\mu$ L # exacerb.	99	60	104	66
Sirocco/Calima eos $<$ 300/ $\mu$ L # exacerb.	69	44	65	32
Zonda # of exacerbation	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 $\geq$ 300/ $\mu$ L # exacerb.	0	0	0	0
Sirocco/Calima eos $<$ 300/ $\mu$ L # exacerb.	0	0	0	0
Zonda # of exacerbation	12	5	13	11

## Statistical analyses

No statistical analyses for this end point

### Secondary: Annual asthma exacerbation rate during on-treatment period, Full analysis set, Excluding MELTEMI patients

End point title	Annual asthma exacerbation rate during on-treatment period, Full analysis set, Excluding MELTEMI patients
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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
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End point timeframe:

From week 0 to week 56 in study treatment 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 <sup>[2]</sup>	793 <sup>[3]</sup>	49 <sup>[4]</sup>	49 <sup>[5]</sup>
Units: count per year				
number (confidence interval 95%)				
Sirocco/Calima patients with EOS $\geq$ 300/ $\mu$ L	0.5 (0.44 to 0.56)	0.49 (0.44 to 0.56)	0 (0 to 0)	0 (0 to 0)
Sirocco/Calima patients with EOS $<$ 300/ $\mu$ L	0.76 (0.66 to 0.87)	0.64 (0.55 to 0.74)	0 (0 to 0)	0 (0 to 0)
Zonda patients	0 (0 to 0)	0 (0 to 0)	0.63 (0.44 to 0.91)	0.68 (0.48 to 0.95)

Notes:

[2] - 519 for EOS $\geq$ 300  
264 for EOS $<$ 300

[3] - 527 for EOS $\geq$ 300  
266 for EOS $<$ 300

[4] - Over all EOS

[5] - 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	518 <sup>[6]</sup>	265 <sup>[7]</sup>	512 <sup>[8]</sup>	281 <sup>[9]</sup>
Units: count per year				

number (confidence interval 95%)				
Sirocco/Calima patients with EOS $\geq$ 300/ $\mu$ L	0.48 (0.42 to 0.56)	0.53 (0.43 to 0.56)	0.59 (0.49 to 0.71)	0.74 (0.59 to 0.94)
Sirocco/Calima patients with EOS $<$ 300/ $\mu$ L	0.74 (0.62 to 0.88)	0.8 (0.64 to 1)	0.59 (0.49 to 0.71)	0.74 (0.59 to 0.94)
Zonda patients	0 (0 to 0)			

Notes:

[6] - 347 for EOS $\geq$ 300  
171 for EOS $<$ 300

[7] - 172 for EOS $\geq$ 300  
93 for EOS $<$ 300

[8] - 339 for EOS $\geq$ 300  
173 for EOS $<$ 300

[9] - 188 for EOS $\geq$ 300  
93 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	31 <sup>[10]</sup>	18 <sup>[11]</sup>	31 <sup>[12]</sup>	18 <sup>[13]</sup>
Units: count per year				
number (confidence interval 95%)				
Sirocco/Calima patients with EOS $\geq$ 300/ $\mu$ L	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)
Sirocco/Calima patients with EOS $<$ 300/ $\mu$ L	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)
Zonda patients	0.6 (0.39 to 0.95)	0.7 (0.38 to 1.3)	0.64 (0.42 to 0.98)	0.75 (0.44 to 1.3)

Notes:

[10] - Over all EOS

[11] - Over all EOS

[12] - Over all EOS

[13] - Over all EOS

## Statistical analyses

No statistical analyses for this end point

### Secondary: Change from baseline in pre-bronchodilator FEV1 (L), Full analysis set, Excluding MELTEMI patients

End point title	Change from baseline in pre-bronchodilator FEV1 (L), Full analysis set, Excluding MELTEMI patients
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

<b>End point values</b>	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 <sup>[14]</sup>	660 <sup>[15]</sup>	38 <sup>[16]</sup>	43 <sup>[17]</sup>
Units: Liter				
arithmetic mean (standard deviation)				
Sirocco/Calima patients with EOS $\geq$ 300/ $\mu$ L	0.038 ( $\pm$ 0.346)	0.040 ( $\pm$ 0.356)	0 ( $\pm$ 0)	0 ( $\pm$ 0)
Sirocco/Calima patients with EOS $<$ 300/ $\mu$ L	-0.017 ( $\pm$ 0.345)	-0.001 ( $\pm$ 0.312)	0 ( $\pm$ 0)	0 ( $\pm$ 0)
Zonda patients	0 ( $\pm$ 0)	0 ( $\pm$ 0)	0.057 ( $\pm$ 0.412)	-0.012 ( $\pm$ 0.314)

Notes:

[14] - 439 for EOS $\geq$ 300

226 for EOS $<$ 300

[15] - 442 for EOS $\geq$ 300

218 for EOS $<$ 300

[16] - Over all EOS

[17] - Over all EOS

<b>End point values</b>	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 <sup>[18]</sup>	221 <sup>[19]</sup>	440 <sup>[20]</sup>	220 <sup>[21]</sup>
Units: Liter				
arithmetic mean (standard deviation)				
Sirocco/Calima patients with EOS $\geq$ 300/ $\mu$ L	-0.006 ( $\pm$ 0.295)	0.131 ( $\pm$ 0.422)	0.019 ( $\pm$ 0.317)	0.081 ( $\pm$ 0.419)
Sirocco/Calima patients with EOS $<$ 300/ $\mu$ L	-0.021 ( $\pm$ 0.376)	-0.011 ( $\pm$ 0.280)	-0.015 ( $\pm$ 0.293)	0.030 ( $\pm$ 0.350)
Zonda patients	0 ( $\pm$ 0)	0 ( $\pm$ 0)	0 ( $\pm$ 0)	0 ( $\pm$ 0)

Notes:

[18] - 297 for EOS $\geq$ 300

147 for EOS $<$ 300

[19] - 142 for EOS $\geq$ 300

79 for EOS $<$ 300

[20] - 291 for EOS $\geq$ 300

149 for EOS $<$ 300

[21] - 151 for EOS $\geq$ 300

69 for EOS $<$ 300

<b>End point values</b>	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 <sup>[22]</sup>	11 <sup>[23]</sup>	28 <sup>[24]</sup>	15 <sup>[25]</sup>
Units: Liter				
arithmetic mean (standard deviation)				
Sirocco/Calima patients with EOS $\geq$ 300/ $\mu$ L	0 ( $\pm$ 0)	0 ( $\pm$ 0)	0 ( $\pm$ 0)	0 ( $\pm$ 0)
Sirocco/Calima patients with EOS $<$ 300/ $\mu$ L	0 ( $\pm$ 0)	0 ( $\pm$ 0)	0 ( $\pm$ 0)	0 ( $\pm$ 0)

Zonda patients	0.013 (± 0.354)	0.167 (± 0.533)	-0.093 (± 0.280)	0.138 (± 0.329)
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Notes:

[22] - Over all EOS

[23] - Over all EOS

[24] - Over all EOS

[25] - Over all EOS

## Statistical analyses

No statistical analyses for this end point

### Secondary: Change from baseline in post-bronchodilator FEV1 (L), Full analysis set, Excluding MELTEMI patients

End point title	Change from baseline in post-bronchodilator FEV1 (L), Full analysis set, Excluding MELTEMI patients <sup>[26]</sup>
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End point description:

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

End point type	Secondary
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End point timeframe:

Week 56

Notes:

[26] - 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: Patients in two arms from study ZONDA were not required to collect post-bronchodilator FEV1, thus this endpoint was not analyzed for those two arms.

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 <sup>[27]</sup>	652 <sup>[28]</sup>	439 <sup>[29]</sup>	220 <sup>[30]</sup>
Units: Liter				
arithmetic mean (standard deviation)				
Sirocco/Calima patients with eos $\geq$ 300/ $\mu$ L	-0.015 (± 0.354)	-0.004 (± 0.329)	-0.066 (± 0.280)	0.089 (± 0.455)
Sirocco/Calima patients with eos $<$ 300/ $\mu$ L	-0.046 (± 0.350)	-0.015 (± 0.316)	-0.058 (± 0.379)	-0.024 (± 0.289)

Notes:

[27] - 440 for EOS $\geq$ 300  
219 for EOS $<$ 300

[28] - 443 for EOS $\geq$ 300  
209 for EOS $<$ 300

[29] - 296 for EOS $\geq$ 300  
143 for EOS $<$ 300

[30] - 144 for EOS $\geq$ 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 <sup>[31]</sup>	214 <sup>[32]</sup>		
Units: Liter				
arithmetic mean (standard deviation)				
Sirocco/Calima patients with eos $\geq$ 300/ $\mu$ L	-0.029 ( $\pm$ 0.281)	0.045 ( $\pm$ 0.401)		
Sirocco/Calima patients with eos $<$ 300/ $\mu$ L	-0.043 ( $\pm$ 0.273)	0.049 ( $\pm$ 0.394)		

Notes:

[31] - 292 for EOS $\geq$ 300  
146 for EOS $<$ 300

[32] - 151 for EOS $\geq$ 300  
63 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, Full analysis set, Excluding MELTEMI patients

End point title	Change from baseline in Asthma Control Questionnaire (ACQ) as a measure of asthma control in overall patients, Full analysis set, Excluding MELTEMI patients
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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
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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 <sup>[33]</sup>	664 <sup>[34]</sup>	39 <sup>[35]</sup>	43 <sup>[36]</sup>
Units: Scale of score				
arithmetic mean (standard deviation)				
Sirocco/Calima patients with eos $\geq$ 300/ $\mu$ L	-0.09 ( $\pm$ 0.91)	-0.12 ( $\pm$ 0.91)	0 ( $\pm$ 0)	0 ( $\pm$ 0)
Sirocco/Calima patients with eos $<$ 300/ $\mu$ L	-0.15 ( $\pm$ 0.86)	-0.10 ( $\pm$ 0.90)	0 ( $\pm$ 0)	0 ( $\pm$ 0)
Zonda patients	0 ( $\pm$ 0)	0 ( $\pm$ 0)	-0.21 ( $\pm$ 0.87)	-0.05 ( $\pm$ 1.04)

Notes:

[33] - 444 for EOS $\geq$ 300  
227 for EOS $<$ 300

[34] - 447 for EOS $\geq$ 300  
217 for EOS $<$ 300

[35] - Over all EOS

[36] - Over all EOS

End point values	SIROCCO/CALIMA	SIROCCO/CALIMA	SIROCCO/CALIMA	SIROCCO/CALIMA
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	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	447 <sup>[37]</sup>	224 <sup>[38]</sup>	444 <sup>[39]</sup>	220 <sup>[40]</sup>
Units: Scale of score				
arithmetic mean (standard deviation)				
Sirocco/Calima patients with eos $\geq$ 300/ $\mu$ L	-0.04 ( $\pm$ 0.83)	-0.20 ( $\pm$ 1.04)	-0.06 ( $\pm$ 0.82)	-0.25 ( $\pm$ 1.06)
Sirocco/Calima patients with eos $<$ 300/ $\mu$ L	-0.16 ( $\pm$ 0.90)	-0.12 ( $\pm$ 0.80)	-0.10 ( $\pm$ 0.83)	-0.09 ( $\pm$ 1.06)
Zonda patients	0 ( $\pm$ 0)	0 ( $\pm$ 0)	0 ( $\pm$ 0)	0 ( $\pm$ 0)

Notes:

[37] - 298 for EOS $\geq$ 300

149 for EOS $<$ 300

[38] - 146 for EOS $\geq$ 300

78 for EOS $<$ 300

[39] - 294 for EOS $\geq$ 300

150 for EOS $<$ 300

[40] - 153 for EOS $\geq$ 300

67 for EOS $<$ 300

<b>End point values</b>	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 <sup>[41]</sup>	11 <sup>[42]</sup>	28 <sup>[43]</sup>	15 <sup>[44]</sup>
Units: Scale of score				
arithmetic mean (standard deviation)				
Sirocco/Calima patients with eos $\geq$ 300/ $\mu$ L	0 ( $\pm$ 0)	0 ( $\pm$ 0)	0 ( $\pm$ 0)	0 ( $\pm$ 0)
Sirocco/Calima patients with eos $<$ 300/ $\mu$ L	0 ( $\pm$ 0)	0 ( $\pm$ 0)	0 ( $\pm$ 0)	0 ( $\pm$ 0)
Zonda patients	-0.05 ( $\pm$ 0.89)	-0.61 ( $\pm$ 0.74)	0.15 ( $\pm$ 1.02)	-0.43 ( $\pm$ 1.00)

Notes:

[41] - Over all EOS

[42] - Over all EOS

[43] - Over all EOS

[44] - 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), Full analysis set, Excluding MELTEMI patients

End point title	Change from baseline in total score of asthma related and general health-related quality of life questionnaire (AQLQ(S)+12), Full analysis set, Excluding MELTEMI patients
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). An increase in score indicates improvement.	
End point type	Secondary

<b>End point values</b>	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 <sup>[45]</sup>	662 <sup>[46]</sup>	37 <sup>[47]</sup>	43 <sup>[48]</sup>
Units: Scale of score				
arithmetic mean (standard deviation)				
Sirocco/Calima patients with eos $\geq$ 300/ $\mu$ L	0.08 ( $\pm$ 0.87)	0.15 ( $\pm$ 0.94)	0 ( $\pm$ 0)	0 ( $\pm$ 0)
Sirocco/Calima patients with eos $<$ 300/ $\mu$ L	0.09 ( $\pm$ 0.85)	0.11 ( $\pm$ 0.95)	0 ( $\pm$ 0)	0 ( $\pm$ 0)
Zonda patients	0 ( $\pm$ 0)	0 ( $\pm$ 0)	0.22 ( $\pm$ 0.92)	0.11 ( $\pm$ 0.98)

Notes:

[45] - 442 for EOS $\geq$ 300  
226 for EOS $<$ 300[46] - 446 for EOS $\geq$ 300  
216 for EOS $<$ 300

[47] - Over all EOS

[48] - Over all EOS

<b>End point values</b>	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 <sup>[49]</sup>	224 <sup>[50]</sup>	442 <sup>[51]</sup>	220 <sup>[52]</sup>
Units: Scale of score				
arithmetic mean (standard deviation)				
Sirocco/Calima patients with eos $\geq$ 300/ $\mu$ L	0.02 ( $\pm$ 0.80)	0.21 ( $\pm$ 0.98)	0.08 ( $\pm$ 0.91)	0.26 ( $\pm$ 1.00)
Sirocco/Calima patients with eos $<$ 300/ $\mu$ L	0.11 ( $\pm$ 0.84)	0.03 ( $\pm$ 0.89)	0.15 ( $\pm$ 0.90)	0.02 ( $\pm$ 1.06)
Zonda patients	0 ( $\pm$ 0)	0 ( $\pm$ 0)	0 ( $\pm$ 0)	0 ( $\pm$ 0)

Notes:

[49] - 296 for EOS $\geq$ 300  
148 for EOS $<$ 300[50] - 146 for EOS $\geq$ 300  
78 for EOS $<$ 300[51] - 293 for EOS $\geq$ 300  
149 for EOS $<$ 300[52] - 153 for EOS $\geq$ 300  
67 for EOS $<$ 300

<b>End point values</b>	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 <sup>[53]</sup>	11 <sup>[54]</sup>	28 <sup>[55]</sup>	15 <sup>[56]</sup>

Units: Scale of score				
arithmetic mean (standard deviation)				
Sirocco/Calima patients with eos $\geq$ 300/ $\mu$ L	0 ( $\pm$ 0)	0 ( $\pm$ 0)	0 ( $\pm$ 0)	0 ( $\pm$ 0)
Sirocco/Calima patients with eos<300/ $\mu$ L	0 ( $\pm$ 0)	0 ( $\pm$ 0)	0 ( $\pm$ 0)	0 ( $\pm$ 0)
Zonda patients	0.13 ( $\pm$ 0.93)	0.43 ( $\pm$ 0.91)	-0.04 ( $\pm$ 0.94)	0.40 ( $\pm$ 1.03)

Notes:

[53] - Over all EOS

[54] - Over all EOS

[55] - Over all EOS

[56] - Over all EOS

## Statistical analyses

No statistical analyses for this end point

### Secondary: Change of blood eosinophil levels' measurement in overall patients, Full analysis set, Excluding MELTEMI patients

End point title	Change of blood eosinophil levels' measurement in overall patients, Full analysis set, Excluding MELTEMI 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 <sup>[57]</sup>	703 <sup>[58]</sup>	39 <sup>[59]</sup>	42 <sup>[60]</sup>
Units: cell/ $\mu$ L				
arithmetic mean (standard deviation)				
Sirocco/Calima patients with eos $\geq$ 300/ $\mu$ L	-148.6 ( $\pm$ 332.91)	-154.1 ( $\pm$ 297.34)	0 ( $\pm$ 0)	0 ( $\pm$ 0)
Sirocco/Calima patients with eos<300/ $\mu$ L	-68.4 ( $\pm$ 234.40)	-74.7 ( $\pm$ 160.29)	0 ( $\pm$ 0)	0 ( $\pm$ 0)
Zonda patients	0 ( $\pm$ 0)	0 ( $\pm$ 0)	-145.1 ( $\pm$ 307.66)	-166.4 ( $\pm$ 351.39)

Notes:

[57] - 462 for EOS $\geq$ 300

229 for EOS<300

[58] - 464 for EOS $\geq$ 300

239 for EOS<300

[59] - Over all EOS

[60] - Over all EOS

End point values	SIROCCO/CALIMA - Benralizumab 30 mg q.4 -	SIROCCO/CALIMA - Benralizumab 30 mg q.4 -	SIROCCO/CALIMA - Benralizumab 30 mg q.8 -	SIROCCO/CALIMA - Benralizumab 30 mg q.8 -

	Pre Benra q.4	Predecessor Placebo	Pre Benra q.8	Predecessor Placebo
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	454 <sup>[61]</sup>	237 <sup>[62]</sup>	461 <sup>[63]</sup>	242 <sup>[64]</sup>
Units: cell/ $\mu$ L				
arithmetic mean (standard deviation)				
Sirocco/Calima patients with eos $\geq$ 300/ $\mu$ L	4.9 ( $\pm$ 177.42)	-449.6 ( $\pm$ 360.6)	-10.1 ( $\pm$ 134.7)	-422.5 ( $\pm$ 330.01)
Sirocco/Calima patients with eos<300/ $\mu$ L	15.7 ( $\pm$ 87.04)	-222.1 ( $\pm$ 325.03)	-2.9 ( $\pm$ 59.11)	-217.4 ( $\pm$ 198.56)
Zonda patients	0 ( $\pm$ 0)	0 ( $\pm$ 0)	0 ( $\pm$ 0)	0 ( $\pm$ 0)

Notes:

[61] - 306 for EOS $\geq$ 300

148 for EOS<300

[62] - 156 for EOS $\geq$ 300

81 for EOS<300

[63] - 302 for EOS $\geq$ 300

159 for EOS<300

[64] - 162 for EOS $\geq$ 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 <sup>[65]</sup>	11 <sup>[66]</sup>	27 <sup>[67]</sup>	15 <sup>[68]</sup>
Units: cell/ $\mu$ L				
arithmetic mean (standard deviation)				
Sirocco/Calima patients with eos $\geq$ 300/ $\mu$ L	0 ( $\pm$ 0)	0 ( $\pm$ 0)	0 ( $\pm$ 0)	0 ( $\pm$ 0)
Sirocco/Calima patients with eos<300/ $\mu$ L	0 ( $\pm$ 0)	0 ( $\pm$ 0)	0 ( $\pm$ 0)	0 ( $\pm$ 0)
Zonda patients	2.5 ( $\pm$ 69.85)	-520.9 ( $\pm$ 360.79)	-17.0 ( $\pm$ 107.48)	-435.3 ( $\pm$ 468.64)

Notes:

[65] - Over all EOS

[66] - Over all EOS

[67] - Over all EOS

[68] - Over all EOS

## Statistical analyses

No statistical analyses for this end point

### Secondary: Change from baseline in EQ-5D-5L visual analog scale, Full analysis set, Excluding MELTEMI patients

End point title	Change from baseline in EQ-5D-5L visual analog scale, Full analysis set, Excluding MELTEMI patients
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	

<b>End point values</b>	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 <sup>[69]</sup>	709 <sup>[70]</sup>	21 <sup>[71]</sup>	28 <sup>[72]</sup>
Units: Scale of score				
arithmetic mean (standard deviation)				
Sirocco/Calima patients with eos $\geq$ 300/ $\mu$ L	6.08 ( $\pm$ 15.68)	6.02 ( $\pm$ 17.68)	0 ( $\pm$ 0)	0 ( $\pm$ 0)
Sirocco/Calima patients with eos $<$ 300/ $\mu$ L	4.38 ( $\pm$ 14.99)	6.69 ( $\pm$ 15.96)	0 ( $\pm$ 0)	0 ( $\pm$ 0)
Zonda patients	0 ( $\pm$ 0)	0 ( $\pm$ 0)	5.00 ( $\pm$ 10.35)	1.36 ( $\pm$ 13.58)

Notes:

[69] - 454 for EOS $\geq$ 300

228 for EOS $<$ 3000

[70] - 468 for EOS $\geq$ 300

241 for EOS $<$ 300

[71] - Over all EOS

[72] - Over all EOS

## Statistical analyses

No statistical analyses for this end point

## Secondary: Work Productivity loss in adults, using Work Productivity and Activity Impairment Questionnaire (WPAI), Full analysis set, Excluding MELTEMI patients

End point title	Work Productivity loss in adults, using Work Productivity and Activity Impairment Questionnaire (WPAI), Full analysis set, Excluding MELTEMI patients
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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.

End point type	Secondary
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End point timeframe:

Baseline and Week 68

<b>End point values</b>	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 <sup>[73]</sup>	793 <sup>[74]</sup>	49 <sup>[75]</sup>	49 <sup>[76]</sup>
Units: percentage				
arithmetic mean (standard deviation)				
Sirocco/Calima patients with eos $\geq$ 300/ $\mu$ L-baseline	25.3 ( $\pm$ 24.70)	25.0 ( $\pm$ 24.15)	0 ( $\pm$ 0)	0 ( $\pm$ 0)

Sirocco/Calima patients with eos $\geq$ 300/ $\mu$ L-wk 68	23.3 ( $\pm$ 26.18)	21.0 ( $\pm$ 25.54)	0 ( $\pm$ 0)	0 ( $\pm$ 0)
Sirocco/Calima patients with eos<300/ $\mu$ L-baseline	31.0 ( $\pm$ 27.06)	32.6 ( $\pm$ 26.29)	0 ( $\pm$ 0)	0 ( $\pm$ 0)
Sirocco/Calima patients with eos<300/ $\mu$ L-wk 68	32.7 ( $\pm$ 27.55)	25.8 ( $\pm$ 24.05)	0 ( $\pm$ 0)	0 ( $\pm$ 0)
Zonda Patients-baseline	0 ( $\pm$ 0)	0 ( $\pm$ 0)	23.5 ( $\pm$ 25.13)	7.1 ( $\pm$ 10.47)
Zonda Patients-wk 68	0 ( $\pm$ 0)	0 ( $\pm$ 0)	18.9 ( $\pm$ 24.94)	21.0 ( $\pm$ 27.13)

Notes:

[73] - BS: 234 for EOS $\geq$ 300

WK68: 236 for EOS $\geq$ 300

BS: 101 for EOS<300

WK68: 97 for EOS<300

[74] - BS: 217 for EOS $\geq$ 300

WK68: 217 for EOS $\geq$ 300

BS: 93 for EOS<300

WK68: 96 for EOS<300

[75] - BS: 16

WK68: 19

[76] - BS: 17

WK68: 20

## Statistical analyses

No statistical analyses for this end point

## Secondary: Classroom Productivity loss in adolescents, using Classroom Impairment Questionnaire (CIQ), Full analysis set, Excluding MELTEMI patients

End point title	Classroom Productivity loss in adolescents, using Classroom Impairment Questionnaire (CIQ), Full analysis set, Excluding MELTEMI patients <sup>[77]</sup>
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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.

End point type	Secondary
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End point timeframe:

Baseline and Week 56

Notes:

[77] - 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: Since two arms from study ZONDA, for which does not have adolescent patients, thus this endpoint was not analyzed for those two arms.

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 <sup>[78]</sup>	61 <sup>[79]</sup>		
Units: Percentage				
arithmetic mean (standard deviation)				
Sirocco/Calima patients with eos $\geq$ 300/ $\mu$ L-Baseline	13.0 ( $\pm$ 19.14)	30.7 ( $\pm$ 31.41)		
Sirocco/Calima patients with eos $\geq$ 300/ $\mu$ L-wk 56	3.8 ( $\pm$ 7.44)	15.2 ( $\pm$ 20.69)		
Sirocco/Calima patients with eos<300/ $\mu$ L-Baseline	42.1 ( $\pm$ 32.50)	35.4 ( $\pm$ 23.92)		

Sirocco/Calima patients with eos<300/ $\mu$ L-wk 56	5.0 ( $\pm$ 7.07)	17.1 ( $\pm$ 20.06)		
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Notes:

[78] - BS: 11 for EOS $\geq$ 300  
 WK56: 8 for EOS $\geq$ 300  
 BS: 4 for EOS<300  
 WK56: 2 for EOS<300  
 [79] - BS: 23 for EOS $\geq$ 300  
 WK56: 24 for EOS $\geq$ 300  
 BS: 19 for EOS<300  
 WK56: 24 for EOS<300

## Statistical analyses

No statistical analyses for this end point

### Secondary: Activity impairment (%), using Work Productivity and Activity Impairment Questionnaire (WPAI), Full analysis set, Excluding MELTEMI patients

End point title	Activity impairment (%), using Work Productivity and Activity Impairment Questionnaire (WPAI), Full analysis set, Excluding MELTEMI patients
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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
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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 <sup>[80]</sup>	793 <sup>[81]</sup>	49 <sup>[82]</sup>	49 <sup>[83]</sup>
Units: percentage				
arithmetic mean (standard deviation)				
Sirocco/Calima patients with eos $\geq$ 300/ $\mu$ L-baseline	31.3 ( $\pm$ 26.44)	31.2 ( $\pm$ 25.63)	0 ( $\pm$ 0)	0 ( $\pm$ 0)
Sirocco/Calima patients with eos $\geq$ 300/ $\mu$ L-wk 68	26.6 ( $\pm$ 26.14)	24.4 ( $\pm$ 25.26)	0 ( $\pm$ 0)	0 ( $\pm$ 0)
Sirocco/Calima patients with eos<300/ $\mu$ L-baseline	39.6 ( $\pm$ 25.75)	36.3 ( $\pm$ 25.72)	0 ( $\pm$ 0)	0 ( $\pm$ 0)
Sirocco/Calima patients with eos<300/ $\mu$ L-wk 68	33.6 ( $\pm$ 26.55)	32.7 ( $\pm$ 26.58)	0 ( $\pm$ 0)	0 ( $\pm$ 0)
Zonda Patients-baseline	0 ( $\pm$ 0)	0 ( $\pm$ 0)	31.5 ( $\pm$ 29.49)	24.5 ( $\pm$ 29.08)
Zonda Patients-wk 68	0 ( $\pm$ 0)	0 ( $\pm$ 0)	28.4 ( $\pm$ 27.85)	39.0 ( $\pm$ 34.36)

Notes:

[80] - BS: 518 for EOS $\geq$ 300  
 WK68: 458 for EOS $\geq$ 300  
 BS: 261 for EOS<300  
 WK68: 239 for EOS<300

[81] - BS: 524 for EOS $\geq$ 300  
 WK68: 454 for EOS $\geq$ 300  
 BS: 264 for EOS $<$ 300  
 WK68: 220 for EOS $<$ 300  
 [82] - BS: 26  
 WK68: 38  
 [83] - BS: 31  
 WK68: 41

## Statistical analyses

No statistical analyses for this end point

### Secondary: Health care encounters in overall patients on study period, Full analysis set, Excluding MELTEMI patients

End point title	Health care encounters in overall patients on study period, Full analysis set, Excluding MELTEMI patients
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End point description:

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

End point type	Secondary
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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 <sup>[84]</sup>	527 <sup>[85]</sup>	49 <sup>[86]</sup>	49 <sup>[87]</sup>
Units: Participants				
Sirocco/Calima patients with eos $\geq$ 300/ $\mu$ L	193	198	0	0
Sirocco/Calima patients with eos $<$ 300/ $\mu$ L	118	102	0	0
Zonda patients	0	0	20	25

Notes:

[84] - 519 for EOS $\geq$ 300  
 264 for EOS $<$ 300

[85] - 527 for EOS $\geq$ 300  
 266 for EOS $<$ 300

[86] - Over all EOS

[87] - Over all EOS

## 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
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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 <sup>[88]</sup>	263 <sup>[89]</sup>	511 <sup>[90]</sup>	279 <sup>[91]</sup>
Units: ng/mL				
geometric mean (geometric coefficient of variation)				
Baseline	714.25 (± 311.38)	0 (± 0)	142.92 (± 353.94)	0 (± 0)
Week 56	930.04 (± 200.59)	865.93 (± 242.55)	173.95 (± 269.62)	162.03 (± 295.05)

Notes:

[88] - 507 for Baseline  
442 for Week 56

[89] - 260 for Baseline  
225 for Week 56

[90] - 503 for Baseline  
440 for Week 56

[91] - 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 <sup>[92]</sup>	16 <sup>[93]</sup>	31 <sup>[94]</sup>	17 <sup>[95]</sup>
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:

[92] - 31 for Baseline  
27 for Week 56

[93] - 16 for Baseline  
10 for Week 56

[94] - 30 for Baseline  
27 for Week 56

[95] - 17 for Baseline  
15 for Week 56

## Statistical analyses

No statistical analyses for this end point

## Secondary: Anti-drug antibodies (ADA) responses over all patients, Full analysis set, Excluding MELTEMI patients

End point title	Anti-drug antibodies (ADA) responses over all patients, Full analysis set, Excluding MELTEMI patients
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/CALI MA - Benralizumab 30 mg q.4 weeks	SIROCCO/CALI MA - 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

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

All adults participants collected events during the entire study period. Adolescents data collection up to last adolescent completed Week 56 visit, which is April 20, 2017.

Assessment type	Systematic
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### Dictionary used

Dictionary name	MedDRA
Dictionary version	20.0

### Reporting groups

Reporting group title	SIROCCO/CALIMA - Benralizumab 30 mg q.4 weeks
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Reporting group description:

Benralizumab administered subcutaneously every 4 weeks

Reporting group title	SIROCCO/CALIMA - Benralizumab 30 mg q.8 weeks
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Reporting group description:

Benralizumab administered subcutaneously every 8 weeks

Reporting group title	ZONDA - Benralizumab 30 mg q.4 weeks
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Reporting group description:

Benralizumab administered subcutaneously every 4 weeks

Reporting group title	ZONDA - Benralizumab 30 mg q.8 weeks
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Reporting group description:

Benralizumab administered subcutaneously every 8 weeks

<b>Serious adverse events</b>	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	101 / 783 (12.90%)	93 / 793 (11.73%)	10 / 49 (20.41%)
number of deaths (all causes)	5	4	0
number of deaths resulting from adverse events	1	0	0
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
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
<b>Benign neoplasm of eyelid</b>			
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
<b>Benign neoplasm of thyroid gland</b>			
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>Chronic myeloid leukaemia</b>			
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>Colon cancer stage 0</b>			
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>Diffuse large B-cell lymphoma stage II</b>			
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
<b>Large intestine benign neoplasm</b>			
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
<b>Lipoma</b>			
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>Nasal cavity cancer</b>			

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
<b>Osteochondroma</b>			
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>Ovarian germ cell teratoma benign</b>			
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
<b>Prostate cancer</b>			
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
<b>Solid pseudopapillary tumour of the pancreas</b>			
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>Thymoma</b>			
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>Uterine leiomyoma</b>			
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
<b>Vascular disorders</b>			
<b>Hypertensive emergency</b>			
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
<b>Phlebitis</b>			

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
<b>Pregnancy, puerperium and perinatal conditions</b>			
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
<b>General disorders and administration site conditions</b>			
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
<b>Immune system disorders</b>			
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
<b>Reproductive system and breast disorders</b>			
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	35 / 783 (4.47%)	26 / 793 (3.28%)	3 / 49 (6.12%)
occurrences causally related to treatment / all	0 / 39	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
<b>Pleural effusion</b>			
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
<b>Pulmonary hypertension</b>			
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>Status asthmaticus</b>			
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
<b>Investigations</b>			
<b>Endocrine test abnormal</b>			
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>Injury, poisoning and procedural complications</b>			
<b>Arthropod bite</b>			
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
<b>Bone contusion</b>			
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>Clavicle fracture</b>			
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
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
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
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
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
<b>Patella fracture</b>			
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
<b>Radius fracture</b>			
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
<b>Rib fracture</b>			
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
<b>Road traffic accident</b>			
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
<b>Subdural haemorrhage</b>			
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
<b>Upper limb fracture</b>			
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>Cardiac disorders</b>			
<b>Acute coronary syndrome</b>			
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
<b>Acute myocardial infarction</b>			

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			
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
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
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
<b>Blood and lymphatic system disorders</b>			
<b>Hypochromic anaemia</b>			
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>Iron deficiency anaemia</b>			
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
<b>Neutropenia</b>			
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>Eye disorders</b>			
<b>Cataract</b>			
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
<b>Gastrointestinal disorders</b>			
<b>Abdominal pain</b>			
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>Abdominal pain lower</b>			
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
<b>Barrett's oesophagus</b>			
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			
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
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
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
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
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
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			
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
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
<b>Cholelithiasis</b>			
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
<b>Hepatitis</b>			
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
<b>Skin and subcutaneous tissue disorders</b>			
<b>Erythema nodosum</b>			
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
<b>Pemphigoid</b>			
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
<b>Rosacea</b>			
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>Urticaria papular</b>			
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
<b>Renal and urinary disorders</b>			
<b>Calculus urinary</b>			
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>Chronic kidney disease</b>			

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
<b>Nephrolithiasis</b>			
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
<b>Ureterolithiasis</b>			
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
<b>Endocrine disorders</b>			
<b>Goitre</b>			
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>Hyperparathyroidism</b>			
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>Musculoskeletal and connective tissue disorders</b>			
<b>Arthralgia</b>			
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
<b>Arthritis</b>			
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>Intervertebral disc protrusion</b>			
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
<b>Infections and infestations</b>			
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
<b>Gastroenteritis salmonella</b>			
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
<b>Influenza</b>			
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
<b>Lower respiratory tract infection</b>			
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
<b>Lower respiratory tract infection viral</b>			
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>Lung infection</b>			
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
<b>Pneumonia</b>			
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
<b>Pneumonia bacterial</b>			
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
<b>Postoperative abscess</b>			

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>Pulmonary sepsis</b>			
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
<b>Respiratory tract infection viral</b>			
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
<b>Sepsis</b>			
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
<b>Sinusitis</b>			
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
<b>Sinusitis bacterial</b>			
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>Urinary tract infection</b>			
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
<b>Urinary tract infection bacterial</b>			
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>Urosepsis</b>			

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>Metabolism and nutrition disorders</b>			
<b>Dehydration</b>			
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>Obesity</b>			
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
<b>Type 2 diabetes mellitus</b>			
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

<b>Serious adverse events</b>	ZONDA - Benralizumab 30 mg q.8 weeks		
<b>Total subjects affected by serious adverse events</b>			
subjects affected / exposed	9 / 49 (18.37%)		
number of deaths (all causes)	1		
number of deaths resulting from adverse events	0		
<b>Neoplasms benign, malignant and unspecified (incl cysts and polyps)</b>			
<b>Adenocarcinoma of colon</b>			
subjects affected / exposed	0 / 49 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
<b>B-cell lymphoma</b>			
subjects affected / exposed	0 / 49 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
<b>Basal cell carcinoma</b>			

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		
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		
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		
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		
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		
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		
<b>Osteochondroma</b>			
subjects affected / exposed	0 / 49 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
<b>Ovarian germ cell teratoma benign</b>			
subjects affected / exposed	1 / 49 (2.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Prostate cancer</b>			
subjects affected / exposed	0 / 49 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
<b>Solid pseudopapillary tumour of the pancreas</b>			
subjects affected / exposed	0 / 49 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
<b>Thymoma</b>			
subjects affected / exposed	0 / 49 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
<b>Uterine leiomyoma</b>			
subjects affected / exposed	0 / 49 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
<b>Vascular disorders</b>			
<b>Hypertensive emergency</b>			
subjects affected / exposed	0 / 49 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
<b>Phlebitis</b>			

subjects affected / exposed	0 / 49 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
<b>Pregnancy, puerperium and perinatal conditions</b>			
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		
<b>General disorders and administration site conditions</b>			
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		
<b>Immune system disorders</b>			
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		
<b>Reproductive system and breast disorders</b>			
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		
<b>Ovarian cyst</b>			
subjects affected / exposed	0 / 49 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
<b>Vaginal fistula</b>			
subjects affected / exposed	0 / 49 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
<b>Vaginal haemorrhage</b>			
subjects affected / exposed	0 / 49 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
<b>Respiratory, thoracic and mediastinal disorders</b>			
<b>Asthma</b>			
subjects affected / exposed	2 / 49 (4.08%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
<b>Asthmatic crisis</b>			
subjects affected / exposed	0 / 49 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
<b>Interstitial lung disease</b>			
subjects affected / exposed	0 / 49 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
<b>Middle lobe syndrome</b>			
subjects affected / exposed	0 / 49 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
<b>Nasal polyps</b>			

subjects affected / exposed	0 / 49 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
<b>Pleural effusion</b>			
subjects affected / exposed	0 / 49 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
<b>Pulmonary hypertension</b>			
subjects affected / exposed	0 / 49 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
<b>Status asthmaticus</b>			
subjects affected / exposed	0 / 49 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
<b>Investigations</b>			
<b>Endocrine test abnormal</b>			
subjects affected / exposed	0 / 49 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
<b>Injury, poisoning and procedural complications</b>			
<b>Arthropod bite</b>			
subjects affected / exposed	0 / 49 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
<b>Bone contusion</b>			
subjects affected / exposed	0 / 49 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
<b>Clavicle fracture</b>			
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			
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			
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			
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			
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		
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		
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			
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		
Syncope			
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		
<b>Blood and lymphatic system disorders</b>			
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		
<b>Eye disorders</b>			
Cataract			
subjects affected / exposed	0 / 49 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
<b>Gastrointestinal disorders</b>			
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		
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		
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				
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 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			
Gastroesophageal 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			
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			
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		
<b>Oesophageal ulcer</b>			
subjects affected / exposed	0 / 49 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
<b>Oesophagitis</b>			
subjects affected / exposed	0 / 49 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
<b>Pancreatitis acute</b>			
subjects affected / exposed	0 / 49 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
<b>Vomiting</b>			
subjects affected / exposed	0 / 49 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
<b>Hepatobiliary disorders</b>			
<b>Bile duct stone</b>			
subjects affected / exposed	0 / 49 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
<b>Cholecystitis</b>			
subjects affected / exposed	0 / 49 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
<b>Cholecystitis acute</b>			
subjects affected / exposed	0 / 49 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
<b>Cholecystitis chronic</b>			

subjects affected / exposed	0 / 49 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
<b>Cholelithiasis</b>			
subjects affected / exposed	0 / 49 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
<b>Hepatitis</b>			
subjects affected / exposed	0 / 49 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
<b>Skin and subcutaneous tissue disorders</b>			
<b>Erythema nodosum</b>			
subjects affected / exposed	0 / 49 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
<b>Pemphigoid</b>			
subjects affected / exposed	1 / 49 (2.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Rosacea</b>			
subjects affected / exposed	0 / 49 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
<b>Urticaria papular</b>			
subjects affected / exposed	0 / 49 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
<b>Renal and urinary disorders</b>			
<b>Calculus urinary</b>			
subjects affected / exposed	0 / 49 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
<b>Chronic kidney disease</b>			

subjects affected / exposed	0 / 49 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
<b>Nephrolithiasis</b>			
subjects affected / exposed	0 / 49 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
<b>Ureterolithiasis</b>			
subjects affected / exposed	0 / 49 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
<b>Endocrine disorders</b>			
<b>Goitre</b>			
subjects affected / exposed	0 / 49 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
<b>Hyperparathyroidism</b>			
subjects affected / exposed	0 / 49 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
<b>Musculoskeletal and connective tissue disorders</b>			
<b>Arthralgia</b>			
subjects affected / exposed	0 / 49 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
<b>Arthritis</b>			
subjects affected / exposed	0 / 49 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
<b>Intervertebral disc protrusion</b>			
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		
<b>Infections and infestations</b>			
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		
<b>Gastroenteritis salmonella</b>			
subjects affected / exposed	0 / 49 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
<b>Influenza</b>			
subjects affected / exposed	0 / 49 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
<b>Lower respiratory tract infection</b>			
subjects affected / exposed	1 / 49 (2.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Lower respiratory tract infection viral</b>			
subjects affected / exposed	0 / 49 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
<b>Lung infection</b>			
subjects affected / exposed	0 / 49 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
<b>Pneumonia</b>			
subjects affected / exposed	1 / 49 (2.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Pneumonia bacterial</b>			
subjects affected / exposed	0 / 49 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
<b>Postoperative abscess</b>			

subjects affected / exposed	0 / 49 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
<b>Pulmonary sepsis</b>			
subjects affected / exposed	0 / 49 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
<b>Respiratory tract infection viral</b>			
subjects affected / exposed	0 / 49 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
<b>Sepsis</b>			
subjects affected / exposed	0 / 49 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
<b>Sinusitis</b>			
subjects affected / exposed	0 / 49 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
<b>Sinusitis bacterial</b>			
subjects affected / exposed	0 / 49 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
<b>Urinary tract infection</b>			
subjects affected / exposed	0 / 49 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
<b>Urinary tract infection bacterial</b>			
subjects affected / exposed	0 / 49 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
<b>Urosepsis</b>			

subjects affected / exposed	0 / 49 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
<b>Metabolism and nutrition disorders</b>			
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 %

<b>Non-serious adverse events</b>	SIROCCO/CALIMA - Benralizumab 30 mg q.4 weeks	SIROCCO/CALIMA - Benralizumab 30 mg q.8 weeks	ZONDA - Benralizumab 30 mg q.4 weeks
<b>Total subjects affected by non-serious adverse events</b>			
subjects affected / exposed	404 / 783 (51.60%)	392 / 793 (49.43%)	33 / 49 (67.35%)
<b>Investigations</b>			
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
<b>Vascular disorders</b>			
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 occurrences (all)	1 / 783 (0.13%) 1	3 / 793 (0.38%) 3	0 / 49 (0.00%) 0
Nervous system disorders Headache subjects affected / exposed occurrences (all)	38 / 783 (4.85%) 54	40 / 793 (5.04%) 54	2 / 49 (4.08%) 2
General disorders and administration site conditions Influenza like illness subjects affected / exposed occurrences (all)	26 / 783 (3.32%) 38	28 / 793 (3.53%) 32	3 / 49 (6.12%) 3
Injection site bruising subjects affected / exposed occurrences (all)	0 / 783 (0.00%) 0	2 / 793 (0.25%) 4	0 / 49 (0.00%) 0
Non-cardiac chest pain subjects affected / exposed occurrences (all)	2 / 783 (0.26%) 2	4 / 793 (0.50%) 6	0 / 49 (0.00%) 0
Oedema peripheral subjects affected / exposed occurrences (all)	4 / 783 (0.51%) 4	6 / 793 (0.76%) 7	0 / 49 (0.00%) 0
Immune system disorders Seasonal allergy subjects affected / exposed occurrences (all)	13 / 783 (1.66%) 15	8 / 793 (1.01%) 8	2 / 49 (4.08%) 2
Eye disorders Conjunctivitis allergic subjects affected / exposed occurrences (all)	4 / 783 (0.51%) 5	8 / 793 (1.01%) 8	3 / 49 (6.12%) 3
Gastrointestinal disorders Diarrhoea subjects affected / exposed occurrences (all)	12 / 783 (1.53%) 14	9 / 793 (1.13%) 9	1 / 49 (2.04%) 1
Gastritis subjects affected / exposed occurrences (all)	6 / 783 (0.77%) 6	7 / 793 (0.88%) 8	2 / 49 (4.08%) 2
Large intestine polyp			

subjects affected / exposed occurrences (all)	1 / 783 (0.13%) 1	1 / 793 (0.13%) 1	2 / 49 (4.08%) 2
Nausea subjects affected / exposed occurrences (all)	10 / 783 (1.28%) 11	5 / 793 (0.63%) 13	2 / 49 (4.08%) 2
Respiratory, thoracic and mediastinal disorders			
Asthma subjects affected / exposed occurrences (all)	62 / 783 (7.92%) 98	53 / 793 (6.68%) 72	4 / 49 (8.16%) 4
Dyspnoea subjects affected / exposed occurrences (all)	6 / 783 (0.77%) 6	9 / 793 (1.13%) 9	3 / 49 (6.12%) 3
Nasal congestion subjects affected / exposed occurrences (all)	2 / 783 (0.26%) 2	12 / 793 (1.51%) 12	0 / 49 (0.00%) 0
Nasal polyps subjects affected / exposed occurrences (all)	5 / 783 (0.64%) 6	4 / 793 (0.50%) 4	2 / 49 (4.08%) 2
Rhinitis allergic subjects affected / exposed occurrences (all)	38 / 783 (4.85%) 43	22 / 793 (2.77%) 31	0 / 49 (0.00%) 0
Psychiatric disorders			
Insomnia subjects affected / exposed occurrences (all)	11 / 783 (1.40%) 12	8 / 793 (1.01%) 8	3 / 49 (6.12%) 3
Musculoskeletal and connective tissue disorders			
Arthralgia subjects affected / exposed occurrences (all)	26 / 783 (3.32%) 32	20 / 793 (2.52%) 20	5 / 49 (10.20%) 5
Back pain subjects affected / exposed occurrences (all)	24 / 783 (3.07%) 25	21 / 793 (2.65%) 21	2 / 49 (4.08%) 2
Infections and infestations			
Acute sinusitis subjects affected / exposed occurrences (all)	27 / 783 (3.45%) 45	44 / 793 (5.55%) 57	2 / 49 (4.08%) 5

Bronchitis subjects affected / exposed occurrences (all)	49 / 783 (6.26%) 65	50 / 793 (6.31%) 73	3 / 49 (6.12%) 7
Bronchitis bacterial subjects affected / exposed occurrences (all)	18 / 783 (2.30%) 23	15 / 793 (1.89%) 21	3 / 49 (6.12%) 3
Chronic sinusitis subjects affected / exposed occurrences (all)	12 / 783 (1.53%) 13	10 / 793 (1.26%) 17	1 / 49 (2.04%) 1
Herpes zoster subjects affected / exposed occurrences (all)	8 / 783 (1.02%) 8	2 / 793 (0.25%) 2	2 / 49 (4.08%) 2
Oral candidiasis subjects affected / exposed occurrences (all)	14 / 783 (1.79%) 20	12 / 793 (1.51%) 15	1 / 49 (2.04%) 1
Respiratory tract infection viral subjects affected / exposed occurrences (all)	8 / 783 (1.02%) 8	12 / 793 (1.51%) 13	2 / 49 (4.08%) 2
Sinusitis subjects affected / exposed occurrences (all)	21 / 783 (2.68%) 23	18 / 793 (2.27%) 22	3 / 49 (6.12%) 3
Upper respiratory tract infection subjects affected / exposed occurrences (all)	60 / 783 (7.66%) 94	55 / 793 (6.94%) 81	0 / 49 (0.00%) 0
Upper respiratory tract infection bacterial subjects affected / exposed occurrences (all)	15 / 783 (1.92%) 17	22 / 793 (2.77%) 27	1 / 49 (2.04%) 1
Urinary tract infection subjects affected / exposed occurrences (all)	14 / 783 (1.79%) 17	7 / 793 (0.88%) 7	0 / 49 (0.00%) 0
Viral upper respiratory tract infection subjects affected / exposed occurrences (all)	121 / 783 (15.45%) 181	129 / 793 (16.27%) 187	14 / 49 (28.57%) 22

<b>Non-serious adverse events</b>	ZONDA - Benralizumab 30 mg q.8 weeks		
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Total subjects affected by non-serious adverse events subjects affected / exposed	38 / 49 (77.55%)		
Investigations Blood creatinine increased subjects affected / exposed occurrences (all)	2 / 49 (4.08%) 2		
Blood pressure increased subjects affected / exposed occurrences (all)	2 / 49 (4.08%) 2		
Vascular disorders Hypertension subjects affected / exposed occurrences (all)	2 / 49 (4.08%) 2		
Peripheral venous disease subjects affected / exposed occurrences (all)	2 / 49 (4.08%) 2		
Nervous system disorders Headache subjects affected / exposed occurrences (all)	4 / 49 (8.16%) 4		
General disorders and administration site conditions Influenza like illness subjects affected / exposed occurrences (all)	1 / 49 (2.04%) 1		
Injection site bruising subjects affected / exposed occurrences (all)	2 / 49 (4.08%) 2		
Non-cardiac chest pain subjects affected / exposed occurrences (all)	2 / 49 (4.08%) 3		
Oedema peripheral subjects affected / exposed occurrences (all)	4 / 49 (8.16%) 6		
Immune system disorders Seasonal allergy subjects affected / exposed occurrences (all)	0 / 49 (0.00%) 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 occurrences (all)	0 / 49 (0.00%) 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			
Acute sinusitis			
subjects affected / exposed	2 / 49 (4.08%)		
occurrences (all)	4		
Bronchitis			
subjects affected / exposed	10 / 49 (20.41%)		
occurrences (all)	16		
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		
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			

subjects affected / exposed	7 / 49 (14.29%)		
occurrences (all)	8		
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:

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### 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: