Clinical trial results:
A Phase IIb, Randomized, Double-Blind, Placebo-Controlled Study to Evaluate the Efficacy, Safety, and Dosing Regimens of MEMP1972A in Adults with Allergic Asthma who are Inadequately Controlled on Inhaled Corticosteroids and a Second Controller (COSTA)

Summary

EudraCT number	2011-003997-10
Trial protocol	BE DE HU BG
Global end of trial date	17 November 2014

Results information

Result version number	v1 (current)
This version publication date	17 April 2016
First version publication date	17 April 2016

Trial information

Trial identification

Sponsor protocol code	GB27980

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01582503
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	F. Hoffmann-La Roche AG
Sponsor organisation address	Grenzacherstrasse 124, Basel, Switzerland, CH-4070
Public contact	Roche Trial Information Hotline, F. Hoffmann-La Roche AG, 41 61 6878333, global.trial_information@roche.com
Scientific contact	Roche Trial Information Hotline, F. Hoffmann-La Roche AG, 41 61 6878333, global.trial_information@roche.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	23 January 2015
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	17 November 2014
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The primary objectives of this study were to evaluate the efficacy and safety of quilizumab in adult participants with allergic asthma inadequately controlled despite high-dose inhaled corticosteroid (ICS) (greater than or equal to [>=] 400 microgram per day [mcg/day] total daily dose of fluticasone propionate or equivalent) and a second controller after 36 weeks of treatment.

Protection of trial subjects:

The study was conducted in accordance with the United States Food and Drug Administration (FDA) regulations, the International Conference on Harmonisation (ICH) E6 Guideline for Good Clinical Practice (GCP), and applicable local, state, and federal laws, as well as other applicable country laws.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	30 April 2012
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	11 Months
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Argentina: 42
Country: Number of subjects enrolled	Canada: 10
Country: Number of subjects enrolled	Mexico: 7
Country: Number of subjects enrolled	New Zealand: 11
Country: Number of subjects enrolled	Peru: 55
Country: Number of subjects enrolled	Romania: 38
Country: Number of subjects enrolled	Russian Federation: 7
Country: Number of subjects enrolled	Ukraine: 35
Country: Number of subjects enrolled	United States: 127
Country: Number of subjects enrolled	Poland: 93
Country: Number of subjects enrolled	Belgium: 15
Country: Number of subjects enrolled	Bulgaria: 104
Country: Number of subjects enrolled	Germany: 21
Country: Number of subjects enrolled	Hungary: 13
Worldwide total number of subjects	578
EEA total number of subjects	284

Notes:

Subjects enrolled per age group	
In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	527
From 65 to 84 years	51
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 1212 participants were screened, out of which 578 participants were randomized to the study treatment.

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Participants received placebo matched to quilizumab subcutaneously on Weeks 0, 4, 8, 12, 16, 20, 24, 28, and 32.

Arm type	Placebo
Investigational medicinal product name	Placebo matched to quilizumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Participants received placebo matched to quilizumab subcutaneously on Weeks 0, 4, 8, 12, 16, 20, 24, 28, and 32.

Arm title	Quilizumab 150 mg

Arm description:

Participants received quilizumab at the dose of 150 milligram (mg) subcutaneously on Weeks 0, 4, 12, and 24.

Arm type	Experimental
Investigational medicinal product name	Quilizumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Participants received quilizumab subcutaneously at specified dose and time.

Arm title	Quilizumab 450 mg

Arm description:

Participants received quilizumab at the dose of 450 mg subcutaneously on Weeks 0, 4, 12, and 24.

Arm type	Experimental

Investigational medicinal product name	Quilizumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Participants received quilizumab subcutaneously at specified dose and time.

Arm title	Quilizumab 300 mg

Arm description:

Participants received quilizumab at the dose of 300 mg subcutaneously on Weeks 0, 4, 8, 12, 16, 20, 24, 28, and 32.

Arm type	Experimental
Investigational medicinal product name	Quilizumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Participants received quilizumab subcutaneously at specified dose and time.

Number of subjects in period 1	Placebo	Quilizumab 150 mg	Quilizumab 450 mg
Started	145	145	145
Completed	44	44	41
Not completed	101	101	104
Consent withdrawn by subject	17	18	16
Physician decision	-	2	2
Study terminated by sponsor	82	76	77
Adverse event	-	2	1
Non-compliance	-	3	1
Lost to follow-up	1	-	5
unspecified	1	-	2
Lack of efficacy	-	-	-

Number of subjects in period 1	Quilizumab 300 mg
Started	143
Completed	41
Not completed	102
Consent withdrawn by subject	11
Physician decision	-
Study terminated by sponsor	83
Adverse event	-
Non-compliance	1
Lost to follow-up	4

unspecified	2
Lack of efficacy	1

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Participants received placebo matched to quilizumab subcutaneously on Weeks 0, 4, 8, 12, 16, 20, 24, 28, and 32.	
Reporting group title	Quilizumab 150 mg
Reporting group description:	
Participants received quilizumab at the dose of 150 milligram (mg) subcutaneously on Weeks 0, 4, 12, and 24.	
Reporting group title	Quilizumab 450 mg
Reporting group description:	
Participants received quilizumab at the dose of 450 mg subcutaneously on Weeks 0, 4, 12, and 24.	
Reporting group title	Quilizumab 300 mg
Reporting group description:	
Participants received quilizumab at the dose of 300 mg subcutaneously on Weeks 0, 4, 8, 12, 16, 20, 24, 28, and 32.	

Reporting group values	Placebo	Quilizumab 150 mg	Quilizumab 450 mg
Number of subjects	145	145	145
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	47.9	46.7	47
standard deviation	± 13	± 13.4	± 13.6
Gender categorical Units: Subjects			
Female	84	89	98
Male	61	56	47

Reporting group values	Quilizumab 300 mg	Total	
Number of subjects	143	578	
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	44.8		
standard deviation	± 12.2	-	
Gender categorical Units: Subjects			
Female	86	357	
Male	57	221	

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
Participants received placebo matched to quilizumab subcutaneously on Weeks 0, 4, 8, 12, 16, 20, 24, 28, and 32.	
Reporting group title	Quilizumab 150 mg
Reporting group description:	
Participants received quilizumab at the dose of 150 milligram (mg) subcutaneously on Weeks 0, 4, 12, and 24.	
Reporting group title	Quilizumab 450 mg
Reporting group description:	
Participants received quilizumab at the dose of 450 mg subcutaneously on Weeks 0, 4, 12, and 24.	
Reporting group title	Quilizumab 300 mg
Reporting group description:	
Participants received quilizumab at the dose of 300 mg subcutaneously on Weeks 0, 4, 8, 12, 16, 20, 24, 28, and 32.	

Primary: Annualized Rate of Asthma Exacerbations

End point title	Annualized Rate of Asthma Exacerbations
End point description:	
An asthma exacerbation is defined as new or increased asthma symptoms (including wheeze, cough, dyspnea, chest tightness, or nocturnal awakenings due to these symptoms) that lead to hospitalization or treatment with systemic corticosteroids defined as: a) Treatment with oral, intravenous, or intramuscular corticosteroids for at least 3 days, or b) Emergency department visit with at least one dose of intravenous or intramuscular corticosteroids. Adjusted exacerbation rates of protocol-defined asthma exacerbations per 52 weeks were reported. Intent-to-treat (ITT) population included all participants who received at least 1 dose of study drug.	
End point type	Primary
End point timeframe:	
Baseline up to Week 36	

End point values	Placebo	Quilizumab 150 mg	Quilizumab 450 mg	Quilizumab 300 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	145	145	145	143
Units: exacerbations per year				
number (not applicable)	0.62	0.66	0.69	0.5

Statistical analyses

Statistical analysis title	Quilizumab 150 mg vs. Placebo
Statistical analysis description:	
Annualized Rate of Asthma Exacerbations: Quilizumab 150 mg vs. Placebo	
Comparison groups	Placebo v Quilizumab 150 mg

Number of subjects included in analysis	290
Analysis specification	Pre-specified
Analysis type	superiority[1]
P-value	= 0.812
Method	Poisson regression
Parameter estimate	Exacerbation rate reduction
Point estimate	-5.7
Confidence interval	
level	90 %
sides	2-sided
lower limit	-54.65
upper limit	27.81

Notes:

[1] - Missing values were imputed using last observation carried forward (LOCF). Model was adjusted for periostin status (less than [<] 50, greater than or equal to [>=] 50), number of prior exacerbations (1, greater than [>] 1), Immunoglobulin E (IgE) level (<200 international units per milliliter [IU/mL], >=200 IU/mL).

Statistical analysis title	Quilizumab 450 mg vs. Placebo

Statistical analysis description:

Annualized Rate of Asthma Exacerbations: Quilizumab 450 mg vs. Placebo

Comparison groups	Placebo v Quilizumab 450 mg
Number of subjects included in analysis	290
Analysis specification	Pre-specified
Analysis type	superiority[2]
P-value	= 0.6474
Method	Poisson regression
Parameter estimate	Exacerbation rate reduction
Point estimate	-11.2
Confidence interval	
level	90 %
sides	2-sided
lower limit	-62.7
upper limit	24.04

Notes:

[2] - Missing values were imputed using LOCF. Model was adjusted for periostin status (<50, >=50), number of prior exacerbations (1, >1), IgE level (<200 IU/mL, >=200 IU/mL).

Statistical analysis title	Quilizumab 300 mg vs. Placebo

Statistical analysis description:

Annualized Rate of Asthma Exacerbations: Quilizumab 300 mg vs. Placebo

Comparison groups	Placebo v Quilizumab 300 mg
Number of subjects included in analysis	288
Analysis specification	Pre-specified
Analysis type	superiority[3]
P-value	= 0.3821
Method	Poisson regression
Parameter estimate	Exacerbation rate reduction
Point estimate	19.6

Confidence interval	
level	90 %
sides	2-sided
lower limit	-21.27
upper limit	46.75

Notes:

[3] - Missing values were imputed using LOCF. Model was adjusted for periostin status (<50, >=50), number of prior exacerbations (1, >1), IgE level (<200 IU/mL, >=200 IU/mL).

Secondary: Percent Change from Baseline in Pre-Bronchodilator Forced Expiratory Volume in 1 Second (FEV1) at Weeks 12 and 36

End point title	Percent Change from Baseline in Pre-Bronchodilator Forced Expiratory Volume in 1 Second (FEV1) at Weeks 12 and 36

End point description:

The percent change from baseline in FEV1 (liters) was calculated at Week 12 and 36 using the formula: (FEV1 at Week 12 or 36 [respectively] minus (-) FEV1 at baseline) / FEV1 at baseline multiplied by (*) 100 for each treatment group. ITT population included all participants who received at least 1 dose of study drug.

End point type	Secondary

End point timeframe:

Baseline, Week 12, and Week 36

End point values	Placebo	Quilizumab 150 mg	Quilizumab 450 mg	Quilizumab 300 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	145	145	145	143
Units: percent change				
arithmetic mean (standard deviation)				
Percent change at Week 12	6.91 (± 23.866)	11.25 (± 30.998)	9.41 (± 23.5)	7.56 (± 25.692)
Percent change at Week 36	7.62 (± 23.674)	13.5 (± 30.473)	7.85 (± 25.549)	7.15 (± 24.773)

Statistical analyses

Statistical analysis title	Week 12: Quilizumab 150 mg vs. Placebo

Statistical analysis description:

Percent change from baseline in FEV1 at Week 12: Quilizumab 150 mg vs. Placebo

Comparison groups	Placebo v Quilizumab 150 mg
Number of subjects included in analysis	290
Analysis specification	Pre-specified
Analysis type	superiority[4]
P-value	= 0.2064
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	3.843

Confidence interval	
level	90 %
sides	2-sided
lower limit	-1.162
upper limit	8.848

Notes:

[4] - Missing values were imputed using LOCF. Model was adjusted for periostin status (<50, >=50), number of prior exacerbations (1, >1), IgE level (<200 IU/mL, >=200 IU/mL) and baseline FEV1 (L).

Statistical analysis title	Week 12: Quilizumab 450 mg vs. Placebo

Statistical analysis description:

Percent change from baseline in FEV1 at Week 12: Quilizumab 450 mg vs. Placebo

Comparison groups	Placebo v Quilizumab 450 mg
Number of subjects included in analysis	290
Analysis specification	Pre-specified
Analysis type	superiority[5]
P-value	= 0.4752
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	2.169
Confidence interval	
level	90 %
sides	2-sided
lower limit	-2.832
upper limit	7.171

Notes:

[5] - Missing values were imputed using LOCF. Model was adjusted for periostin status (<50, >=50), number of prior exacerbations (1, >1), IgE level (<200 IU/mL, >=200 IU/mL) and baseline FEV1 (L).

Statistical analysis title	Week 12: Quilizumab 300 mg vs. Placebo

Statistical analysis description:

Percent change from baseline in FEV1 at Week 12: Quilizumab 300 mg vs. Placebo

Comparison groups	Placebo v Quilizumab 300 mg
Number of subjects included in analysis	288
Analysis specification	Pre-specified
Analysis type	superiority[6]
P-value	= 0.721
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	1.092
Confidence interval	
level	90 %
sides	2-sided
lower limit	-3.941
upper limit	6.124

Notes:

[6] - Missing values were imputed using LOCF. Model was adjusted for periostin status (<50, >=50), number of prior exacerbations (1, >1), IgE level (<200 IU/mL, >=200 IU/mL) and baseline FEV1 (L).

Statistical analysis title	Week 36: Quilizumab 150 mg vs. Placebo

Statistical analysis description:

Percent change from baseline in FEV1 at Week 36: Quilizumab 150 mg vs. Placebo

Comparison groups	Quilizumab 150 mg v Placebo

Number of subjects included in analysis	290
Analysis specification	Pre-specified
Analysis type	superiority[7]
P-value	= 0.0679
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	5.593
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.556
upper limit	10.63

Notes:

[7] - Missing values were imputed using LOCF. Model was adjusted for periostin status (<50, >=50), number of prior exacerbations (1, >1), IgE level (<200 IU/mL, >=200 IU/mL) and baseline FEV1 (L).

Statistical analysis title	Week 36: Quilizumab 450 mg vs. Placebo
Statistical analysis description:	
Percent change from baseline in FEV1 at Week 36: Quilizumab 450 mg vs. Placebo	
Comparison groups	Placebo v Quilizumab 450 mg
Number of subjects included in analysis	290
Analysis specification	Pre-specified
Analysis type	superiority[8]
P-value	= 0.9833
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	0.064
Confidence interval	
level	90 %
sides	2-sided
lower limit	-4.969
upper limit	5.097

Notes:

[8] - Missing values were imputed using LOCF. Model was adjusted for periostin status (<50, >=50), number of prior exacerbations (1, >1), IgE level (<200 IU/mL, >=200 IU/mL) and baseline FEV1 (L).

Statistical analysis title	Week 36: Quilizumab 300 mg vs. Placebo
Statistical analysis description:	
Percent change from baseline in FEV1 at Week 36: Quilizumab 300 mg vs. Placebo	
Comparison groups	Placebo v Quilizumab 300 mg
Number of subjects included in analysis	288
Analysis specification	Pre-specified
Analysis type	superiority[9]
P-value	= 0.9631
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	0.142
Confidence interval	
level	90 %
sides	2-sided
lower limit	-4.922
upper limit	5.207

Notes:

[9] - Missing values were imputed using LOCF. Model was adjusted for periostin status (<50, >=50), number of prior exacerbations
(1, >1), IgE level (<200 IU/mL, >=200 IU/mL) and baseline FEV1 (L).

Secondary: Change from Baseline in Daytime Asthma Symptoms Score at Weeks 12 and 36

End point title	Change from Baseline in Daytime Asthma Symptoms Score at Weeks 12 and 36

End point description:

Daytime asthma symptoms were calculated from assessments recorded on participant diaries. The daytime asthma symptoms score ranges from 0 to 4, with higher scores indicating more severe symptoms. Daily scores were averaged over the previous 1 week (7 days) prior to the timepoint of interest, with the exception of the baseline value which was derived based on the last 14 days prior to randomization. ITT population included all participants who received at least 1 dose of study drug.

End point type	Secondary

End point timeframe:

Baseline, Week 12, and Week 36

End point values	Placebo	Quilizumab 150 mg	Quilizumab 450 mg	Quilizumab 300 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	145	145	145	143
Units: units on a scale				
arithmetic mean (standard deviation)				
Change at Week 12	-0.54 (± 0.746)	-0.51 (± 0.66)	-0.48 (± 0.793)	-0.51 (± 0.712)
Change at Week 36	-0.68 (± 0.863)	-0.64 (± 0.783)	-0.64 (± 0.898)	-0.7 (± 0.809)

Statistical analyses

Statistical analysis title	Week 12: Quilizumab 150 mg vs. Placebo

Statistical analysis description:

Change from baseline in Daytime Asthma Symptoms Score at Week 12: Quilizumab 150 mg vs. Placebo

Comparison groups	Placebo v Quilizumab 150 mg
Number of subjects included in analysis	290
Analysis specification	Pre-specified
Analysis type	superiority[10]
P-value	= 0.6506
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	0.037
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.097
upper limit	0.171

Notes:

[10] - Missing values were imputed using LOCF. Model was adjusted for periostin status (<50, >=50), number of prior exacerbations (1, >1), IgE level (<200 IU/mL, >=200 IU/mL) and baseline daytime asthma symptom score.

Statistical analysis title	Week 12: Quilizumab 450 mg vs. Placebo
Statistical analysis description:	
Change from baseline in Daytime Asthma Symptoms Score at Week 12: Quilizumab 450 mg vs. Placebo	
Comparison groups	Placebo v Quilizumab 450 mg
Number of subjects included in analysis	290
Analysis specification	Pre-specified
Analysis type	superiority[11]
P-value	= 0.5042
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	0.054
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.08
upper limit	0.188

Notes:

[11] - Missing values were imputed using LOCF. Model was adjusted for periostin status (<50, >=50), number of prior exacerbations (1, >1), IgE level (<200 IU/mL, >=200 IU/mL) and baseline daytime asthma symptom score.

Statistical analysis title	Week 12: Quilizumab 300 mg vs. Placebo
Statistical analysis description:	
Change from baseline in Daytime Asthma Symptoms Score at Week 12: Quilizumab 300 mg vs. Placebo	
Comparison groups	Placebo v Quilizumab 300 mg
Number of subjects included in analysis	288
Analysis specification	Pre-specified
Analysis type	superiority[12]
P-value	= 0.8466
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	0.016
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.119
upper limit	0.15

Notes:

[12] - Missing values were imputed using LOCF. Model was adjusted for periostin status (<50, >=50), number of prior exacerbations (1, >1), IgE level (<200 IU/mL, >=200 IU/mL) and baseline daytime asthma symptom score.

Statistical analysis title	Week 36: Quilizumab 150 mg vs. Placebo
Statistical analysis description:	
Change from baseline in Daytime Asthma Symptoms Score at Week 36: Quilizumab 150 mg vs. Placebo	
Comparison groups	Placebo v Quilizumab 150 mg

Number of subjects included in analysis	290
Analysis specification	Pre-specified
Analysis type	superiority[13]
P-value	= 0.5522
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	0.053
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.094
upper limit	0.201

Notes:

[13] - Missing values were imputed using LOCF. Model was adjusted for periostin status (<50, >=50), number of prior exacerbations (1, >1), IgE level (<200 IU/mL, >=200 IU/mL) and baseline daytime asthma symptom score.

Statistical analysis title	Week 36: Quilizumab 450 mg vs. Placebo

Statistical analysis description:

Change from baseline in Daytime Asthma Symptoms Score at Week 36: Quilizumab 450 mg vs. Placebo

Comparison groups	Placebo v Quilizumab 450 mg
Number of subjects included in analysis	290
Analysis specification	Pre-specified
Analysis type	superiority[14]
P-value	= 0.6961
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	0.035
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.112
upper limit	0.182

Notes:

[14] - Missing values were imputed using LOCF. Model was adjusted for periostin status (<50, >=50), number of prior exacerbations (1, >1), IgE level (<200 IU/mL, >=200 IU/mL) and baseline daytime asthma symptom score.

Statistical analysis title	Week 36: Quilizumab 300 mg vs. Placebo

Statistical analysis description:

Change from baseline in Daytime Asthma Symptoms Score at Week 36: Quilizumab 300 mg vs. Placebo

Comparison groups	Placebo v Quilizumab 300 mg
Number of subjects included in analysis	288
Analysis specification	Pre-specified
Analysis type	superiority[15]
P-value	= 0.6895
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	-0.036

Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.184
upper limit	0.112

Notes:

[15] - Missing values were imputed using LOCF. Model was adjusted for periostin status (<50, >=50), number of prior exacerbations (1, >1), IgE level (<200 IU/mL, >=200 IU/mL) and baseline daytime asthma symptom score.

Secondary: Proportion of Well-controlled Weeks

End point title	Proportion of Well-controlled Weeks

End point description:

"Well-controlled" week was defined by documentation in the daily diary, as the participant having had no night-time awakenings due to asthma symptoms and less than or equal to (<=) 2 days of short-acting beta agonist (SABA) use per week. ITT population included all participants who received at least 1 dose of study drug.

End point type	Secondary

End point timeframe:

Week 24 up to Week 36

End point values	Placebo	Quilizumab 150 mg	Quilizumab 450 mg	Quilizumab 300 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	145	145	145	143
Units: ratio				
arithmetic mean (standard deviation)	0.329 (± 0.394)	0.306 (± 0.383)	0.362 (± 0.413)	0.34 (± 0.395)

Statistical analyses

Statistical analysis title	Quilizumab 150 mg vs. Placebo

Statistical analysis description:

Proportion of Well-Controlled Weeks from Week 24 to Week 36: Quilizumab 150 mg vs. Placebo

Comparison groups	Placebo v Quilizumab 150 mg
Number of subjects included in analysis	290
Analysis specification	Pre-specified
Analysis type	superiority[16]
P-value	= 0.5819
Method	Wilcoxon rank sum test
Parameter estimate	Mean difference (final values)
Point estimate	-0.023
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.098
upper limit	0.053

Notes:

[16] - Model was adjusted for periostin status (<50, >=50), number of prior exacerbations (1, >1) and IgE level (<200 IU/mL, >=200 IU/mL).

Statistical analysis title	Quilizumab 450 mg vs. Placebo

Statistical analysis description:

Proportion of Well-Controlled Weeks from Week 24 to Week 36: Quilizumab 450 mg vs. Placebo

Comparison groups	Placebo v Quilizumab 450 mg
Number of subjects included in analysis	290
Analysis specification	Pre-specified
Analysis type	superiority[17]
P-value	= 0.4941
Method	Wilcoxon rank sum test
Parameter estimate	Mean difference (final values)
Point estimate	0.033
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.045
upper limit	0.111

Notes:

[17] - Model was adjusted for periostin status (<50, >=50), number of prior exacerbations (1, >1) and IgE level (<200 IU/mL, >=200 IU/mL).

Statistical analysis title	Quilizumab 300 mg vs. Placebo

Statistical analysis description:

Proportion of Well-Controlled Weeks from Week 24 to Week 36: Quilizumab 300 mg vs. Placebo

Comparison groups	Placebo v Quilizumab 300 mg
Number of subjects included in analysis	288
Analysis specification	Pre-specified
Analysis type	superiority[18]
P-value	= 0.9591
Method	Wilcoxon rank sum test
Parameter estimate	Mean difference (final values)
Point estimate	0.011
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.066
upper limit	0.088

Notes:

[18] - Model was adjusted for periostin status (<50, >=50), number of prior exacerbations (1, >1) and IgE level (<200 IU/mL, >=200 IU/mL).

Secondary: Number of Participants with Treatment−induced Anti-therapeutic Antibodies (ATAs) and Treatment−enhanced ATAs to Quilizumab

End point title	Number of Participants with Treatment−induced Anti-therapeutic Antibodies (ATAs) and Treatment−enhanced ATAs to Quilizumab

End point description:

Treatment-induced ATA = a negative or missing baseline ATA result(s) and at least 1 positive postbaseline ATA result. Treatment-enhanced ATA = a positive ATA result at baseline with one or more postbaseline titer results that are at least 0.60 transducing units (t.u.) greater than the baseline titer result. ITT population included all participants who received at least 1 dose of study drug. N (number of subjects analyzed) = number of participants who were evaluable for this outcome measure.

End point type	Secondary

End point timeframe:

Baseline up to Week 36

End point values	Placebo	Quilizumab 150 mg	Quilizumab 450 mg	Quilizumab 300 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	143	142	144	141
Units: participants				
number (not applicable)				
Treatment-induced ATAs	7	2	2	2
Treatment-enhanced ATAs	0	0	1	0

Statistical analyses

No statistical analyses for this end point

Secondary: Serum Quilizumab Concentrations at Weeks 4, 12, 24, and 36

End point title	Serum Quilizumab Concentrations at Weeks 4, 12, 24, and

End point description:

Pharmacokinetics (PK)-evaluable population included all participants who received any amount of quilizumab. Only participants who received quilizumab were to be analyzed for this outcome measure. N (number of subjects analyzed) = number of participants who were evaluable for this outcome measure.

End point type	Secondary

End point timeframe:

Pre-dose and 2 hours post-dose on Weeks 4, 12, 24, and 36

Notes:

[19] - 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: Only participants who received quilizumab were to be analyzed for this outcome measure.

End point values	Quilizumab 150 mg	Quilizumab 450 mg	Quilizumab 300 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	140	143	141	
Units: microgram per milliliter				
arithmetic mean (standard deviation)				
Week 4	5.68 (± 2.34)	17.1 (± 7.04)	11.6 (± 4.54)	
Week 12	2.55 (± 1.99)	7.2 (± 3.8)	16.7 (± 6.67)	
Week 24	1.31 (± 4.57)	2.25 (± 2.21)	16.8 (± 7.71)	
Week 36	0.743 (± 1.75)	2.23 (± 3.4)	18.2 (± 8.65)	

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum Observed Serum Quilizumab Concentration after Doses at Week 4 (Cmax, Week 5) and Week 24 (Cmax, Week 25)

End point title	Maximum Observed Serum Quilizumab Concentration after Doses at Week 4 (Cmax, Week 5) and Week 24 (Cmax, Week 25)[20]

End point description:

PK-evaluable population included all participants who received any amount of quilizumab. Only participants who received quilizumab were to be analyzed for this outcome measure. N (number of subjects analyzed) = number of participants who were evaluable for this outcome measure.

End point type	Secondary

End point timeframe:

2 hours post-dose on Week 4, pre-dose on Week 5, 2 hours post-dose on Week 24, and pre-dose on Week 25

Notes:

[20] - 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: Only participants who received quilizumab were to be analyzed for this outcome measure.

End point values	Quilizumab 150 mg	Quilizumab 450 mg	Quilizumab 300 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	140	143	141	
Units: microgram per milliliter				
arithmetic mean (standard deviation)				
Cmax, Week 5	18 (± 7.78)	51.6 (± 19.5)	34 (± 12.6)	
Cmax, Week 25	14.3 (± 5.49)	38.3 (± 15.4)	36.8 (± 15.4)	

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Reach Maximum Observed Serum Quilizumab Concentration after Doses at Week 4 (tmax, Week 5) and Week 24 (tmax, Week 25)

End point title	Time to Reach Maximum Observed Serum Quilizumab Concentration after Doses at Week 4 (tmax, Week 5) and Week 24 (tmax, Week 25)[21]

End point description:

PK-evaluable population included all participants who received any amount of quilizumab. Only participants who received quilizumab were to be analyzed for this outcome measure. N (number of subjects analyzed) = number of participants who were evaluable for this outcome measure.

End point type	Secondary

End point timeframe:

2 hours post-dose on Week 4, pre-dose on Week 5, 2 hours post-dose on Week 24, and pre-dose on Week 25

Notes:

[21] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only participants who received quilizumab were to be analyzed for this outcome measure.

End point values	Quilizumab 150 mg	Quilizumab 450 mg	Quilizumab 300 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	140	143	141	
Units: days				
arithmetic mean (standard deviation)				
tmax, Week 5	36.4 (± 4.25)	36.2 (± 2.99)	36.2 (± 3.51)	
tmax, Week 25	176 (± 6.5)	177 (± 5.47)	176 (± 5.08)	

Statistical analyses

No statistical analyses for this end point

Secondary: Elimination Half-Life of Quilizumab

End point title	Elimination Half-Life of Quilizumab[22]

End point description:

PK-evaluable population included all participants who received any amount of quilizumab. Only participants who received quilizumab were to be analyzed for this outcome measure. N (number of subjects analyzed) = number of participants who were evaluable for this outcome measure.

End point type	Secondary

End point timeframe:

Pre-dose and 2 hours post-dose on Baseline (Week 0), Weeks 4, 5, 12, 24, 25, 32, 36, 42, 48, 60, 84

Notes:

[22] - 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: Only participants who received quilizumab were to be analyzed for this outcome measure.

End point values	Quilizumab 150 mg	Quilizumab 450 mg	Quilizumab 300 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	140	143	141	
Units: days				
arithmetic mean (standard deviation)	18.7 (± 2.45)	17.6 (± 2.89)	16.4 (± 2.42)	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: Baseline up to Week 84	
Assessment type	Non-systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	17
Reporting groups	
Reporting group title	Placebo
Reporting group description: Participants received placebo matched to quilizumab subcutaneously on Weeks 0, 4, 8, 12, 16, 20, 24, 28, and 32.	
Reporting group title	Quilizumab 150 mg
Reporting group description: Participants received quilizumab at the dose of 150 milligram (mg) subcutaneously on Weeks 0, 4, 12, and 24.	
Reporting group title	Quilizumab 450 mg
Reporting group description: Participants received quilizumab at the dose of 450 mg subcutaneously on Weeks 0, 4, 12, and 24.	
Reporting group title	Quilizumab 300 mg
Reporting group description: Participants received quilizumab at the dose of 300 mg subcutaneously on Weeks 0, 4, 8, 12, 16, 20, 24, 28, and 32.	

Serious adverse events	Placebo	Quilizumab 150 mg	Quilizumab 450 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	12 / 145 (8.28%)	11 / 145 (7.59%)	10 / 145 (6.90%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Breast cancer			
subjects affected / exposed	0 / 145 (0.00%)	1 / 145 (0.69%)	1 / 145 (0.69%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung adenocarcinoma			
subjects affected / exposed	0 / 145 (0.00%)	0 / 145 (0.00%)	1 / 145 (0.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Uterine leiomyoma			

subjects affected / exposed	1 / 145 (0.69%)	0 / 145 (0.00%)	0 / 145 (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
Surgical and medical procedures			
Abortion induced			
subjects affected / exposed	0 / 145 (0.00%)	1 / 145 (0.69%)	0 / 145 (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
Hysterectomy			
subjects affected / exposed	0 / 145 (0.00%)	1 / 145 (0.69%)	0 / 145 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	0 / 145 (0.00%)	1 / 145 (0.69%)	1 / 145 (0.69%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Drug hypersensitivity			
subjects affected / exposed	0 / 145 (0.00%)	1 / 145 (0.69%)	0 / 145 (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
Social circumstances			
Convalescent			
subjects affected / exposed	1 / 145 (0.69%)	0 / 145 (0.00%)	0 / 145 (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
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	5 / 145 (3.45%)	2 / 145 (1.38%)	6 / 145 (4.14%)
occurrences causally related to treatment / all	0 / 5	0 / 6	0 / 6
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Major depression			

subjects affected / exposed	0 / 145 (0.00%)	0 / 145 (0.00%)	0 / 145 (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
Injury, poisoning and procedural complications			
Hip fracture			
subjects affected / exposed	0 / 145 (0.00%)	0 / 145 (0.00%)	1 / 145 (0.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post−traumatic neck syndrome			
subjects affected / exposed	0 / 145 (0.00%)	0 / 145 (0.00%)	0 / 145 (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
Radius fracture			
subjects affected / exposed	0 / 145 (0.00%)	0 / 145 (0.00%)	0 / 145 (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
Postoperative hernia			
subjects affected / exposed	1 / 145 (0.69%)	0 / 145 (0.00%)	0 / 145 (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
Seroma			
subjects affected / exposed	1 / 145 (0.69%)	0 / 145 (0.00%)	0 / 145 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Cardiac failure congestive			
subjects affected / exposed	0 / 145 (0.00%)	0 / 145 (0.00%)	1 / 145 (0.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mitral valve prolapse			
subjects affected / exposed	0 / 145 (0.00%)	0 / 145 (0.00%)	0 / 145 (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

Nervous system disorders			
Epilepsy			
subjects affected / exposed	0 / 145 (0.00%)	0 / 145 (0.00%)	0 / 145 (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
Gastrointestinal disorders			
Gastritis			
subjects affected / exposed	0 / 145 (0.00%)	0 / 145 (0.00%)	0 / 145 (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
Pancreatitis			
subjects affected / exposed	0 / 145 (0.00%)	1 / 145 (0.69%)	0 / 145 (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
Colitis			
subjects affected / exposed	1 / 145 (0.69%)	0 / 145 (0.00%)	0 / 145 (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			
Gallbladder enlargement			
subjects affected / exposed	0 / 145 (0.00%)	1 / 145 (0.69%)	0 / 145 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Renal colic			
subjects affected / exposed	0 / 145 (0.00%)	1 / 145 (0.69%)	0 / 145 (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
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 145 (0.69%)	0 / 145 (0.00%)	0 / 145 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intervertebral disc protrusion			

subjects affected / exposed	1 / 145 (0.69%)	0 / 145 (0.00%)	0 / 145 (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
Ankylosing spondylitis			
subjects affected / exposed	0 / 145 (0.00%)	0 / 145 (0.00%)	0 / 145 (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
Spinal osteoarthritis			
subjects affected / exposed	0 / 145 (0.00%)	0 / 145 (0.00%)	0 / 145 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Pneumonia			
subjects affected / exposed	0 / 145 (0.00%)	1 / 145 (0.69%)	1 / 145 (0.69%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	0 / 145 (0.00%)	0 / 145 (0.00%)	0 / 145 (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
Diverticulitis			
subjects affected / exposed	0 / 145 (0.00%)	1 / 145 (0.69%)	0 / 145 (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
Mastitis			
subjects affected / exposed	0 / 145 (0.00%)	1 / 145 (0.69%)	0 / 145 (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
Subcutaneous abscess			
subjects affected / exposed	0 / 145 (0.00%)	1 / 145 (0.69%)	0 / 145 (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
Tooth infection			

subjects affected / exposed	0 / 145 (0.00%)	0 / 145 (0.00%)	0 / 145 (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
Cervicitis			
subjects affected / exposed	1 / 145 (0.69%)	0 / 145 (0.00%)	0 / 145 (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
Lobar pneumonia			
subjects affected / exposed	1 / 145 (0.69%)	0 / 145 (0.00%)	0 / 145 (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
Parametritis			
subjects affected / exposed	1 / 145 (0.69%)	0 / 145 (0.00%)	0 / 145 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Quilizumab 300 mg		
Total subjects affected by serious adverse events			
subjects affected / exposed	16 / 143 (11.19%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Breast cancer			
subjects affected / exposed	0 / 143 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Lung adenocarcinoma			
subjects affected / exposed	0 / 143 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Uterine leiomyoma			
subjects affected / exposed	0 / 143 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Surgical and medical procedures			
Abortion induced			
subjects affected / exposed	0 / 143 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hysterectomy			
subjects affected / exposed	0 / 143 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	0 / 143 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Immune system disorders			
Drug hypersensitivity			
subjects affected / exposed	0 / 143 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Social circumstances			
Convalescent			
subjects affected / exposed	0 / 143 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	6 / 143 (4.20%)		
occurrences causally related to treatment / all	0 / 7		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Major depression			
subjects affected / exposed	1 / 143 (0.70%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural			

complications				
Hip fracture				
subjects affected / exposed	0 / 143 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Post−traumatic neck syndrome				
subjects affected / exposed	1 / 143 (0.70%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Radius fracture				
subjects affected / exposed	1 / 143 (0.70%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Postoperative hernia				
subjects affected / exposed	0 / 143 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Seroma				
subjects affected / exposed	0 / 143 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiac disorders				
Cardiac failure congestive				
subjects affected / exposed	0 / 143 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Mitral valve prolapse				
subjects affected / exposed	1 / 143 (0.70%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Nervous system disorders				
Epilepsy				

subjects affected / exposed	1 / 143 (0.70%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Gastritis			
subjects affected / exposed	1 / 143 (0.70%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pancreatitis			
subjects affected / exposed	0 / 143 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Colitis			
subjects affected / exposed	0 / 143 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Gallbladder enlargement			
subjects affected / exposed	0 / 143 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Renal colic			
subjects affected / exposed	0 / 143 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 143 (0.70%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Intervertebral disc protrusion			

subjects affected / exposed	1 / 143 (0.70%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Ankylosing spondylitis				
subjects affected / exposed	1 / 143 (0.70%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Spinal osteoarthritis				
subjects affected / exposed	1 / 143 (0.70%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Infections and infestations				
Pneumonia				
subjects affected / exposed	0 / 143 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cellulitis				
subjects affected / exposed	1 / 143 (0.70%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Diverticulitis				
subjects affected / exposed	0 / 143 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Mastitis				
subjects affected / exposed	0 / 143 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Subcutaneous abscess				
subjects affected / exposed	0 / 143 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Tooth infection				

subjects affected / exposed	1 / 143 (0.70%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cervicitis			
subjects affected / exposed	0 / 143 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Lobar pneumonia			
subjects affected / exposed	0 / 143 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Parametritis			
subjects affected / exposed	0 / 143 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Placebo	Quilizumab 150 mg	Quilizumab 450 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	90 / 145 (62.07%)	96 / 145 (66.21%)	86 / 145 (59.31%)
Nervous system disorders			
Headache			
subjects affected / exposed	9 / 145 (6.21%)	10 / 145 (6.90%)	8 / 145 (5.52%)
occurrences (all)	10	28	12
General disorders and administration site conditions			
Injection site pain			
subjects affected / exposed	6 / 145 (4.14%)	9 / 145 (6.21%)	11 / 145 (7.59%)
occurrences (all)	26	37	33
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	59 / 145 (40.69%)	61 / 145 (42.07%)	52 / 145 (35.86%)
occurrences (all)	126	135	125
Infections and infestations			

Nasopharyngitis			
subjects affected / exposed	26 / 145 (17.93%)	20 / 145 (13.79%)	27 / 145 (18.62%)
occurrences (all)	41	36	42
Upper respiratory tract infection			
subjects affected / exposed	16 / 145 (11.03%)	15 / 145 (10.34%)	17 / 145 (11.72%)
occurrences (all)	22	25	22
Bronchitis			
subjects affected / exposed	18 / 145 (12.41%)	9 / 145 (6.21%)	11 / 145 (7.59%)
occurrences (all)	22	12	16
Sinusitis			
subjects affected / exposed	14 / 145 (9.66%)	10 / 145 (6.90%)	9 / 145 (6.21%)
occurrences (all)	23	18	13
Pharyngitis			
subjects affected / exposed	6 / 145 (4.14%)	7 / 145 (4.83%)	8 / 145 (5.52%)
occurrences (all)	9	7	12
Respiratory tract infection			
subjects affected / exposed	4 / 145 (2.76%)	5 / 145 (3.45%)	4 / 145 (2.76%)
occurrences (all)	4	8	6
Rhinitis			
subjects affected / exposed	2 / 145 (1.38%)	4 / 145 (2.76%)	2 / 145 (1.38%)
occurrences (all)	2	5	3

Non-serious adverse events	Quilizumab 300 mg		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	81 / 143 (56.64%)		
Nervous system disorders			
Headache			
subjects affected / exposed	7 / 143 (4.90%)		
occurrences (all)	9		
General disorders and administration site conditions			
Injection site pain			
subjects affected / exposed	6 / 143 (4.20%)		
occurrences (all)	45		
Respiratory, thoracic and mediastinal disorders			
Asthma			

subjects affected / exposed	51 / 143 (35.66%)		
occurrences (all)	104		
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	22 / 143 (15.38%)		
occurrences (all)	35		
Upper respiratory tract infection			
subjects affected / exposed	12 / 143 (8.39%)		
occurrences (all)	15		
Bronchitis			
subjects affected / exposed	15 / 143 (10.49%)		
occurrences (all)	20		
Sinusitis			
subjects affected / exposed	8 / 143 (5.59%)		
occurrences (all)	13		
Pharyngitis			
subjects affected / exposed	9 / 143 (6.29%)		
occurrences (all)	10		
Respiratory tract infection			
subjects affected / exposed	8 / 143 (5.59%)		
occurrences (all)	19		
Rhinitis			
subjects affected / exposed	9 / 143 (6.29%)		
occurrences (all)	14		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

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.

None reported

Notes: