



Clinical trial results:

A Phase 2b, Randomized, Double-blinded, Placebo-controlled, Dose-ranging Study to Evaluate the Efficacy and Safety of Tralokinumab in Adult Subjects with Moderate-to-Severe Atopic Dermatitis

Summary

EudraCT number	2014-003725-17
Trial protocol	DE PL
Global end of trial date	05 February 2016

Results information

Result version number	v1 (current)
This version publication date	12 May 2018
First version publication date	25 May 2017

Trial information

Trial identification

Sponsor protocol code	D2213C00001
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02347176
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	MedImmune, LLC
Sponsor organisation address	Milstein Building, Granta Park, Cambridge, United Kingdom,
Public contact	Rene van der Merwe, Senior Director, Clinical Development, Respiratory and Inflammation, MedImmune, LLC, +44 3013984095, information.center@astrazeneca.com
Scientific contact	Rene van der Merwe, Senior Director, Clinical Development, Respiratory and Inflammation, MedImmune, LLC, +44 3013984095, information.center@astrazeneca.com

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	05 February 2016
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	05 February 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The objective of study was to evaluate the efficacy of Tralokinumab Dose 1, 2 and 3, tested hierarchically, compared with placebo in adults with moderate to severe AD, assessed using the absolute change in Eczema Area and Severity Index (EASI) from baseline at Week 12, and using the percentage of participants achieving Investigator's Global Assessment (IGA) response of 0 (clear) or 1 (almost clear) and at least a 2 grade reduction from baseline at Week 12.

Protection of trial subjects:

The conduct of this clinical study met all local and regulatory requirements. The study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and are consistent with International Conference on Harmonization guideline: Good Clinical Practice, and applicable regulatory requirements. Participants signed informed consent form and could withdraw from the study at any time without any disadvantage and without having to provide a reason for this decision. Only investigators qualified by training and experience were selected as appropriate experts to investigate the study drug.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	23 January 2015
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Australia: 33
Country: Number of subjects enrolled	Canada: 11
Country: Number of subjects enrolled	Germany: 40
Country: Number of subjects enrolled	Japan: 25
Country: Number of subjects enrolled	Poland: 15
Country: Number of subjects enrolled	United States: 80
Worldwide total number of subjects	204
EEA total number of subjects	55

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37	0

wk	
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	197
From 65 to 84 years	7
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

A total of 299 participants participated in the study at 55 sites worldwide, including 24 sites in the USA, 8 sites in Germany, 6 sites each in Japan, Poland, and Canada, and 5 sites in Australia.

Pre-assignment

Screening details:

95 participants were considered screen failures and 204 participants were randomized and treated in the study.

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
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Arm title	Placebo
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Arm description:

Placebo was administered subcutaneously to participants.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Placebo was administered subcutaneously to participants.

Arm title	Tralokinumab Dose 1
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Arm description:

Tralokinumab Dose 1 was administered subcutaneously once every 2 Weeks (Q2W) for 12 weeks.

Arm type	Experimental
Investigational medicinal product name	Tralokinumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Tralokinumab Dose 1 was administered subcutaneously once every 2 Weeks (Q2W) for 12 weeks.

Arm title	Tralokinumab Dose 2
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Arm description:

Tralokinumab Dose 2 was administered subcutaneously once every 2 Weeks (Q2W) for 12 weeks.

Arm type	Experimental
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Investigational medicinal product name	Tralokinumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use
Dosage and administration details:	
Tralokinumab Dose 2 was administered subcutaneously once every 2 Weeks (Q2W) for 12 weeks.	
Arm title	Tralokinumab Dose 3

Arm description:

Tralokinumab Dose 3 was administered subcutaneously once every 2 Weeks (Q2W) for 12 weeks.

Arm type	Experimental
Investigational medicinal product name	Tralokinumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Tralokinumab Dose 3 was administered subcutaneously once every 2 Weeks (Q2W) for 12 weeks.

Number of subjects in period 1	Placebo	Tralokinumab Dose 1	Tralokinumab Dose 2
Started	51	50	51
Completed	39	40	43
Not completed	12	10	8
Consent withdrawn by subject	9	5	5
Unspecified	1	2	2
Lost to follow-up	2	3	1

Number of subjects in period 1	Tralokinumab Dose 3
Started	52
Completed	48
Not completed	4
Consent withdrawn by subject	3
Unspecified	-
Lost to follow-up	1

Baseline characteristics

Reporting groups

Reporting group title	Placebo
Reporting group description: Placebo was administered subcutaneously to participants.	
Reporting group title	Tralokinumab Dose 1
Reporting group description: Tralokinumab Dose 1 was administered subcutaneously once every 2 Weeks (Q2W) for 12 weeks.	
Reporting group title	Tralokinumab Dose 2
Reporting group description: Tralokinumab Dose 2 was administered subcutaneously once every 2 Weeks (Q2W) for 12 weeks.	
Reporting group title	Tralokinumab Dose 3
Reporting group description: Tralokinumab Dose 3 was administered subcutaneously once every 2 Weeks (Q2W) for 12 weeks.	

Reporting group values	Placebo	Tralokinumab Dose 1	Tralokinumab Dose 2
Number of subjects	51	50	51
Age categorical Units: Subjects			
Adults (18-64 years)	48	48	51
From 65-84 years	3	2	0
Age Continuous Units: Years			
arithmetic mean	39.4	39.1	37.1
standard deviation	± 14.5	± 15.1	± 14.0
Gender, Male/Female Units: Participants			
Male	22	29	26
Female	29	21	25

Reporting group values	Tralokinumab Dose 3	Total	
Number of subjects	52	204	
Age categorical Units: Subjects			
Adults (18-64 years)	50	197	
From 65-84 years	2	7	
Age Continuous Units: Years			
arithmetic mean	35.7	-	
standard deviation	± 14.6		
Gender, Male/Female Units: Participants			
Male	33	110	
Female	19	94	

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description: Placebo was administered subcutaneously to participants.	
Reporting group title	Tralokinumab Dose 1
Reporting group description: Tralokinumab Dose 1 was administered subcutaneously once every 2 Weeks (Q2W) for 12 weeks.	
Reporting group title	Tralokinumab Dose 2
Reporting group description: Tralokinumab Dose 2 was administered subcutaneously once every 2 Weeks (Q2W) for 12 weeks.	
Reporting group title	Tralokinumab Dose 3
Reporting group description: Tralokinumab Dose 3 was administered subcutaneously once every 2 Weeks (Q2W) for 12 weeks.	

Primary: Absolute Change From Baseline in Eczema Area and Severity Index (EASI) Total Score at Week 12

End point title	Absolute Change From Baseline in Eczema Area and Severity Index (EASI) Total Score at Week 12
End point description: EASI evaluates 4 natural anatomical regions for severity and extent of key disease signs and focuses on the key acute and chronic signs of inflammation (erythema, induration/papulation, excoriation, and lichenification). The maximum total score is 72, with higher values indicating more severe disease. The data presented here is Adjusted mean change after excluding the data from participants who took prohibited medications. The intent-to-treat (ITT) population included all randomized and treated participants, grouped according to assigned treatment. Here, "N" is number of participants analysed for this outcome measure.	
End point type	Primary
End point timeframe: Week 12	

End point values	Placebo	Tralokinumab Dose 1	Tralokinumab Dose 2	Tralokinumab Dose 3
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	40	43	44	48
Units: units on a scale				
arithmetic mean (standard error)	-10.78 (± 1.398)	-13.67 (± 1.386)	-15.14 (± 1.361)	-15.72 (± 1.334)

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v Tralokinumab Dose 1

Number of subjects included in analysis	83
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.143
Method	ANCOVA
Parameter estimate	Adj Mean Difference
Point estimate	-2.89
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.78
upper limit	0.99
Variability estimate	Standard error of the mean
Dispersion value	1.968

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo v Tralokinumab Dose 2
Number of subjects included in analysis	84
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.027
Method	ANCOVA
Parameter estimate	Adj Mean Difference
Point estimate	-4.36
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.22
upper limit	-0.51
Variability estimate	Standard error of the mean
Dispersion value	1.951

Statistical analysis title	Statistical Analysis 3
Comparison groups	Placebo v Tralokinumab Dose 3
Number of subjects included in analysis	88
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.011
Method	ANCOVA
Parameter estimate	Adj Mean Difference
Point estimate	-4.94
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.76
upper limit	-1.13

Variability estimate	Standard error of the mean
Dispersion value	1.932

Primary: Percentage of Participants Achieving Investigator's Global Assessment (IGA) Response of 0 (Clear) or 1 (Almost Clear) and at Least a 2-Grade Reduction From Baseline at Week 12

End point title	Percentage of Participants Achieving Investigator's Global Assessment (IGA) Response of 0 (Clear) or 1 (Almost Clear) and at Least a 2-Grade Reduction From Baseline at Week 12
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End point description:

The IGA allows investigators to assess overall disease severity at one given time point and consists of a 6-point severity scale from clear to very severe disease (0 = clear, 1 = almost clear, 2 = mild disease, 3 = moderate disease, 4 = severe disease, and 5 = very severe disease). A participant has IGA response if they achieve a score of 0 (clear) or 1 (almost clear) and at least a 2-grade reduction from baseline. The intent-to-treat (ITT) population included all randomized and treated participants, grouped according to assigned treatment. Here, "N" is number of participants analysed for this outcome measure.

End point type	Primary
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End point timeframe:

Week 12

End point values	Placebo	Tralokinumab Dose 1	Tralokinumab Dose 2	Tralokinumab Dose 3
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	50	50	51	51
Units: Percentage of participant				
number (not applicable)	11.8	11.6	19.4	26.4

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v Tralokinumab Dose 1
Number of subjects included in analysis	100
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.976
Method	ANCOVA
Parameter estimate	Odds ratio (OR)
Point estimate	0.98
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.29
upper limit	3.32

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo v Tralokinumab Dose 2
Number of subjects included in analysis	101
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.283
Method	ANCOVA
Parameter estimate	Odds ratio (OR)
Point estimate	1.84
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.6
upper limit	5.6

Statistical analysis title	Statistical Analysis 3
Comparison groups	Placebo v Tralokinumab Dose 3
Number of subjects included in analysis	101
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.063
Method	ANCOVA
Parameter estimate	Odds ratio (OR)
Point estimate	2.79
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.95
upper limit	8.2

Secondary: Number of Participants With Treatment Emergent Adverse Events (TEAEs) and Treatment Emergent Serious Adverse Events (TESAEs)

End point title	Number of Participants With Treatment Emergent Adverse Events (TEAEs) and Treatment Emergent Serious Adverse Events (TESAEs)
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End point description:

An adverse event (AE) present at baseline that worsened in intensity after administration of investigational product or events absent at baseline that emerged after administration of study drug until Week 22. A serious adverse event (SAE) is an AE resulting in any of the following outcomes or deemed significant for any other reason: death; initial or prolonged inpatient hospitalization; life-threatening situation (immediate risk of dying); persistent or significant disability/incapacity; congenital anomaly/birth defect in the offspring of a participant who received Tralokinumab. Treatment-emergent adverse events between administration of investigational product and Week 22 that were absent before treatment or that worsened relative to pre-treatment state. As-treated population included all treated participants, grouped according to actual treatment received.

End point type	Secondary
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End point timeframe:

From Study Drug Administration to Week 22

End point values	Placebo	Tralokinumab Dose 1	Tralokinumab Dose 2	Tralokinumab Dose 3
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	51	50	51	52
Units: Participant				
TEAEs	31	36	35	30
TESAEs	1	3	2	0

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Vital Signs and Physical Examination Abnormalities Reported as Treatment Emergent Adverse Events

End point title	Number of Participants With Vital Signs and Physical Examination Abnormalities Reported as Treatment Emergent Adverse Events
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End point description:

Vital sign parameters included blood pressure, temperature, pulse rate, and respiratory rate. TEAEs were present at baseline that worsened in intensity after administration of study drug or events absent at baseline that emerged after administration of study drug until Week 22. As-treated population included all treated participants, grouped according to actual treatment received.

End point type	Secondary
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End point timeframe:

From Study Drug Administration to Week 22

End point values	Placebo	Tralokinumab Dose 1	Tralokinumab Dose 2	Tralokinumab Dose 3
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	51	50	51	52
Units: Participant				
Blood pressure increased	0	1	1	0
Pyrexia	1	0	1	0
Acute coronary syndrome	0	1	0	0
Angina pectoris	1	0	0	0
Hypertension	0	0	1	0
Pallor	0	0	0	1

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Clinical Laboratory Abnormalities Reported as Treatment Emergent Adverse Events

End point title	Number of Participants With Clinical Laboratory Abnormalities Reported as Treatment Emergent Adverse Events
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End point description:

An abnormal laboratory finding which required an action or intervention by the investigator, or a finding judged by the investigator to represent a change beyond the range of normal physiologic fluctuation were reported as an adverse event. Treatment-emergent adverse events between first dose of study drug and 10 weeks after the last dose that were absent before treatment or that worsened relative to pre-treatment state. Laboratory evaluations (haematology, serum chemistry and urinalysis) of blood and urine samples were performed. As-treated population included all treated participants, grouped according to actual treatment received.

End point type	Secondary
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End point timeframe:

From Study Drug Administration to Week 22

End point values	Placebo	Tralokinumab Dose 1	Tralokinumab Dose 2	Tralokinumab Dose 3
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	51	50	51	52
Units: Participant				
Anaemia	0	1	0	0
Lymphopenia	1	0	0	0
Alanine aminotransferase increased	0	1	0	0
Aspartate aminotransferase increased	0	1	0	0
Blood alkaline phosphatase increased	0	0	1	0
Blood creatinine increased	0	1	0	0
Blood immunoglobulin E increased	0	0	1	0
Gamma-glutamyltransferase increased	0	1	0	0
Hepatic function abnormal	0	1	0	0
Hyperbilirubinaemia	1	0	0	0
Liver function test abnormal	0	0	1	0
Glycosuria	0	1	0	0
Leukocyturia	1	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Electrocardiogram (ECG) Abnormalities Reported as Treatment Emergent Adverse Events

End point title	Number of Participants With Electrocardiogram (ECG) Abnormalities Reported as Treatment Emergent Adverse Events
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End point description:

AEs observed in participants with clinically significant ECG abnormalities were assessed. ECG parameters included heart rate, RR, PR, QRS and QT intervals. Treatment-emergent adverse events between administration of investigational product and Week 22 that were absent before treatment or that worsened relative to pre-treatment state. As-treated population included all treated participants, grouped according to actual treatment received.

End point type	Secondary
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End point timeframe:

From Study Drug Administration to Week 22

End point values	Placebo	Tralokinumab Dose 1	Tralokinumab Dose 2	Tralokinumab Dose 3
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	51	50	51	52
Units: Participant	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Achieving 50 percent (%) Reduction From Baseline in Eczema Area and Severity Index (EASI) at Week 12

End point title	Percentage of Participants Achieving 50 percent (%) Reduction From Baseline in Eczema Area and Severity Index (EASI) at Week 12
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End point description:

EASI50 responder is defined as a participant who achieves at least a 50% reduction in EASI score from baseline. The intent-to-treat (ITT) population included all randomized and treated participants, grouped according to assigned treatment. Here, "N" is number of participants analyzed for this outcome measure.

End point type	Secondary
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End point timeframe:

Week 12

End point values	Placebo	Tralokinumab Dose 1	Tralokinumab Dose 2	Tralokinumab Dose 3
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	41	45	47	48
Units: Percentage of participant				
number (not applicable)	61.0	64.4	72.3	75.0

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute Change From Baseline in Scoring of Atopic Dermatitis (SCORAD) at Week 12

End point title	Absolute Change From Baseline in Scoring of Atopic Dermatitis (SCORAD) at Week 12
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End point description:

The SCORAD is a clinical tool for assessing the severity (that is, extent, intensity) of AD. The tool

evaluates the extent and intensity of the AD lesions, along with participant symptoms. The maximum total score is 103, with higher values indicating more severe disease. The data presented here is Adjusted mean change after excluding the data from subjects who took prohibited medications. The intent-to-treat (ITT) population included all randomized and treated participants, grouped according to assigned treatment. Here, "N" is number of participants analyzed for this outcome measure.

End point type	Secondary
End point timeframe:	
Week 12	

End point values	Placebo	Tralokinumab Dose 1	Tralokinumab Dose 2	Tralokinumab Dose 3
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	40	43	44	48
Units: units on a scale				
arithmetic mean (standard error)	-16.67 (\pm 2.224)	-21.97 (\pm 2.204)	-26.09 (\pm 2.168)	-26.50 (\pm 2.123)

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Achieving 50 percent (%) Reduction From Baseline in SCORAD at Week 12

End point title	Percentage of Participants Achieving 50 percent (%) Reduction From Baseline in SCORAD at Week 12
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End point description:

SCORAD50 responder is defined as a participant who achieves at least a 50% reduction in SCORAD score from baseline. The intent-to-treat (ITT) population included all randomized and treated participants, grouped according to assigned treatment. Here, "N" is number of participants analyzed for this outcome measure.

End point type	Secondary
End point timeframe:	
Week 12	

End point values	Placebo	Tralokinumab Dose 1	Tralokinumab Dose 2	Tralokinumab Dose 3
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	41	45	47	48
Units: Percentage of participant				
number (not applicable)	26.8	35.6	46.8	43.8

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Pruritus Numeric Rating Scale (NRS) (7-day mean score) at Week 12

End point title	Change From Baseline in Pruritus Numeric Rating Scale (NRS) (7-day mean score) at Week 12
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End point description:

Pruritus assessed using an NRS (0 - 10) with 0= no itch and 10= worst imaginable itch. Daily pruritus assessments were summarized as weekly peak score and a change from baseline in weekly peak score was calculated. The data presented here is Adjusted mean change after excluding the data from subjects who took prohibited medications. The intent-to-treat (ITT) population included all randomized and treated participants, grouped according to assigned treatment. Here, "N" is number of participants analyzed for this outcome measure.

End point type	Secondary
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End point timeframe:

Week 12

End point values	Placebo	Tralokinumab Dose 1	Tralokinumab Dose 2	Tralokinumab Dose 3
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	38	38	42	42
Units: units on a scale				
arithmetic mean (standard error)	-1.03 (± 0.270)	-1.80 (± 0.266)	-1.59 (± 0.260)	-2.17 (± 0.256)

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From Study Drug Administration to Week 22

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	18.1
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Reporting groups

Reporting group title	Placebo
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Reporting group description:

Placebo was administered subcutaneously to participants.

Reporting group title	Tralokinumab Dose 1
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Reporting group description:

Tralokinumab Dose 1 was administered subcutaneously once every 2 Weeks (Q2W) for 12 weeks.

Reporting group title	Tralokinumab Dose 2
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Reporting group description:

Tralokinumab Dose 2 was administered subcutaneously once every 2 Weeks (Q2W) for 12 weeks.

Reporting group title	Tralokinumab Dose 3
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Reporting group description:

Tralokinumab Dose 3 was administered subcutaneously once every 2 Weeks (Q2W) for 12 weeks.

Serious adverse events	Placebo	Tralokinumab Dose 1	Tralokinumab Dose 2
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 51 (3.92%)	3 / 50 (6.00%)	2 / 51 (3.92%)
number of deaths (all causes)	0	1	0
number of deaths resulting from adverse events			
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	1 / 51 (1.96%)	0 / 50 (0.00%)	0 / 51 (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
General disorders and administration site conditions			
Death			
subjects affected / exposed	0 / 51 (0.00%)	1 / 50 (2.00%)	0 / 51 (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
Gastrointestinal disorders			
Upper gastrointestinal haemorrhage			

subjects affected / exposed	0 / 51 (0.00%)	1 / 50 (2.00%)	0 / 51 (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
Reproductive system and breast disorders			
Ovarian cyst			
subjects affected / exposed	0 / 51 (0.00%)	0 / 50 (0.00%)	1 / 51 (1.96%)
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 polyp			
subjects affected / exposed	0 / 51 (0.00%)	0 / 50 (0.00%)	1 / 51 (1.96%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	0 / 51 (0.00%)	1 / 50 (2.00%)	0 / 51 (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
Hepatic function abnormal			
subjects affected / exposed	0 / 51 (0.00%)	1 / 50 (2.00%)	0 / 51 (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	1 / 51 (1.96%)	0 / 50 (0.00%)	1 / 51 (1.96%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Serious adverse events			
Tralokinumab Dose 3			
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 52 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Cardiac disorders			
Angina pectoris			

subjects affected / exposed	0 / 52 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Death			
subjects affected / exposed	0 / 52 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Upper gastrointestinal haemorrhage			
subjects affected / exposed	0 / 52 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Reproductive system and breast disorders			
Ovarian cyst			
subjects affected / exposed	0 / 52 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Uterine polyp			
subjects affected / exposed	0 / 52 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	0 / 52 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hepatic function abnormal			
subjects affected / exposed	0 / 52 (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	0 / 52 (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: 1 %

Non-serious adverse events	Placebo	Tralokinumab Dose 1	Tralokinumab Dose 2
Total subjects affected by non-serious adverse events			
subjects affected / exposed	15 / 51 (29.41%)	20 / 50 (40.00%)	21 / 51 (41.18%)
Investigations			
Blood immunoglobuline increased			
subjects affected / exposed	1 / 51 (1.96%)	2 / 50 (4.00%)	3 / 51 (5.88%)
occurrences (all)	1	2	3
Nervous system disorders			
Headache			
subjects affected / exposed	2 / 51 (3.92%)	3 / 50 (6.00%)	4 / 51 (7.84%)
occurrences (all)	3	6	4
Skin and subcutaneous tissue disorders			
Dermatitis atopic			
subjects affected / exposed	4 / 51 (7.84%)	3 / 50 (6.00%)	3 / 51 (5.88%)
occurrences (all)	5	3	4
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	6 / 51 (11.76%)	11 / 50 (22.00%)	8 / 51 (15.69%)
occurrences (all)	9	12	9
Sinusitis			
subjects affected / exposed	1 / 51 (1.96%)	1 / 50 (2.00%)	2 / 51 (3.92%)
occurrences (all)	1	1	2
Upper respiratory tract infection			
subjects affected / exposed	5 / 51 (9.80%)	5 / 50 (10.00%)	6 / 51 (11.76%)
occurrences (all)	6	7	9

Non-serious adverse events	Tralokinumab Dose 3		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	22 / 52 (42.31%)		
Investigations			

Blood immunoglobuline increased subjects affected / exposed occurrences (all)	1 / 52 (1.92%) 1		
Nervous system disorders Headache subjects affected / exposed occurrences (all)	4 / 52 (7.69%) 4		
Skin and subcutaneous tissue disorders Dermatitis atopic subjects affected / exposed occurrences (all)	3 / 52 (5.77%) 4		
Infections and infestations Nasopharyngitis subjects affected / exposed occurrences (all) Sinusitis subjects affected / exposed occurrences (all) Upper respiratory tract infection subjects affected / exposed occurrences (all)	13 / 52 (25.00%) 20 3 / 52 (5.77%) 3 4 / 52 (7.69%) 6		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
25 March 2015	Protocol Amendment 1: The major changes were made as per Food and Drug Administration (FDA) suggestion to establish the efficacy based on the primary endpoint of Investigator's Global Assessment (IGA) severity scale, clarification on usage of lower potency steroids, and eligibility criteria updated. Minor editing and correction of typographical errors were also addressed.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported