Clinical trial results:
AN OPEN-LABEL, SINGLE-ARM STUDY TO ASSESS THE SAFETY AND EFFICACY OF LEBRIKIZUMAB IN ADOLESCENT PATIENTS WITH MODERATE-TO-SEVERE ATOPIC DERMATITIS

Summary

EudraCT number	2019-004301-28
Trial protocol	PL
Global end of trial date	22 June 2022

Results information

Result version number	v2 (current)
This version publication date	19 February 2023
First version publication date	05 January 2023
Version creation reason	• Correction of full data set Adjusted the data per ctgov changes.

Trial information

Trial identification

Sponsor protocol code	J2T-DM-KGAE

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04250350
WHO universal trial number (UTN)	-
Other trial identifiers	Trial Number: 17804

Notes:

Sponsors

Sponsor organisation name	Eli Lilly and Company
Sponsor organisation address	Lilly Corporate Center, Indianapolis, IN, United States, 46285
Public contact	Available Mon Fri 9 AM 5 PM EST, Eli Lilly and Company, 1 877CTLilly,
Scientific contact	Available Mon Fri 9 AM 5 PM EST, Eli Lilly and Company, 1 8772854559,

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-002536-PIP01-18
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	22 June 2022
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	22 June 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

This is an open-label, single arm study of 52 weeks duration. The study will assess the safety and efficacy of lebrikizumab in adolescent participants (≥12 to <18 years weighing ≥40 kilograms) with moderate-to-severe atopic dermatitis (AD) who are candidates for systemic therapy.

Protection of trial subjects:

This study was conducted in accordance with International Conference on Harmonization (ICH) Good Clinical Practice, and the principles of the Declaration of Helsinki, in addition to following the laws and regulations of the country or countries in which a study is conducted.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	11 February 2020
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	Poland: 63
Country: Number of subjects enrolled	Australia: 12
Country: Number of subjects enrolled	Canada: 20
Country: Number of subjects enrolled	United States: 111
Worldwide total number of subjects	206
EEA total number of subjects	63

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)	206
Adults (18-64 years)	0

From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

NA

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Lebrikizumab 250 mg

Arm description:

Participants received two subcutaneous (SC) injections of 250 mg Lebrikizumab at Baseline and Week 2 followed by a single injection every 2 weeks (Q2W) from Week 4 up to (but not including) Week 52.

Arm type	Experimental
Investigational medicinal product name	Lebrikizumab
Investigational medicinal product code	
Other name	LY3650150, DRM06
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Administered via subcutaneous injection

Number of subjects in period 1	Lebrikizumab 250 mg
Started	206
Completed	172
Not completed	34
Consent withdrawn by subject	13
Physician decision	1
Adverse event, non-fatal	5
Participant moved out of the country/non-complianc	3
Lost to follow-up	8
Lack of efficacy	4

Baseline characteristics

Reporting groups	
Reporting group title	Overall Study
Reporting group description:	
All enrolled or randomized participants who received at least one dose of study drug.	

Reporting group values	Overall Study	Total	
Number of subjects	206	206	
Age categorical Units: Subjects			
<=18 years	206	206	
Between 18 and 65 years	0	0	
>=65 years	0	0	
Age continuous Units: years			
arithmetic mean	14.6		
standard deviation	± 1.79	-	
Gender categorical Units: Subjects			
Female	108	108	
Male	98	98	
Region of Enrollment Units: Subjects			
Canada	20	20	
United States	111	111	
Poland	63	63	
Australia	12	12	
Weight Units: Subjects			
<60 kg	92	92	
>=60 - <100 kg	95	95	
>= 100 kg	19	19	
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	2	2	
Asian	24	24	
Native Hawaiian or Other Pacific Islander	0	0	
White	138	138	
Black or African American	26	26	
More than one race	11	11	
Unknown or Not Reported	5	5	

Subject analysis sets	
Subject analysis set title	Lebrikizumab 250 mg
Subject analysis set type	Safety analysis

Subject analysis set description:

Participants received 250 mg Lebrikizumab SC at baseline and Week 2. From Week 4 onwards, all participants received 250 mg lebrikizumab SC every 2 weeks up to (but not including) Week 52.

Reporting group values	Lebrikizumab 250 mg		
Number of subjects	206		
Age categorical Units: Subjects			
<=18 years	206		
Between 18 and 65 years	0		
>=65 years	0		
Age continuous Units: years			
arithmetic mean	14.6		
standard deviation	± 1.79		
Gender categorical Units: Subjects			
Female	108		
Male	98		
Region of Enrollment Units: Subjects			
Canada	20		
United States	111		
Poland	63		
Australia	12		
Weight Units: Subjects			
<60 kg	92		
>=60 - <100 kg	95		
>= 100 kg	19		
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	2		
Asian	24		
Native Hawaiian or Other Pacific Islander	0		
White	138		
Black or African American	26		
More than one race	11		
Unknown or Not Reported	5		

End points

End points reporting groups

Reporting group title	Lebrikizumab 250 mg

Reporting group description:

Participants received two subcutaneous (SC) injections of 250 mg Lebrikizumab at Baseline and Week 2 followed by a single injection every 2 weeks (Q2W) from Week 4 up to (but not including) Week 52.

Subject analysis set title	Lebrikizumab 250 mg
Subject analysis set type	Safety analysis

Subject analysis set description:

Participants received 250 mg Lebrikizumab SC at baseline and Week 2. From Week 4 onwards, all participants received 250 mg lebrikizumab SC every 2 weeks up to (but not including) Week 52.

Primary: Percentage of Participants Discontinued from Study Treatment Due to Adverse Events (AEs)

End point title	Percentage of Participants Discontinued from Study Treatment Due to Adverse Events (AEs)[1]

End point description:

The percentage of participants who discontinued from study treatment due to 1 or more AEs assessed is summarized cumulatively. A summary of all SAE's, regardless of causality, is located in the Reported Adverse Events section.
Analysis Population Description (APD): All enrolled participants.

End point type	Primary

End point timeframe:

Week 52

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: No statistical analyses were performed for this endpoint.

End point values	Lebrikizumab 250 mg			
Subject group type	Reporting group			
Number of subjects analysed	206			
Units: percentage of participants				
number (not applicable)	2.4			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with an Investigator Global Assessment (IGA) Score of 0 or 1 and a Reduction ≥2-points from Baseline

End point title	Percentage of Participants with an Investigator Global Assessment (IGA) Score of 0 or 1 and a Reduction ≥2-points from Baseline

End point description:

The IGA measures the investigator's global assessment of the participant's overall severity of their AD, based on a static, numeric 5-point scale from 0 (clear skin) to 4 (severe disease). The score is based on an overall assessment of the degree of erythema, papulation/induration, oozing/crusting, and lichenification.
APD: All participants with evaluable data for IGA score of 0 or 1.

End point type	Secondary

End point timeframe:

Week 52

End point values	Lebrikizumab 250 mg			
Subject group type	Reporting group			
Number of subjects analysed	206			
Units: percentage of participants				
number (confidence interval 95%)	62.6 (55.6 to 69.6)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Achieving ≥75% Reduction from Baseline in Eczema Area and Severity Instrument (EASI) Score (EASI-75)

End point title	Percentage of Participants Achieving ≥75% Reduction from Baseline in Eczema Area and Severity Instrument (EASI) Score (EASI-75)

End point description:

The EASI assesses objective physician estimates of 2 dimensions of atopic dermatitis - disease extent and clinical signs affected: 0 = 0%; 1 = 1-9%; 2 = 10-29%; 3 = 30-49%; 4 = 50-69%; 5 = 70-89%; 6 = 90-100% and the severity of 4 clinical signs: (1) erythema, (2) edema/papulation, (3) excoriation, and (4) lichenification each on a scale of 0 to 3 (0 = none, absent; 1 = mild; 2 = moderate; 3 = severe) at 4 body sites (head/neck, trunk, upper limbs, and lower limbs). Half scores are allowed between severities 1, 2, and 3. The final EASI score was obtained by weight-averaging these 4 scores and will range from 0 to 72 (severe).
The EASI responder is defined as a participant who achieves a ≥ 75% improvement from baseline in the EASI score.
APD: All participants with evaluable data for EASI-75.

End point type	Secondary

End point timeframe:

Week 52

End point values	Lebrikizumab 250 mg			
Subject group type	Reporting group			
Number of subjects analysed	206			
Units: percentage of participants				
number (confidence interval 95%)	81.9 (76.5 to 87.4)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage Change from Baseline in EASI score

End point title	Percentage Change from Baseline in EASI score

End point description:

The EASI assesses objective physician estimates of 2 dimensions of atopic dermatitis - disease extent and clinical signs affected: 0 = 0%; 1 = 1-9%; 2 = 10-29%; 3 = 30-49%; 4 = 50-69%; 5 = 70-89%; 6 = 90-100% and the severity of 4 clinical signs: (1) erythema, (2) edema/papulation, (3) excoriation, and (4) lichenification each on a scale of 0 to 3 (0 = none, absent; 1 = mild; 2 = moderate; 3 = severe) at 4 body sites (head/neck, trunk, upper limbs, and lower limbs). Half scores are allowed between severities 1, 2, and 3. The final EASI score was obtained by weight-averaging these 4 scores and will range from 0 to 72 (severe).
APD: All participants with evaluable data for EASI score.

End point type	Secondary

End point timeframe:

Baseline, Week 52

End point values	Lebrikizumab 250 mg			
Subject group type	Reporting group			
Number of subjects analysed	206			
Units: percentage change				
arithmetic mean (confidence interval 95%)	-86.0 (-89.1 to -83.0)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Achieving EASI-50 (≥50 reduction from Baseline in EASI score)

End point title	Percentage of Participants Achieving EASI-50 (≥50 reduction from Baseline in EASI score)

End point description:

The EASI assesses objective physician estimates of 2 dimensions of atopic dermatitis - disease extent and clinical signs affected: 0 = 0%; 1 = 1-9%; 2 = 10-29%; 3 = 30-49%; 4 = 50-69%; 5 = 70-89%; 6 = 90-100% and the severity of 4 clinical signs: (1) erythema, (2) edema/papulation, (3) excoriation, and (4) lichenification each on a scale of 0 to 3 (0 = none, absent; 1 = mild; 2 = moderate; 3 = severe) at 4 body sites (head/neck, trunk, upper limbs, and lower limbs). Half scores are allowed between severities 1, 2, and 3. The final EASI score was obtained by weight-averaging these 4 scores and will range from 0 to 72 (severe).
The EASI responder is defined as a participant who achieves a ≥ 50% improvement from baseline in the EASI score. Percentage change from baseline was calculated.
APD: All participants with evaluable data for EASI-50.

End point type	Secondary

End point timeframe:

Week 52

End point values	Lebrikizumab 250 mg			
Subject group type	Reporting group			
Number of subjects analysed	206			
Units: percentage of participants				
number (confidence interval 95%)	94.4 (91.1 to 97.7)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Achieving EASI-90 (≥90% reduction from baseline in EASI score)

End point title	Percentage of Participants Achieving EASI-90 (≥90% reduction from baseline in EASI score)

End point description:

The EASI assesses objective physician estimates of 2 dimensions of atopic dermatitis - disease extent and clinical signs affected: 0 = 0%; 1 = 1-9%; 2 = 10-29%; 3 = 30-49%; 4 = 50-69%; 5 = 70-89%; 6 = 90-100% and the severity of 4 clinical signs: (1) erythema, (2) edema/papulation, (3) excoriation, and (4) lichenification each on a scale of 0 to 3 (0 = none, absent; 1 = mild; 2 = moderate; 3 = severe) at 4 body sites (head/neck, trunk, upper limbs, and lower limbs). Half scores are allowed between severities 1, 2, and 3. The final EASI score was obtained by weight-averaging these 4 scores and will range from 0 to 72 (severe).
The EASI responder is defined as a participant who achieves a ≥ 90% improvement from baseline in the EASI score.
APD: All participants with evaluable data for EASI-90.

End point type	Secondary

End point timeframe:

Week 52

End point values	Lebrikizumab 250 mg			
Subject group type	Reporting group			
Number of subjects analysed	206			
Units: percentage of participants				
number (confidence interval 95%)	61.4 (54.5 to 68.3)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Body Surface Area (BSA)

End point title	Change from Baseline in Body Surface Area (BSA)

End point description:

The BSA affected by AD will be assessed for 4 separate body regions: head and neck, trunk (including genital region), upper extremities, and lower extremities (including the buttocks). Each body region will be assessed for disease extent ranging from 0% to 100% involvement. BSA was calculated using the

participant's palm using the 1% rule, 1 palm was equivalent to 1% with estimates of the number of palms it takes to cover the affected AD area. Maximum number of palms were 10 palms for head and neck (10%), 20 palms for upper extremities (20%), 30 palms for trunk, including axilla and groin (30%), 40 palms for lower extremities, including buttocks (40%). Percent of BSA for a body region was calculated as = total number of palms in a body region * % surface area equivalent to 1 palm. Overall percent BSA of all 4 body regions ranges from 0% to 100 % with higher values representing greater severity of AD.
APD: All participants with evaluable data for BSA.

End point type	Secondary

End point timeframe:

Baseline, Week 52

End point values	Lebrikizumab 250 mg			
Subject group type	Reporting group			
Number of subjects analysed	172			
Units: percentage of body surface area				
arithmetic mean (standard deviation)	-37.63 (± 21.071)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Patient-Reported Outcomes Information System (PROMIS) Anxiety

End point title	Change from Baseline in Patient-Reported Outcomes Information System (PROMIS) Anxiety

End point description:

PROMIS® is a set of person-centered measures that evaluates and monitors physical, mental, and social health in adults and children. Participants ≤17 years will complete pediatric versions for the duration of the study. PROMIS anxiety has 8 questions on Emotion Distress-Anxiety (or Pediatric Anxiety Symptom). Each question has 5 response options with values from 1 to 5. Total raw scores were converted to T-Scores (mean = 50 and a standard deviation = 10) with higher scores representing greater anxiety.
APD: All participants with evaluable data for PROMIS Anxiety.

End point type	Secondary

End point timeframe:

Baseline, Week 52

End point values	Lebrikizumab 250 mg			
Subject group type	Reporting group			
Number of subjects analysed	170			
Units: T-Score				
arithmetic mean (standard deviation)	-6.34 (± 9.979)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Patient-Reported Outcomes Information System (PROMIS) Depression

End point title	Change From Baseline in Patient-Reported Outcomes Information System (PROMIS) Depression

End point description:

PROMIS is a set of person-centered measures that evaluates and monitors physical, mental, and social health in adults and children. The PROMIS measures will be completed by the participant in the study clinic. PROMIS depression has 8 questions on Emotion Distress-Depression. Questions are measured on a 5-point scale with 1 being "Never" and 5 being "Always". Responses for each section will be summed and converted to T-Scores using the Assessment Center PROMIS Scoring Service, which rescales the raw score to a standardized T-Score with a population mean of 50 and a standard deviation of 10. Total raw scores were converted to T-scores with higher scores indicating greater severity of symptoms.
APD: All participants evaluable data for PROMIS Depression.

End point type	Secondary

End point timeframe:

Baseline, Week 52

End point values	Lebrikizumab 250 mg			
Subject group type	Reporting group			
Number of subjects analysed	169			
Units: T-score				
arithmetic mean (standard deviation)	-3.43 (± 9.057)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Dermatology Life Quality Index (DLQI)

End point title	Change from Baseline in Dermatology Life Quality Index (DLQI)

End point description:

The DLQI questionnaire designed for participants aged 17 years or more is a 10-item, validated questionnaire used to assess the impact of skin disease on the quality of life of an affected person. The 10 questions cover the following topics: symptoms, embarrassment, shopping and home care, clothes, social and leisure, sport, work or study, close relationships, sex, and treatment, over the previous week. Response categories include "Not at all," "A little," "A lot," and "Very much," with corresponding scores of 0, 1, 2, and 3 respectively. Questions 3-10 also have an additional response category of "Not relevant" which is scored as "0". Questions are scored from 0 to 3, giving a possible total score range from 0 (no impact of skin disease on quality of life) to 30 (maximum impact on quality of life). A high score is indicative of a poor quality of life.

APD: All participants with evaluable data for DLQI.

End point type	Secondary

End point timeframe:

Baseline, Week 52

End point values	Lebrikizumab 250 mg			
Subject group type	Reporting group			
Number of subjects analysed	35			
Units: score on a scale				
arithmetic mean (confidence interval 95%)	-8.92 (-10.8 to -7.1)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Children’s Dermatology Life Quality Index (CDLQI)

End point title	Change From Baseline in Children’s Dermatology Life Quality Index (CDLQI)

End point description:

The CDLQI questionnaire is designed for use in children (4 to 16 years of age). It consists of 10 items that are grouped into 6 domains: symptoms & feelings, leisure, school or holidays, personal relationships, sleep, & treatment. The scoring of each question is: Very much =3; Quite a lot = 2; Only a little = 1; Not at all = 0. CDLQI total score is calculated by summing all 10 items responses and has a range of 0 to 30 (higher scores are indicative of greater impairment).
APD: All participants with evaluable data for CDLQI.

End point type	Secondary

End point timeframe:

Baseline, Week 52

End point values	Lebrikizumab 250 mg			
Subject group type	Reporting group			
Number of subjects analysed	168			
Units: score on a scale				
arithmetic mean (confidence interval 95%)	-6.45 (-7.4 to -5.5)			

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacokinetics (PK): Average Serum Concentration of Lebrikizumab

End point title	Pharmacokinetics (PK): Average Serum Concentration of Lebrikizumab

End point description:

PK: Average Serum Concentration of Lebrikizumab was evaluated. Ctrough sample was defined as collected 14 days ± 7 days after the prior dose, based on the dosing interval of 14 days and allowed visit windows in the protocol.
APD: All participants with evaluable PK data at Week 52.

End point type	Secondary

End point timeframe:

Predose: Week 52

End point values	Lebrikizumab 250 mg			
Subject group type	Reporting group			
Number of subjects analysed	138			
Units: microgram per milliliter (µg/mL)				
arithmetic mean (standard deviation)	82.3 (± 39.8)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Baseline up to Week 52

Adverse event reporting additional description:

All participants who received at least one dose of study drug. Gender specific events only occurring in male or female participants have had the number of participants At Risk adjusted accordingly.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	25.0

Reporting groups

Reporting group title	Lebrikizumab 250mg

Reporting group description:

Participants received two SC injections of 250 mg Lebrikizumab at Baseline and Week 2 followed by a single injection Q2W from Week 4 up to (but not including) Week 52.

Serious adverse events	Lebrikizumab 250mg		
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 206 (2.43%)		
number of deaths (all causes)	1		
number of deaths resulting from adverse events	0		
Injury, poisoning and procedural complications			
multiple injuries			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	1 / 206 (0.49%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
cardiac arrest			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	1 / 206 (0.49%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Reproductive system and breast disorders			
testicular torsion			
alternative dictionary used:			

MedDRA 25.0			
subjects affected / exposed[1]	1 / 98 (1.02%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
bile duct stone			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	1 / 206 (0.49%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
dermatitis atopic			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	1 / 206 (0.49%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Notes:

[1] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.
Justification: Gender specific events only occurring in male or female participants have had the number of participants at risk adjusted accordingly.

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Lebrikizumab 250mg		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	133 / 206 (64.56%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
cutaneous t-cell lymphoma			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	1 / 206 (0.49%)		
occurrences (all)	1		
lipoma			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	1 / 206 (0.49%)		
occurrences (all)	1		
skin papilloma			
alternative dictionary used: MedDRA 25.0			

subjects affected / exposed	2 / 206 (0.97%)		
occurrences (all)	2		
Vascular disorders			
hypertension			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	4 / 206 (1.94%)		
occurrences (all)	4		
General disorders and administration site conditions			
fatigue			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	3 / 206 (1.46%)		
occurrences (all)	5		
injection site erythema			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	2 / 206 (0.97%)		
occurrences (all)	3		
injection site pain			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	3 / 206 (1.46%)		
occurrences (all)	8		
injection site reaction			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	2 / 206 (0.97%)		
occurrences (all)	3		
malaise			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	1 / 206 (0.49%)		
occurrences (all)	1		
pain			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	1 / 206 (0.49%)		
occurrences (all)	1		
pyrexia			
alternative dictionary used: MedDRA 25.0			

subjects affected / exposed	4 / 206 (1.94%)		
occurrences (all)	4		
vaccination site erythema	Additional description: NA		
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	1 / 206 (0.49%)		
occurrences (all)	1		
Immune system disorders			
drug hypersensitivity			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	1 / 206 (0.49%)		
occurrences (all)	1		
food allergy			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	1 / 206 (0.49%)		
occurrences (all)	1		
hypersensitivity			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	2 / 206 (0.97%)		
occurrences (all)	2		
multiple allergies			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	1 / 206 (0.49%)		
occurrences (all)	1		
seasonal allergy			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	1 / 206 (0.49%)		
occurrences (all)	1		
Reproductive system and breast disorders			
dysmenorrhoea			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed[2]	1 / 108 (0.93%)		
occurrences (all)	3		
heavy menstrual bleeding			
alternative dictionary used: MedDRA 25.0			

subjects affected / exposed[3]	2 / 108 (1.85%)		
occurrences (all)	2		
menstruation irregular			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed[4]	2 / 108 (1.85%)		
occurrences (all)	2		
polymenorrhoea			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed[5]	1 / 108 (0.93%)		
occurrences (all)	1		
Respiratory, thoracic and mediastinal disorders			
adenoidal hypertrophy			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	1 / 206 (0.49%)		
occurrences (all)	1		
catarrh			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	1 / 206 (0.49%)		
occurrences (all)	1		
cough			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	7 / 206 (3.40%)		
occurrences (all)	8		
epistaxis			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	4 / 206 (1.94%)		
occurrences (all)	4		
nasal congestion			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	3 / 206 (1.46%)		
occurrences (all)	3		
oropharyngeal pain			
alternative dictionary used: MedDRA 25.0			

subjects affected / exposed	4 / 206 (1.94%)		
occurrences (all)	4		
rhinitis allergic			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	1 / 206 (0.49%)		
occurrences (all)	1		
rhinorrhoea			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	3 / 206 (1.46%)		
occurrences (all)	3		
tonsillar hypertrophy			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	1 / 206 (0.49%)		
occurrences (all)	1		
Psychiatric disorders			
anxiety			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	1 / 206 (0.49%)		
occurrences (all)	2		
attention deficit hyperactivity disorder			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	2 / 206 (0.97%)		
occurrences (all)	2		
depression			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	2 / 206 (0.97%)		
occurrences (all)	2		
insomnia	Additional description: NA		
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	2 / 206 (0.97%)		
occurrences (all)	3		
persistent depressive disorder			
alternative dictionary used: MedDRA 25.0			

subjects affected / exposed	1 / 206 (0.49%)		
occurrences (all)	1		
social anxiety disorder			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	1 / 206 (0.49%)		
occurrences (all)	1		
Investigations			
alanine aminotransferase increased			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	4 / 206 (1.94%)		
occurrences (all)	5		
aspartate aminotransferase increased			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	1 / 206 (0.49%)		
occurrences (all)	1		
gamma-glutamyltransferase increased			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	1 / 206 (0.49%)		
occurrences (all)	1		
mean cell haemoglobin concentration decreased			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	1 / 206 (0.49%)		
occurrences (all)	1		
neutrophil count increased			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	1 / 206 (0.49%)		
occurrences (all)	1		
platelet count increased			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	1 / 206 (0.49%)		
occurrences (all)	1		
white blood cell count increased	Additional description: NA		
alternative dictionary used: MedDRA 25.0			

subjects affected / exposed	1 / 206 (0.49%)		
occurrences (all)	1		
Injury, poisoning and procedural complications			
animal bite			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	1 / 206 (0.49%)		
occurrences (all)	1		
clavicle fracture			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	1 / 206 (0.49%)		
occurrences (all)	1		
contusion			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	1 / 206 (0.49%)		
occurrences (all)	1		
foot fracture			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	1 / 206 (0.49%)		
occurrences (all)	1		
hand fracture			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	1 / 206 (0.49%)		
occurrences (all)	1		
head injury			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	1 / 206 (0.49%)		
occurrences (all)	1		
ligament sprain	Additional description: NA		
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	2 / 206 (0.97%)		
occurrences (all)	2		
muscle strain			
alternative dictionary used: MedDRA 25.0			

subjects affected / exposed	1 / 206 (0.49%)		
occurrences (all)	1		
nail injury			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	1 / 206 (0.49%)		
occurrences (all)	1		
post procedural complication			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	1 / 206 (0.49%)		
occurrences (all)	1		
procedural dizziness			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	1 / 206 (0.49%)		
occurrences (all)	2		
radius fracture			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	1 / 206 (0.49%)		
occurrences (all)	1		
skin abrasion	Additional description: NA		
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	1 / 206 (0.49%)		
occurrences (all)	1		
thermal burn			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	1 / 206 (0.49%)		
occurrences (all)	1		
sunburn	Additional description: NA		
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	2 / 206 (0.97%)		
occurrences (all)	2		
vaccination complication	Additional description: NA		
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	2 / 206 (0.97%)		
occurrences (all)	2		

wound	Additional description: NA		
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	1 / 206 (0.49%)		
occurrences (all)	1		
Congenital, familial and genetic disorders			
thyroglossal cyst			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	1 / 206 (0.49%)		
occurrences (all)	1		
type v hyperlipidaemia			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	1 / 206 (0.49%)		
occurrences (all)	1		
Cardiac disorders			
sinus arrhythmia	Additional description: NA		
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	1 / 206 (0.49%)		
occurrences (all)	1		
Nervous system disorders			
dizziness			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	1 / 206 (0.49%)		
occurrences (all)	1		
headache			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	12 / 206 (5.83%)		
occurrences (all)	15		
loss of consciousness			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	1 / 206 (0.49%)		
occurrences (all)	1		
paraesthesia			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	1 / 206 (0.49%)		
occurrences (all)	1		

somnolence			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	2 / 206 (0.97%)		
occurrences (all)	2		
tremor			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	1 / 206 (0.49%)		
occurrences (all)	1		
Blood and lymphatic system disorders			
eosinophilia			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	8 / 206 (3.88%)		
occurrences (all)	9		
haemolytic anaemia			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	1 / 206 (0.49%)		
occurrences (all)	1		
leukopenia	Additional description: NA		
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	2 / 206 (0.97%)		
occurrences (all)	2		
leukocytosis	Additional description: NA		
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	1 / 206 (0.49%)		
occurrences (all)	1		
lymphadenopathy			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	1 / 206 (0.49%)		
occurrences (all)	1		
neutropenia			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	2 / 206 (0.97%)		
occurrences (all)	2		
Ear and labyrinth disorders			

tinnitus			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	1 / 206 (0.49%)		
occurrences (all)	1		
Eye disorders			
atopic keratoconjunctivitis			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	1 / 206 (0.49%)		
occurrences (all)	1		
cataract			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	1 / 206 (0.49%)		
occurrences (all)	3		
conjunctivitis allergic			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	4 / 206 (1.94%)		
occurrences (all)	8		
episcleritis	Additional description: NA		
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	1 / 206 (0.49%)		
occurrences (all)	1		
eye irritation			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	1 / 206 (0.49%)		
occurrences (all)	1		
eyelids pruritus			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	2 / 206 (0.97%)		
occurrences (all)	2		
ocular hyperaemia			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	1 / 206 (0.49%)		
occurrences (all)	1		
retinal detachment			
alternative dictionary used: MedDRA 25.0			

subjects affected / exposed	1 / 206 (0.49%)			
occurrences (all)	1			
uveitis				
alternative dictionary used: MedDRA 25.0				
subjects affected / exposed	1 / 206 (0.49%)			
occurrences (all)	1			
Gastrointestinal disorders				
abdominal discomfort	Additional description: NA			
alternative dictionary used: MedDRA 25.0				
subjects affected / exposed	1 / 206 (0.49%)			
occurrences (all)	1			
abdominal pain	Additional description: NA			
alternative dictionary used: MedDRA 25.0				
subjects affected / exposed	3 / 206 (1.46%)			
occurrences (all)	4			
angular cheilitis				
alternative dictionary used: MedDRA 25.0				
subjects affected / exposed	1 / 206 (0.49%)			
occurrences (all)	1			
dental caries				
alternative dictionary used: MedDRA 25.0				
subjects affected / exposed	2 / 206 (0.97%)			
occurrences (all)	2			
diarrhoea				
alternative dictionary used: MedDRA 25.0				
subjects affected / exposed	6 / 206 (2.91%)			
occurrences (all)	9			
dyspepsia				
alternative dictionary used: MedDRA 25.0				
subjects affected / exposed	1 / 206 (0.49%)			
occurrences (all)	1			
gastritis				
alternative dictionary used: MedDRA 25.0				

subjects affected / exposed	1 / 206 (0.49%)		
occurrences (all)	1		
nausea			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	5 / 206 (2.43%)		
occurrences (all)	5		
toothache			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	2 / 206 (0.97%)		
occurrences (all)	2		
vomiting	Additional description: NA		
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	2 / 206 (0.97%)		
occurrences (all)	2		
Hepatobiliary disorders			
hypertransaminasaemia			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	1 / 206 (0.49%)		
occurrences (all)	1		
Skin and subcutaneous tissue disorders			
acne	Additional description: NA		
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	7 / 206 (3.40%)		
occurrences (all)	7		
alopecia			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	1 / 206 (0.49%)		
occurrences (all)	1		
alopecia areata			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	1 / 206 (0.49%)		
occurrences (all)	1		
angioedema			
alternative dictionary used: MedDRA 25.0			

subjects affected / exposed	1 / 206 (0.49%)			
occurrences (all)	1			
dandruff				
alternative dictionary used: MedDRA 25.0				
subjects affected / exposed	1 / 206 (0.49%)			
occurrences (all)	1			
dermatitis				
alternative dictionary used: MedDRA 25.0				
subjects affected / exposed	1 / 206 (0.49%)			
occurrences (all)	1			
dermatitis atopic				
alternative dictionary used: MedDRA 25.0				
subjects affected / exposed	26 / 206 (12.62%)			
occurrences (all)	38			
drug eruption				
alternative dictionary used: MedDRA 25.0				
subjects affected / exposed	1 / 206 (0.49%)			
occurrences (all)	1			
eczema				
alternative dictionary used: MedDRA 25.0				
subjects affected / exposed	3 / 206 (1.46%)			
occurrences (all)	3			
erythema				
alternative dictionary used: MedDRA 25.0				
subjects affected / exposed	1 / 206 (0.49%)			
occurrences (all)	1			
hyperhidrosis				
alternative dictionary used: MedDRA 25.0				
subjects affected / exposed	2 / 206 (0.97%)			
occurrences (all)	2			
ingrowing nail				
alternative dictionary used: MedDRA 25.0				
subjects affected / exposed	2 / 206 (0.97%)			
occurrences (all)	2			

milia			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	1 / 206 (0.49%)		
occurrences (all)	1		
night sweats			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	1 / 206 (0.49%)		
occurrences (all)	1		
perioral dermatitis			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	1 / 206 (0.49%)		
occurrences (all)	1		
pruritus			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	5 / 206 (2.43%)		
occurrences (all)	5		
rash erythematous			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	1 / 206 (0.49%)		
occurrences (all)	1		
seborrhoeic dermatitis			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	1 / 206 (0.49%)		
occurrences (all)	1		
skin exfoliation			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	1 / 206 (0.49%)		
occurrences (all)	1		
urticaria			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	6 / 206 (2.91%)		
occurrences (all)	8		
Renal and urinary disorders			

dysuria			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	1 / 206 (0.49%)		
occurrences (all)	1		
Musculoskeletal and connective tissue disorders			
arthralgia			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	2 / 206 (0.97%)		
occurrences (all)	2		
muscle spasms			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	1 / 206 (0.49%)		
occurrences (all)	1		
myalgia			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	2 / 206 (0.97%)		
occurrences (all)	2		
neck pain			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	1 / 206 (0.49%)		
occurrences (all)	1		
Infections and infestations			
bronchitis			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	2 / 206 (0.97%)		
occurrences (all)	2		
covid-19			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	19 / 206 (9.22%)		
occurrences (all)	19		
cellulitis			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	1 / 206 (0.49%)		
occurrences (all)	1		
conjunctivitis			

alternative dictionary used: MedDRA 25.0				
subjects affected / exposed	10 / 206 (4.85%)			
occurrences (all)	12			
conjunctivitis bacterial				
alternative dictionary used: MedDRA 25.0				
subjects affected / exposed	1 / 206 (0.49%)			
occurrences (all)	1			
cystitis				
alternative dictionary used: MedDRA 25.0				
subjects affected / exposed	1 / 206 (0.49%)			
occurrences (all)	1			
ear infection				
alternative dictionary used: MedDRA 25.0				
subjects affected / exposed	1 / 206 (0.49%)			
occurrences (all)	1			
eczema herpeticum				
alternative dictionary used: MedDRA 25.0				
subjects affected / exposed	1 / 206 (0.49%)			
occurrences (all)	1			
epididymitis				
alternative dictionary used: MedDRA 25.0				
subjects affected / exposed[6]	1 / 98 (1.02%)			
occurrences (all)	1			
gastroenteritis				
alternative dictionary used: MedDRA 25.0				
subjects affected / exposed	1 / 206 (0.49%)			
occurrences (all)	1			
herpes dermatitis				
alternative dictionary used: MedDRA 25.0				
subjects affected / exposed	5 / 206 (2.43%)			
occurrences (all)	11			
herpes ophthalmic				
alternative dictionary used: MedDRA 25.0				

subjects affected / exposed	1 / 206 (0.49%)			
occurrences (all)	1			
herpes simplex				
alternative dictionary used: MedDRA 25.0				
subjects affected / exposed	3 / 206 (1.46%)			
occurrences (all)	7			
hordeolum				
alternative dictionary used: MedDRA 25.0				
subjects affected / exposed	1 / 206 (0.49%)			
occurrences (all)	1			
impetigo				
alternative dictionary used: MedDRA 25.0				
subjects affected / exposed	3 / 206 (1.46%)			
occurrences (all)	3			
nasopharyngitis				
alternative dictionary used: MedDRA 25.0				
subjects affected / exposed	20 / 206 (9.71%)			
occurrences (all)	28			
oral herpes				
alternative dictionary used: MedDRA 25.0				
subjects affected / exposed	11 / 206 (5.34%)			
occurrences (all)	22			
otitis media				
alternative dictionary used: MedDRA 25.0				
subjects affected / exposed	2 / 206 (0.97%)			
occurrences (all)	2			
paronychia				
alternative dictionary used: MedDRA 25.0				
subjects affected / exposed	3 / 206 (1.46%)			
occurrences (all)	5			
pelvic inflammatory disease				
alternative dictionary used: MedDRA 25.0				
subjects affected / exposed[7]	1 / 108 (0.93%)			
occurrences (all)	1			

pharyngitis			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	1 / 206 (0.49%)		
occurrences (all)	1		
pharyngitis streptococcal			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	1 / 206 (0.49%)		
occurrences (all)	1		
sinusitis	Additional description: NA		
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	4 / 206 (1.94%)		
occurrences (all)	4		
staphylococcal skin infection	Additional description: NA		
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	1 / 206 (0.49%)		
occurrences (all)	2		
tinea versicolour			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	1 / 206 (0.49%)		
occurrences (all)	1		
tooth abscess			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	1 / 206 (0.49%)		
occurrences (all)	1		
upper respiratory tract infection			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	13 / 206 (6.31%)		
occurrences (all)	15		
urinary tract infection			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	3 / 206 (1.46%)		
occurrences (all)	3		
wound infection	Additional description: NA		
alternative dictionary used: MedDRA 25.0			

subjects affected / exposed	1 / 206 (0.49%)		
occurrences (all)	1		
Metabolism and nutrition disorders			
decreased appetite			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	3 / 206 (1.46%)		
occurrences (all)	3		
gluten sensitivity			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	1 / 206 (0.49%)		
occurrences (all)	1		
vitamin d deficiency	Additional description: NA		
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	1 / 206 (0.49%)		
occurrences (all)	1		

Notes:

[2] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: Gender specific events only occurring in male or female participants have had the number of participants at risk adjusted accordingly.
[3] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: Gender specific events only occurring in male or female participants have had the number of participants at risk adjusted accordingly.
[4] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: Gender specific events only occurring in male or female participants have had the number of participants at risk adjusted accordingly.
[5] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: Gender specific events only occurring in male or female participants have had the number of participants at risk adjusted accordingly.
[6] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: Gender specific events only occurring in male or female participants have had the number of participants at risk adjusted accordingly.
[7] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: Gender specific events only occurring in male or female participants have had the number of participants at risk adjusted accordingly.

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

None reported