Clinical trial results:
A Randomized, Double-Blind, Placebo-Controlled, Parallel-Group, Dose-Ranging Study Investigating the Efficacy, Safety, and Pharmacokinetic Profile of ANB020 Administered to Adult Subjects With Moderate-to-Severe Atopic Dermatitis

Summary

EudraCT number	2018-000331-27
Trial protocol	GB DE CZ PL
Global end of trial date	03 December 2019

Results information

Result version number	v2 (current)
This version publication date	01 June 2023
First version publication date	26 March 2021
Version creation reason	• Correction of full data set Minor updates made for consistency.

Trial information

Trial identification

Sponsor protocol code	ANB020-005

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03533751
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	AnaptysBio, Inc
Sponsor organisation address	10421 Pacific Center Court, Suite 200, San Diego, United States, CA 92121
Public contact	AnaptysBio Clinical Trials Information, AnaptysBio, Inc, +1 8583626295, clinicaltrialinfo@anaptysbio.com
Scientific contact	AnaptysBio Clinical Trials Information, AnaptysBio, Inc, +1 8583626295, clinicaltrialinfo@anaptysbio.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	03 December 2019
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	03 December 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective of this study was to evaluate the effects of etokimab (ANB020) on skin lesions.

Protection of trial subjects:

This study was conducted in accordance with the protocol and with the following:
• Consensus ethical principles derived from international guidelines including the Declaration of Helsinki and Council for International Organizations of Medical Sciences International Ethical Guidelines;
• Applicable International Council for Harmonisation Good Clinical Practice Guidelines;
• Applicable laws and regulations.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	19 June 2018
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	Canada: 21
Country: Number of subjects enrolled	United States: 134
Country: Number of subjects enrolled	Germany: 19
Country: Number of subjects enrolled	Poland: 47
Country: Number of subjects enrolled	Czechia: 46
Country: Number of subjects enrolled	United Kingdom: 35
Worldwide total number of subjects	302
EEA total number of subjects	112

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)	279
From 65 to 84 years	23
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This study was conducted at 75 centers in the United States, United Kingdom, Canada, Czech Republic, Germany, and Poland. The study enrolled adults with moderate to severe atopic dermatitis (AD). The study included a treatment period of 16 weeks (Week 0 to 16) followed by a safety follow-up for 8 weeks (Week 16 to Week 24).

Pre-assignment

Screening details:

Participants were equally randomized on Day 1 to one of five treatment groups. Two participants in the etokimab 300 mg/placebo 150 mg subcutaneous (SC) every 8 weeks (Q8W) group were randomized to treatment but never received treatment (1 participant withdrew consent prior to dosing and 1 participant was lost to follow-up prior to dosing).

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Participants received matching placebo to etokimab, administered SC Q4W for up to 16 weeks.

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

Dosage and administration details:

Placebo was formulated as a sterile solution in single use glass vials containing 1.2 milliliters (mL) of solution.

Arm title	Etokimab 20 mg SC Q4W

Arm description:

Participants received etokimab 20 milligrams (mg) administered SC every 4 weeks (Q4W) for up to 16 weeks.

Arm type	Experimental
Investigational medicinal product name	Etokimab
Investigational medicinal product code	ANB020
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Etokimab was formulated as a sterile solution in single use glass vials containing 1.2 mL of solution.

Arm title	Etokimab 300 mg / 150 mg SC Q8W

Arm description:

Participants received a 300 mg loading dose of etokimab on Day 1 then 150 mg etokimab administered SC Q8W for up to 16 weeks. At Weeks 4 and 12 participants received placebo.

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

Dosage and administration details:

Placebo was formulated as a sterile solution in single use glass vials containing 1.2 mL of solution.

Investigational medicinal product name	Etokimab
Investigational medicinal product code	ANB020
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Etokimab was formulated as a sterile solution in single use glass vials containing 1.2 mL of solution.

Arm title	Etokimab 300 mg / 150 mg SC Q4W

Arm description:

Participants received a 300 mg loading dose of etokimab on Day 1 then 150 mg etokimab administered SC Q4W for up to 16 weeks.

Arm type	Experimental
Investigational medicinal product name	Etokimab
Investigational medicinal product code	ANB020
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Etokimab was formulated as a sterile solution in single use glass vials containing 1.2 mL of solution.

Arm title	Etokimab 600 mg / 300 mg SC Q4W

Arm description:

Participants received a 600 mg loading dose of etokimab on Day 1 then 300 mg etokimab administered SC Q4W for up to 16 weeks.

Arm type	Experimental
Investigational medicinal product name	Etokimab
Investigational medicinal product code	ANB020
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Etokimab was formulated as a sterile solution in single use glass vials containing 1.2 mL of solution.

Number of subjects in period 1[1]	Placebo	Etokimab 20 mg SC Q4W	Etokimab 300 mg / 150 mg SC Q8W
Started	60	61	59
Completed	41	36	39
Not completed	19	25	20
Consent withdrawn by subject	12	6	10
Physician decision	-	2	1

Adverse event, non-fatal	4	7	2
Other	-	2	1
Use of any excluded/prohibited medications	-	1	-
Lost to follow-up	3	7	5
Sponsor decision	-	-	1

Number of subjects in period 1[1]	Etokimab 300 mg / 150 mg SC Q4W	Etokimab 600 mg / 300 mg SC Q4W
Started	60	60
Completed	40	37
Not completed	20	23
Consent withdrawn by subject	9	10
Physician decision	2	1
Adverse event, non-fatal	4	5
Other	-	3
Use of any excluded/prohibited medications	-	1
Lost to follow-up	4	3
Sponsor decision	1	-

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: The worldwide number enrolled includes all participants randomized (ie, 302 participants) to treatment. Two participants were randomized but never received study drug. Baseline period is based on participants who were randomized and who received study drug (ie, 300 participants).

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Participants received matching placebo to etokimab, administered SC Q4W for up to 16 weeks.	
Reporting group title	Etokimab 20 mg SC Q4W
Reporting group description:	
Participants received etokimab 20 milligrams (mg) administered SC every 4 weeks (Q4W) for up to 16 weeks.	
Reporting group title	Etokimab 300 mg / 150 mg SC Q8W
Reporting group description:	
Participants received a 300 mg loading dose of etokimab on Day 1 then 150 mg etokimab administered SC Q8W for up to 16 weeks. At Weeks 4 and 12 participants received placebo.	
Reporting group title	Etokimab 300 mg / 150 mg SC Q4W
Reporting group description:	
Participants received a 300 mg loading dose of etokimab on Day 1 then 150 mg etokimab administered SC Q4W for up to 16 weeks.	
Reporting group title	Etokimab 600 mg / 300 mg SC Q4W
Reporting group description:	
Participants received a 600 mg loading dose of etokimab on Day 1 then 300 mg etokimab administered SC Q4W for up to 16 weeks.	

Reporting group values	Placebo	Etokimab 20 mg SC Q4W	Etokimab 300 mg / 150 mg SC Q8W
Number of subjects	60	61	59
Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age continuous Units: years			
arithmetic mean	39.5	40.1	39.7
standard deviation	± 15.92	± 16.76	± 14.38
Gender categorical Units: Subjects			
Female	29	25	36
Male	31	36	23
Race Units: Subjects			
American Indian or Alaska Native	0	1	0
Asian	5	2	0

Black or African American	6	9	10
White	49	48	46
Other	0	1	3
Ethnicity Units: Subjects			
Hispanic or Latino	10	11	8
Not Hispanic or Latino	50	49	51
Not Reported	0	1	0
Unknown	0	0	0
Validated Investigator Global Assessment Scale for Atopic Dermatitis (vIGA-AD)			
The vIGA-AD is a 5-point scale to evaluate AD severity: • 0: Clear - No inflammatory signs of AD (erythema, induration/papulation, lichenification, oozing/crusting) • 1: Almost clear - Barely perceptible erythema, induration/papulation, minimal lichenification • 2: Mild - Slight but definite erythema, induration/papulation, or lichenification. No oozing/crusting • 3: Moderate - Clearly perceptible erythema, induration/papulation, or lichenification. Oozing or crusting may be present • 4: Severe - Marked erythema, induration/papulation, or lichenification. Oozing or crusting may be present			
Units: Subjects			
Grade 0 (Clear)	0	0	0
Grade 1 (Almost clear)	0	0	0
Grade 2 (Mild)	0	0	0
Grade 3 (Moderate)	49	36	43
Grade 4 (Severe)	10	25	16
Missing	1	0	0
Eczema Area and Severity Index (EASI)			
EASI measures the extent and severity of atopic eczema of 4 body regions: head/neck, trunk, upper limbs and lower limbs. For each region, percentage of skin affected and the severity (scored as none [0], mild [1], moderate [2], severe [3]) for symptoms such as redness (erythema), thickness (induration, papulation, edema), scratching (excoriation) and lichenification (lined skin) are assessed. Total score is calculated by summing the EASI scores of 6 symptoms across 4 body regions. The EASI score ranges from 0 (no disease) to 72 (worse disease). In placebo group, 59 participants were evaluable.			
Units: units on a scale			
arithmetic mean	26.6	29.8	27.1
standard deviation	± 11.45	± 12.08	± 10.38

Reporting group values	Etokimab 300 mg / 150 mg SC Q4W	Etokimab 600 mg / 300 mg SC Q4W	Total
Number of subjects	60	60	300
Age categorical Units: Subjects			
In utero			0
Preterm newborn infants (gestational age < 37 wks)			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)			0
From 65-84 years			0
85 years and over			0

Age continuous Units: years			
arithmetic mean	38.9	37.1	
standard deviation	± 14.61	± 14.78	-
Gender categorical Units: Subjects			
Female	24	32	146
Male	36	28	154
Race Units: Subjects			
American Indian or Alaska Native	0	2	3
Asian	0	6	13
Black or African American	4	6	35
White	55	45	243
Other	1	1	6
Ethnicity Units: Subjects			
Hispanic or Latino	8	7	44
Not Hispanic or Latino	50	53	253
Not Reported	1	0	2
Unknown	1	0	1
Validated Investigator Global Assessment Scale for Atopic Dermatitis (vIGA-AD)			
The vIGA-AD is a 5-point scale to evaluate AD severity: • 0: Clear - No inflammatory signs of AD (erythema, induration/papulation, lichenification, oozing/crusting) • 1: Almost clear - Barely perceptible erythema, induration/papulation, minimal lichenification • 2: Mild - Slight but definite erythema, induration/papulation, or lichenification. No oozing/crusting • 3: Moderate - Clearly perceptible erythema, induration/papulation, or lichenification. Oozing or crusting may be present • 4: Severe - Marked erythema, induration/papulation, or lichenification. Oozing or crusting may be present			
Units: Subjects			
Grade 0 (Clear)	0	0	0
Grade 1 (Almost clear)	0	0	0
Grade 2 (Mild)	0	0	0
Grade 3 (Moderate)	43	38	209
Grade 4 (Severe)	17	22	90
Missing	0	0	1
Eczema Area and Severity Index (EASI)			
EASI measures the extent and severity of atopic eczema of 4 body regions: head/neck, trunk, upper limbs and lower limbs. For each region, percentage of skin affected and the severity (scored as none [0], mild [1], moderate [2], severe [3]) for symptoms such as redness (erythema), thickness (induration, papulation, edema), scratching (excoriation) and lichenification (lined skin) are assessed. Total score is calculated by summing the EASI scores of 6 symptoms across 4 body regions. The EASI score ranges from 0 (no disease) to 72 (worse disease). In placebo group, 59 participants were evaluable.			
Units: units on a scale			
arithmetic mean	32.2	29.5	
standard deviation	± 13.06	± 12.19	-

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
Participants received matching placebo to etokimab, administered SC Q4W for up to 16 weeks.	
Reporting group title	Etokimab 20 mg SC Q4W
Reporting group description:	
Participants received etokimab 20 milligrams (mg) administered SC every 4 weeks (Q4W) for up to 16 weeks.	
Reporting group title	Etokimab 300 mg / 150 mg SC Q8W
Reporting group description:	
Participants received a 300 mg loading dose of etokimab on Day 1 then 150 mg etokimab administered SC Q8W for up to 16 weeks. At Weeks 4 and 12 participants received placebo.	
Reporting group title	Etokimab 300 mg / 150 mg SC Q4W
Reporting group description:	
Participants received a 300 mg loading dose of etokimab on Day 1 then 150 mg etokimab administered SC Q4W for up to 16 weeks.	
Reporting group title	Etokimab 600 mg / 300 mg SC Q4W
Reporting group description:	
Participants received a 600 mg loading dose of etokimab on Day 1 then 300 mg etokimab administered SC Q4W for up to 16 weeks.	

Primary: Percent Change From Baseline to Week 16 in Eczema Area and Severity Index (EASI) Score

End point title	Percent Change From Baseline to Week 16 in Eczema Area and Severity Index (EASI) Score
End point description:	
EASI measures the extent and severity of atopic eczema based on assessments of 4 body regions: head/neck, trunk, upper limbs and lower limbs. For each region the percentage of skin affected and the severity (scored as none [0], mild [1], moderate [2], or severe [3]) for symptoms such as redness (erythema), thickness (induration, papulation, and edema), scratching (excoriation), and lichenification (lined skin) are assessed. Total score is calculated by summing the EASI scores of 6 symptoms across 4 body regions. The EASI score ranges from 0 (no disease) to 72 (worse disease). The full analysis set included all randomized subjects who received 1 dose of etokimab or placebo and had baseline and post-baseline EASI scores. Missing data were imputed using multiple imputation.	
End point type	Primary
End point timeframe:	
Baseline and Week 16	

End point values	Placebo	Etokimab 20 mg SC Q4W	Etokimab 300 mg / 150 mg SC Q8W	Etokimab 300 mg / 150 mg SC Q4W
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	60	61	59	60
Units: percent change				
least squares mean (standard error)	-49.38 (± 7.124)	-41.63 (± 6.707)	-55.70 (± 6.206)	-47.40 (± 6.091)

End point values	Etokimab 600 mg / 300 mg SC Q4W			
Subject group type	Reporting group			
Number of subjects analysed	60			
Units: percent change				
least squares mean (standard error)	-44.56 (± 7.811)			

Statistical analyses

Statistical analysis title	Placebo Vs Etokimab 20 mg SC Q4W
Statistical analysis description:	
The p-value was obtained using mixed effect analysis of covariance (ANCOVA) model with treatment as fixed effect and baseline EASI as covariate.	
Comparison groups	Placebo v Etokimab 20 mg SC Q4W
Number of subjects included in analysis	121
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4498
Method	ANCOVA
Parameter estimate	Least squares (LS) mean difference
Point estimate	7.75
Confidence interval	
level	95 %
sides	2-sided
lower limit	-12.4066
upper limit	27.8983
Variability estimate	Standard error of the mean
Dispersion value	10.235

Statistical analysis title	Placebo Vs Etokimab 300 mg / 150 mg SC Q8W
Statistical analysis description:	
The p-value was obtained using mixed effect ANCOVA model with treatment as fixed effect and baseline EASI as covariate.	
Comparison groups	Placebo v Etokimab 300 mg / 150 mg SC Q8W
Number of subjects included in analysis	119
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.501
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	-6.32

Confidence interval	
level	95 %
sides	2-sided
lower limit	-24.774
upper limit	12.1262
Variability estimate	Standard error of the mean
Dispersion value	9.39

Statistical analysis title	Placebo Vs Etokimab 300 mg / 150 mg SC Q4W

Statistical analysis description:

The p-value was obtained using mixed effect ANCOVA model with treatment as fixed effect and baseline EASI as covariate.

Comparison groups	Placebo v Etokimab 300 mg / 150 mg SC Q4W
Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8349
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	1.97
Confidence interval	
level	95 %
sides	2-sided
lower limit	-16.6037
upper limit	20.5476
Variability estimate	Standard error of the mean
Dispersion value	9.454

Statistical analysis title	Placebo Vs Etokimab 600 mg / 300 mg SC Q4W

Statistical analysis description:

The p-value was obtained using mixed effect ANCOVA model with treatment as fixed effect and baseline EASI as covariate.

Comparison groups	Placebo v Etokimab 600 mg / 300 mg SC Q4W
Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6662
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	4.82
Confidence interval	
level	95 %
sides	2-sided
lower limit	-17.1892
upper limit	26.8275
Variability estimate	Standard error of the mean
Dispersion value	11.154

Secondary: Number of Participants With a 50% Reduction From Baseline in Eczema Area and Severity Index Score (EASI 50 Response) at Week 16

End point title	Number of Participants With a 50% Reduction From Baseline in Eczema Area and Severity Index Score (EASI 50 Response) at Week 16

End point description:

EASI measures the extent and severity of atopic eczema based on assessments of 4 body regions: head/neck, trunk, upper limbs and lower limbs. For each region the percentage of skin affected and the severity (scored as none [0], mild [1], moderate [2], or severe [3]) for symptoms such as redness (erythema), thickness (induration, papulation, and edema), scratching (excoriation), and lichenification (lined skin) are assessed. Total score is calculated by summing the EASI scores of 6 symptoms across 4 body regions. The EASI score ranges from 0 (no disease) to 72 (worse disease). Full Analysis Set. Participants with missing data were counted as non-responders.

End point type	Secondary

End point timeframe:

Baseline and Week 16

End point values	Placebo	Etokimab 20 mg SC Q4W	Etokimab 300 mg / 150 mg SC Q8W	Etokimab 300 mg / 150 mg SC Q4W
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	60	61	59	60
Units: subjects	21	19	27	21

End point values	Etokimab 600 mg / 300 mg SC Q4W			
Subject group type	Reporting group			
Number of subjects analysed	60			
Units: subjects	18			

Statistical analyses

Statistical analysis title	Placebo Vs Etokimab 20 mg SC Q4W

Statistical analysis description:

Inferential statistics from a logistic regression model with treatment as fixed effect and baseline EASI as a covariate.

Comparison groups	Placebo v Etokimab 20 mg SC Q4W

Number of subjects included in analysis	121
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7992
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.91
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.42
upper limit	1.9509

Statistical analysis title	Placebo Vs Etokimab 300 mg / 150 mg SC Q8W

Statistical analysis description:

Inferential statistics from a logistic regression model with treatment as fixed effect and baseline EASI as a covariate.

Comparison groups	Placebo v Etokimab 300 mg / 150 mg SC Q8W
Number of subjects included in analysis	119
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2197
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.59
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.757
upper limit	3.3572

Statistical analysis title	Placebo Vs Etokimab 300 mg / 150 mg SC Q4W

Statistical analysis description:

Inferential statistics from a logistic regression model with treatment as fixed effect and baseline EASI as a covariate.

Comparison groups	Placebo v Etokimab 300 mg / 150 mg SC Q4W
Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7197
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.15

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.5345
upper limit	2.4774

Statistical analysis title	Placebo Vs Etokimab 600 mg / 300 mg SC Q4W

Statistical analysis description:

Inferential statistics from a logistic regression model with treatment as fixed effect and baseline EASI as a covariate.

Comparison groups	Placebo v Etokimab 600 mg / 300 mg SC Q4W
Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6772
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.85
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.391
upper limit	1.8404

Secondary: Number of Participants With a 75% Reduction From Baseline in Eczema Area and Severity Index Score (EASI 75 Response) at Week 16

End point title	Number of Participants With a 75% Reduction From Baseline in Eczema Area and Severity Index Score (EASI 75 Response) at Week 16

End point description:

EASI measures the extent and severity of atopic eczema based on assessments of 4 body regions: head/neck, trunk, upper limbs and lower limbs. For each region the percentage of skin affected and the severity (scored as none [0], mild [1], moderate [2], or severe [3]) for symptoms such as redness (erythema), thickness (induration, papulation, and edema), scratching (excoriation), and lichenification (lined skin) are assessed. Total score is calculated by summing the EASI scores of 6 symptoms across 4 body regions. The EASI score ranges from 0 (no disease) to 72 (worse disease). Full Analysis Set. Participants with missing data were counted as non-responders.

End point type	Secondary

End point timeframe:

Baseline and Week 16

End point values	Placebo	Etokimab 20 mg SC Q4W	Etokimab 300 mg / 150 mg SC Q8W	Etokimab 300 mg / 150 mg SC Q4W
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	60	61	59	60
Units: subjects	10	10	14	12

End point values	Etokimab 600 mg / 300 mg SC Q4W			
Subject group type	Reporting group			
Number of subjects analysed	60			
Units: subjects	11			

Statistical analyses

Statistical analysis title	Placebo Vs Etokimab 20 mg SC Q4W
Statistical analysis description:	
Inferential statistics from a logistic regression model with treatment as fixed effect and baseline EASI as a covariate.	
Comparison groups	Placebo v Etokimab 20 mg SC Q4W
Number of subjects included in analysis	121
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9537
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.03
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.3922
upper limit	2.6994

Statistical analysis title	Placebo Vs Etokimab 300 mg / 150 mg SC Q8W
Statistical analysis description:	
Inferential statistics from a logistic regression model with treatment as fixed effect and baseline EASI as a covariate.	
Comparison groups	Placebo v Etokimab 300 mg / 150 mg SC Q8W
Number of subjects included in analysis	119
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3316
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.57

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.6323
upper limit	3.8895

Statistical analysis title	Placebo Vs Etokimab 300 mg / 150 mg SC Q4W

Statistical analysis description:

Inferential statistics from a logistic regression model with treatment as fixed effect and baseline EASI as a covariate.

Comparison groups	Placebo v Etokimab 300 mg / 150 mg SC Q4W
Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5166
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.36
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.5331
upper limit	3.4944

Statistical analysis title	Placebo Vs Etokimab 600 mg / 300 mg SC Q4W

Statistical analysis description:

Inferential statistics from a logistic regression model with treatment as fixed effect and baseline EASI as a covariate.

Comparison groups	Placebo v Etokimab 600 mg / 300 mg SC Q4W
Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7426
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.17
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.4545
upper limit	3.0223

Secondary: Number of Participants With a 90% Reduction From Baseline in Eczema Area and Severity Index Score (EASI 90 Response) at Week 16

End point title	Number of Participants With a 90% Reduction From Baseline in

	Eczema Area and Severity Index Score (EASI 90 Response) at Week 16

End point description:

EASI measures the extent and severity of atopic eczema based on assessments of 4 body regions: head/neck, trunk, upper limbs and lower limbs. For each region the percentage of skin affected and the severity (scored as none [0], mild [1], moderate [2], or severe [3]) for symptoms such as redness (erythema), thickness (induration, papulation, and edema), scratching (excoriation), and lichenification (lined skin) are assessed. Total score is calculated by summing the EASI scores of 6 symptoms across 4 body regions. The EASI score ranges from 0 (no disease) to 72 (worse disease). Full Analysis Set. Participants with missing data were counted as non-responders.

End point type	Secondary

End point timeframe:

Baseline and Week 16

End point values	Placebo	Etokimab 20 mg SC Q4W	Etokimab 300 mg / 150 mg SC Q8W	Etokimab 300 mg / 150 mg SC Q4W
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	60	61	59	60
Units: subjects	3	5	7	7

End point values	Etokimab 600 mg / 300 mg SC Q4W			
Subject group type	Reporting group			
Number of subjects analysed	60			
Units: subjects	2			

Statistical analyses

Statistical analysis title	Placebo Vs Etokimab 20 mg SC Q4W

Statistical analysis description:

Inferential statistics from a logistic regression model with treatment as fixed effect and baseline EASI as a covariate.

Comparison groups	Placebo v Etokimab 20 mg SC Q4W
Number of subjects included in analysis	121
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4543
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.76
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.3998
upper limit	7.7615

Statistical analysis title	Placebo Vs Etokimab 300 mg / 150 mg SC Q8W
Statistical analysis description:	
Inferential statistics from a logistic regression model with treatment as fixed effect and baseline EASI as a covariate.	
Comparison groups	Placebo v Etokimab 300 mg / 150 mg SC Q8W
Number of subjects included in analysis	119
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1874
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.57
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.6314
upper limit	10.4827

Statistical analysis title	Placebo Vs Etokimab 300 mg / 150 mg SC Q4W
Statistical analysis description:	
Inferential statistics from a logistic regression model with treatment as fixed effect and baseline EASI as a covariate.	
Comparison groups	Placebo v Etokimab 300 mg / 150 mg SC Q4W
Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1721
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.69
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.6506
upper limit	11.0814

Statistical analysis title	Placebo Vs Etokimab 600 mg / 300 mg SC Q4W
Statistical analysis description:	
Inferential statistics from a logistic regression model with treatment as fixed effect and baseline EASI as a covariate.	
Comparison groups	Placebo v Etokimab 600 mg / 300 mg SC Q4W

Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6755
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.68
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.1086
upper limit	4.2141

Secondary: Number of Participants Who Achieved a Reduction of ≥ 2 Points From Baseline in the Validated Investigator's Global Assessment for Atopic Dermatitis (vIGA-AD) at Week 16

End point title	Number of Participants Who Achieved a Reduction of ≥ 2 Points From Baseline in the Validated Investigator's Global Assessment for Atopic Dermatitis (vIGA-AD) at Week 16

End point description:

The vIGA-AD is a static 5-point scale to evaluate AD severity globally:
0: Clear - No inflammatory signs of AD (no erythema, no induration/papulation, no lichenification, no oozing/crusting). Postinflammatory hyperpigmentation and/or hypopigmentation may be present
1: Almost clear - Barely perceptible erythema, barely perceptible induration/papulation, and/or minimal lichenification. No oozing or crusting
2: Mild - Slight but definite erythema (pink), slight but definite induration/papulation, and/or slight but definite lichenification. No oozing or crusting
3: Moderate - Clearly perceptible erythema (dull red), clearly perceptible induration/papulation, and/or clearly perceptible lichenification. Oozing and crusting may be present
4: Severe - Marked erythema (deep or bright red), marked induration/papulation, and/or marked lichenification. Disease is widespread in extent. Oozing or crusting may be present.
Number of participants with ≥2 points reduction in vIGA-AD is presented.

End point type	Secondary

End point timeframe:

Baseline and Week 16

End point values	Placebo	Etokimab 20 mg SC Q4W	Etokimab 300 mg / 150 mg SC Q8W	Etokimab 300 mg / 150 mg SC Q4W
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	60[1]	61[2]	59[3]	60[4]
Units: subjects	8	7	8	10

Notes:

[1] - Full Analysis Set. Participants with missing data were counted as non-responders.

[2] - Full Analysis Set. Participants with missing data were counted as non-responders.

[3] - Full Analysis Set. Participants with missing data were counted as non-responders.

[4] - Full Analysis Set. Participants with missing data were counted as non-responders.

End point values	Etokimab 600 mg / 300 mg SC Q4W			

Subject group type	Reporting group			
Number of subjects analysed	60[5]			
Units: subjects	9			

Notes:

[5] - Full Analysis Set. Participants with missing data were counted as non-responders.

Statistical analyses

Statistical analysis title	Placebo Vs Etokimab 20 mg SC Q4W

Statistical analysis description:

Inferential statistics based on a Logistic regression model with treatment as fixed effect and baseline test score as covariate.

Comparison groups	Placebo v Etokimab 20 mg SC Q4W
Number of subjects included in analysis	121
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6058
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.75
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.2481
upper limit	2.2543

Statistical analysis title	Placebo Vs Etokimab 300 mg / 150 mg SC Q8W

Statistical analysis description:

Inferential statistics based on a Logistic regression model with treatment as fixed effect and baseline test score as covariate.

Comparison groups	Placebo v Etokimab 300 mg / 150 mg SC Q8W
Number of subjects included in analysis	119
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9521
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.97
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.3356
upper limit	2.7923

Statistical analysis title	Placebo Vs Etokimab 300 mg / 150 mg SC Q4W

Statistical analysis description:

Inferential statistics based on a Logistic regression model with treatment as fixed effect and baseline

test score as covariate.

Comparison groups	Placebo v Etokimab 300 mg / 150 mg SC Q4W
Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6905
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.23
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.4457
upper limit	3.3878

Statistical analysis title	Placebo Vs Etokimab 600 mg / 300 mg SC Q4W

Statistical analysis description:

Inferential statistics based on a Logistic regression model with treatment as fixed effect and baseline test score as covariate.

Comparison groups	Placebo v Etokimab 600 mg / 300 mg SC Q4W
Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9399
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.3671
upper limit	2.9518

Secondary: Number of Participants Who Achieved a vIGA-AD Response of 0 (Clear) or 1 (Almost Clear) at Week 16

End point title	Number of Participants Who Achieved a vIGA-AD Response of 0 (Clear) or 1 (Almost Clear) at Week 16

End point description:

vIGA-AD is static 5-point scale to evaluate AD severity globally:
0: Clear - No inflammatory signs of AD (no erythema, no induration/papulation, no lichenification, no oozing/crusting). Postinflammatory hyperpigmentation and/or hypopigmentation may be present
1: Almost clear - Barely perceptible erythema, barely perceptible induration/papulation, and/or minimal lichenification. No oozing or crusting
2: Mild - Slight but definite erythema (pink), slight but definite induration/papulation, and/or slight but definite lichenification. No oozing or crusting
3: Moderate- Clearly perceptible erythema (dull red), clearly perceptible induration/papulation, and/or clearly perceptible lichenification. Oozing and crusting may be present
4: Severe- Marked erythema (deep or bright red), marked induration/papulation, and/or marked lichenification. Disease is widespread. Oozing or crusting may be present.
Participants who achieved vIGA-AD response of 0 (clear) or 1 (almost clear) are reported.

End point type	Secondary

End point timeframe:

Week 16

End point values	Placebo	Etokimab 20 mg SC Q4W	Etokimab 300 mg / 150 mg SC Q8W	Etokimab 300 mg / 150 mg SC Q4W
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	60[6]	61[7]	59[8]	60[9]
Units: subjects	5	5	6	8

Notes:

[6] - Full Analysis Set. Participants with missing data were counted as non-responders.

[7] - Full Analysis Set. Participants with missing data were counted as non-responders.

[8] - Full Analysis Set. Participants with missing data were counted as non-responders.

[9] - Full Analysis Set. Participants with missing data were counted as non-responders.

End point values	Etokimab 600 mg / 300 mg SC Q4W			
Subject group type	Reporting group			
Number of subjects analysed	60[10]			
Units: subjects	6			

Notes:

[10] - Full Analysis Set. Participants with missing data were counted as non-responders.

Statistical analyses

Statistical analysis title	Placebo Vs Etokimab 20 mg SC Q4W

Statistical analysis description:

Inferential statistics based on a Logistic regression model with treatment as fixed effect and baseline test score as covariate.

Comparison groups	Placebo v Etokimab 20 mg SC Q4W
Number of subjects included in analysis	121
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7659
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.22
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.329
upper limit	4.5268

Statistical analysis title	Placebo Vs Etokimab 300 mg / 150 mg SC Q8W

Statistical analysis description:

Inferential statistics based on a Logistic regression model with treatment as fixed effect and baseline

test score as covariate.

Comparison groups	Placebo v Etokimab 300 mg / 150 mg SC Q8W
Number of subjects included in analysis	119
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6273
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.36
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.3895
upper limit	4.776

Statistical analysis title	Placebo Vs Etokimab 300 mg / 150 mg SC Q4W

Statistical analysis description:

Inferential statistics based on a Logistic regression model with treatment as fixed effect and baseline test score as covariate.

Comparison groups	Placebo v Etokimab 300 mg / 150 mg SC Q4W
Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2967
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.88
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.5734
upper limit	6.1879

Statistical analysis title	Placebo Vs Etokimab 600 mg / 300 mg SC Q4W

Statistical analysis description:

Inferential statistics based on a Logistic regression model with treatment as fixed effect and baseline test score as covariate.

Comparison groups	Placebo v Etokimab 600 mg / 300 mg SC Q4W
Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5544
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.46

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.4152
upper limit	5.1476

Secondary: Number of Participants Who Achieved a Reduction of ≥ 4 Points From Baseline in Weekly Averaged Peak Numerical Rating Scale (NRS) for Pruritus Score at Week 16

End point title	Number of Participants Who Achieved a Reduction of ≥ 4 Points From Baseline in Weekly Averaged Peak Numerical Rating Scale (NRS) for Pruritus Score at Week 16

End point description:

Participants were asked to rate itch (pruritis) intensity at its worst (peak) during the past 24 hours on an 11-point scale from 0 (no itch) to 10 (worst imaginable itch) in a daily electronic diary. Weekly average was calculated as the average of the 7 days before each visit. Full Analysis Set. Participants with missing data were counted as non-responders.

End point type	Secondary

End point timeframe:

Baseline and Week 16

End point values	Placebo	Etokimab 20 mg SC Q4W	Etokimab 300 mg / 150 mg SC Q8W	Etokimab 300 mg / 150 mg SC Q4W
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	60	61	59	60
Units: subjects	5	6	8	9

End point values	Etokimab 600 mg / 300 mg SC Q4W			
Subject group type	Reporting group			
Number of subjects analysed	60			
Units: subjects	9			

Statistical analyses

Statistical analysis title	Placebo Vs Etokimab 20 mg SC Q4W

Statistical analysis description:

Inferential statistics based on a Logistic regression model with treatment as fixed effect and baseline test score as covariate.

Comparison groups	Placebo v Etokimab 20 mg SC Q4W

Number of subjects included in analysis	121
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.86
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.12
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.3175
upper limit	3.9513

Statistical analysis title	Placebo Vs Etokimab 300 mg / 150 mg SC Q8W

Statistical analysis description:

Inferential statistics based on a Logistic regression model with treatment as fixed effect and baseline test score as covariate.

Comparison groups	Placebo v Etokimab 300 mg / 150 mg SC Q8W
Number of subjects included in analysis	119
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3222
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.84
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.5511
upper limit	6.1214

Statistical analysis title	Placebo Vs Etokimab 300 mg / 150 mg SC Q4W

Statistical analysis description:

Inferential statistics based on a Logistic regression model with treatment as fixed effect and baseline test score as covariate.

Comparison groups	Placebo v Etokimab 300 mg / 150 mg SC Q4W
Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2564
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.98

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.6089
upper limit	6.431

Statistical analysis title	Placebo Vs Etokimab 600 mg / 300 mg SC Q4W

Statistical analysis description:

Inferential statistics based on a Logistic regression model with treatment as fixed effect and baseline test score as covariate.

Comparison groups	Placebo v Etokimab 600 mg / 300 mg SC Q4W
Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2912
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.89
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.5806
upper limit	6.1275

Secondary: Percent Change From Baseline in Peak Weekly Averaged Numerical Rating Scale (NRS) for Pruritus Score at Week 16

End point title	Percent Change From Baseline in Peak Weekly Averaged Numerical Rating Scale (NRS) for Pruritus Score at Week 16

End point description:

Participants were asked to rate itch (pruritis) intensity at its worst (peak) during the past 24 hours on an 11-point scale from 0 (no itch) to 10 (worst imaginable itch) in a daily electronic diary. Weekly average was calculated as the average of the 7 days before each visit. Full Analysis Set with available data were analyzed. Missing data were imputed using multiple imputation.

End point type	Secondary

End point timeframe:

Baseline and Week 16

End point values	Placebo	Etokimab 20 mg SC Q4W	Etokimab 300 mg / 150 mg SC Q8W	Etokimab 300 mg / 150 mg SC Q4W
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	56	58	52	54
Units: percent change				
least squares mean (standard error)	-21.13 (± 5.964)	-22.30 (± 6.211)	-17.69 (± 6.530)	-30.39 (± 6.176)

End point values	Etokimab 600 mg / 300 mg SC Q4W			
Subject group type	Reporting group			
Number of subjects analysed	54			
Units: percent change				
least squares mean (standard error)	-27.18 (± 6.192)			

Statistical analyses

Statistical analysis title	Placebo Vs Etokimab 20 mg SC Q4W
Statistical analysis description:	
The p-value was obtained using mixed effect ANCOVA model with treatment as fixed effect and baseline Peak Weekly Averaged NRS as covariate.	
Comparison groups	Placebo v Etokimab 20 mg SC Q4W
Number of subjects included in analysis	114
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8927
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	-1.17
Confidence interval	
level	95 %
sides	2-sided
lower limit	-18.2117
upper limit	15.8686
Variability estimate	Standard error of the mean
Dispersion value	8.679

Statistical analysis title	Placebo Vs Etokimab 300 mg / 150 mg SC Q8W
Statistical analysis description:	
The p-value was obtained using mixed effect ANCOVA model with treatment as fixed effect and baseline Peak Weekly Averaged NRS as covariate.	
Comparison groups	Placebo v Etokimab 300 mg / 150 mg SC Q8W
Number of subjects included in analysis	108
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7035
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	3.43

Confidence interval	
level	95 %
sides	2-sided
lower limit	-14.2767
upper limit	21.1463
Variability estimate	Standard error of the mean
Dispersion value	9.019

Statistical analysis title	Placebo Vs Etokimab 300 mg / 150 mg SC Q4W

Statistical analysis description:

The p-value was obtained using mixed effect ANCOVA model with treatment as fixed effect and baseline Peak Weekly Averaged NRS as covariate.

Comparison groups	Placebo v Etokimab 300 mg / 150 mg SC Q4W
Number of subjects included in analysis	110
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2819
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	-9.27
Confidence interval	
level	95 %
sides	2-sided
lower limit	-26.159
upper limit	7.6237
Variability estimate	Standard error of the mean
Dispersion value	8.608

Statistical analysis title	Placebo Vs Etokimab 600 mg / 300 mg SC Q4W

Statistical analysis description:

The p-value was obtained using mixed effect ANCOVA model with treatment as fixed effect and baseline Peak Weekly Averaged NRS as covariate.

Comparison groups	Placebo v Etokimab 600 mg / 300 mg SC Q4W
Number of subjects included in analysis	110
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4793
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	-6.06
Confidence interval	
level	95 %
sides	2-sided
lower limit	-22.8452
upper limit	10.7333
Variability estimate	Standard error of the mean
Dispersion value	8.557

Secondary: Percent Change From Baseline in Scoring Atopic Dermatitis (SCORAD) Score at Week 16

End point title	Percent Change From Baseline in Scoring Atopic Dermatitis (SCORAD) Score at Week 16

End point description:

SCORAD is a clinical tool used to assess the extent and severity of eczema (SCORing Atopic Dermatitis). The extent is assessed using the rule of 9 to calculate the affected area (A) as extent of disease (0 [no disease]-102 [worst disease]). The intensity part of the SCORAD (B) consists of 6 items: erythema, oedema/papulation, excoriations, lichenification, oozing/crusts and dryness, each graded on a scale from 0 (none) to 3 (severe), for a total score of 0 (none) to 18 (severe intensity). Subjective items (C) include daily pruritus and sleeplessness, each scored on a visual analogue scale (VAS) from 0 to 10 (itch: 0 [no itch] to 10 [worst imaginable itch] and sleeplessness: 0 [no sleeplessness] to 10 [worst imaginable sleeplessness]) (total score 0-20). SCORAD is calculated as A/5 + 7B/2 + C, and ranges from 0 (no AD present) to 103.4 (worst). Full Analysis Set. Missing data were imputed using multiple imputation.

End point type	Secondary

End point timeframe:

Baseline and Week 16

End point values	Placebo	Etokimab 20 mg SC Q4W	Etokimab 300 mg / 150 mg SC Q8W	Etokimab 300 mg / 150 mg SC Q4W
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	60	61	59	60
Units: percent change				
least squares mean (standard error)	-37.99 (± 4.764)	-31.42 (± 4.605)	-39.22 (± 4.294)	-35.48 (± 4.401)

End point values	Etokimab 600 mg / 300 mg SC Q4W			
Subject group type	Reporting group			
Number of subjects analysed	60			
Units: percent change				
least squares mean (standard error)	-31.23 (± 4.927)			

Statistical analyses

Statistical analysis title	Placebo Vs Etokimab 20 mg SC Q4W

Statistical analysis description:

The p-value was obtained using mixed effect ANCOVA model with treatment as fixed effect and baseline SCORAD as covariate.

Comparison groups	Placebo v Etokimab 20 mg SC Q4W

Number of subjects included in analysis	121
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3262
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	6.57
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.5723
upper limit	19.7054
Variability estimate	Standard error of the mean
Dispersion value	6.677

Statistical analysis title	Placebo Vs Etokimab 300 mg / 150 mg SC Q8W

Statistical analysis description:

The p-value was obtained using mixed effect ANCOVA model with treatment as fixed effect and baseline SCORAD as covariate.

Comparison groups	Placebo v Etokimab 300 mg / 150 mg SC Q8W
Number of subjects included in analysis	119
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8465
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	-1.23
Confidence interval	
level	95 %
sides	2-sided
lower limit	-13.7439
upper limit	11.2782
Variability estimate	Standard error of the mean
Dispersion value	6.366

Statistical analysis title	Placebo Vs Etokimab 300 mg / 150 mg SC Q4W

Statistical analysis description:

The p-value was obtained using mixed effect ANCOVA model with treatment as fixed effect and baseline SCORAD as covariate.

Comparison groups	Placebo v Etokimab 300 mg / 150 mg SC Q4W
Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6947
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	2.51

Confidence interval	
level	95 %
sides	2-sided
lower limit	-10.0587
upper limit	15.082
Variability estimate	Standard error of the mean
Dispersion value	6.396

Statistical analysis title	Placebo Vs Etokimab 600 mg / 300 mg SC Q4W

Statistical analysis description:

The p-value was obtained using mixed effect ANCOVA model with treatment as fixed effect and baseline SCORAD as covariate.

Comparison groups	Placebo v Etokimab 600 mg / 300 mg SC Q4W
Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3288
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	6.76
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.8451
upper limit	20.3626
Variability estimate	Standard error of the mean
Dispersion value	6.909

Secondary: Change From Baseline in Dermatology Life Quality Index (DLQI) Score at Week 16

End point title	Change From Baseline in Dermatology Life Quality Index (DLQI) Score at Week 16

End point description:

The DLQI is a 10-item validated questionnaire used to assess the impact of AD disease symptoms and treatment on quality of life (QoL). It consists of 10 questions evaluating impact of skin diseases on different aspects of a participant’s QoL over the prior week, including symptoms and feelings, daily activities, leisure, work or school, personal relationships, and the side effects of treatment. Each item is scored on a 4-point scale (0 = not at all/not relevant; 1 = a little; 2 = a lot; and 3 = very much). Item scores are added to provide a total score, ranging from 0 to 30, with higher scores indicating greater impairment of QoL. A negative change from Baseline indicates improvement. Full Analysis Set with available data were analyzed. Missing data were imputed using multiple imputation.

End point type	Secondary

End point timeframe:

Baseline and Week 16

End point values	Placebo	Etokimab 20 mg SC Q4W	Etokimab 300 mg / 150 mg SC Q8W	Etokimab 300 mg / 150 mg SC Q4W
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	60	61	59	59
Units: units on a scale				
least squares mean (standard error)	-5.61 (± 0.946)	-5.35 (± 0.966)	-6.52 (± 0.945)	-6.05 (± 0.945)

End point values	Etokimab 600 mg / 300 mg SC Q4W			
Subject group type	Reporting group			
Number of subjects analysed	60			
Units: units on a scale				
least squares mean (standard error)	-5.18 (± 1.036)			

Statistical analyses

Statistical analysis title	Placebo Vs Etokimab 20 mg SC Q4W

Statistical analysis description:

The p-value was obtained using mixed effect ANCOVA model with treatment as fixed effect and baseline DLQI score as covariate.

Comparison groups	Placebo v Etokimab 20 mg SC Q4W
Number of subjects included in analysis	121
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8497
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	0.26
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.4081
upper limit	2.9218
Variability estimate	Standard error of the mean
Dispersion value	1.355

Statistical analysis title	Placebo Vs Etokimab 300 mg / 150 mg SC Q8W

Statistical analysis description:

The p-value was obtained using mixed effect ANCOVA model with treatment as fixed effect and baseline DLQI score as covariate.

Comparison groups	Placebo v Etokimab 300 mg / 150 mg SC Q8W

Number of subjects included in analysis	119
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5016
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	-0.91
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.5636
upper limit	1.7473
Variability estimate	Standard error of the mean
Dispersion value	1.35

Statistical analysis title	Placebo Vs Etokimab 300 mg / 150 mg SC Q4W

Statistical analysis description:

The p-value was obtained using mixed effect ANCOVA model with treatment as fixed effect and baseline DLQI score as covariate.

Comparison groups	Placebo v Etokimab 300 mg / 150 mg SC Q4W
Number of subjects included in analysis	119
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7511
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	-0.44
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.167
upper limit	2.287
Variability estimate	Standard error of the mean
Dispersion value	1.386

Statistical analysis title	Placebo Vs Etokimab 600 mg / 300 mg SC Q4W

Statistical analysis description:

The p-value was obtained using mixed effect ANCOVA model with treatment as fixed effect and baseline DLQI score as covariate.

Comparison groups	Placebo v Etokimab 600 mg / 300 mg SC Q4W
Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7558
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	0.43

Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.3133
upper limit	3.1824
Variability estimate	Standard error of the mean
Dispersion value	1.396

Secondary: Number of Participants Who Experienced an Adverse Event (AE)

End point title	Number of Participants Who Experienced an Adverse Event (AE)

End point description:

An AE is any untoward medical occurrence in a clinical trial participant, temporally associated with the use of study treatment, whether or not considered related to the study treatment. A treatment-emergent adverse event (TEAE) is any AE that started or worsened in severity on or after the date and time of the study drug administration. A serious adverse event (SAE) is as any untoward medical occurrence that, at any dose:
- Results in death;
- Is life-threatening;
- Requires inpatient hospitalization or prolongation of existing hospitalization;
- Results in persistent disability/incapacity;
- Is a congenital anomaly/birth defect.

The safety analysis set included all randomized subjects who received 1 dose of etokimab or placebo.

End point type	Secondary

End point timeframe:

From first dose to Week 24

End point values	Placebo	Etokimab 20 mg SC Q4W	Etokimab 300 mg / 150 mg SC Q8W	Etokimab 300 mg / 150 mg SC Q4W
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	60	61	59	60
Units: subjects				
Any TEAEs	38	40	41	42
Serious TEAE	1	2	3	3

End point values	Etokimab 600 mg / 300 mg SC Q4W			
Subject group type	Reporting group			
Number of subjects analysed	60			
Units: subjects				
Any TEAEs	43			
Serious TEAE	3			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
From first dose to Week 24	
Adverse event reporting additional description:	
Safety Analysis Set	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	22.0

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Participants received matching placebo to etokimab, administered SC Q4W for up to 16 weeks.	
Reporting group title	Etokimab 20 mg SC Q4W
Reporting group description:	
Participants received etokimab 20 mg administered SC Q4W for up to 16 weeks.	
Reporting group title	Etokimab 600 mg / 300 mg SC Q4W
Reporting group description:	
Participants received a 600 mg loading dose of etokimab on Day 1 then 300 mg etokimab administered SC Q4W for up to 16 weeks.	
Reporting group title	Etokimab 300 mg / 150 mg SC Q4W
Reporting group description:	
Participants received a 300 mg loading dose of etokimab on Day 1 then 150 mg etokimab administered SC Q4W for up to 16 weeks.	
Reporting group title	Etokimab 300 mg / 150 mg SC Q8W
Reporting group description:	
Participants received a 300 mg loading dose of etokimab on Day 1 then 150 mg etokimab administered SC Q8W for up to 16 weeks. At Weeks 4 and 12 participants received placebo.	

Serious adverse events	Placebo	Etokimab 20 mg SC Q4W	Etokimab 600 mg / 300 mg SC Q4W
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 60 (1.67%)	2 / 61 (3.28%)	3 / 60 (5.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Investigations			
Troponin I Increased			
subjects affected / exposed	0 / 60 (0.00%)	1 / 61 (1.64%)	0 / 60 (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
Surgical and medical procedures			
Hysterectomy			

subjects affected / exposed	1 / 60 (1.67%)	0 / 61 (0.00%)	0 / 60 (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
Skin and subcutaneous tissue disorders			
Dermatitis Atopic			
subjects affected / exposed	0 / 60 (0.00%)	0 / 61 (0.00%)	3 / 60 (5.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dermatitis Exfoliative Generalised			
subjects affected / exposed	0 / 60 (0.00%)	0 / 61 (0.00%)	0 / 60 (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
Musculoskeletal and connective tissue disorders			
Joint Instability			
subjects affected / exposed	0 / 60 (0.00%)	0 / 61 (0.00%)	0 / 60 (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			
Cellulitis			
subjects affected / exposed	0 / 60 (0.00%)	1 / 61 (1.64%)	0 / 60 (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
Eczema Herpeticum			
subjects affected / exposed	0 / 60 (0.00%)	0 / 61 (0.00%)	0 / 60 (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

Serious adverse events	Etokimab 300 mg / 150 mg SC Q4W	Etokimab 300 mg / 150 mg SC Q8W	
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 60 (5.00%)	3 / 59 (5.08%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Investigations			
Troponin I Increased			

subjects affected / exposed	0 / 60 (0.00%)	0 / 59 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			
Hysterectomy			
subjects affected / exposed	0 / 60 (0.00%)	0 / 59 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Dermatitis Atopic			
subjects affected / exposed	1 / 60 (1.67%)	2 / 59 (3.39%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dermatitis Exfoliative Generalised			
subjects affected / exposed	1 / 60 (1.67%)	0 / 59 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Joint Instability			
subjects affected / exposed	0 / 60 (0.00%)	1 / 59 (1.69%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Cellulitis			
subjects affected / exposed	0 / 60 (0.00%)	0 / 59 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eczema Herpeticum			
subjects affected / exposed	1 / 60 (1.67%)	0 / 59 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Placebo	Etokimab 20 mg SC Q4W	Etokimab 600 mg / 300 mg SC Q4W
Total subjects affected by non-serious adverse events			
subjects affected / exposed	24 / 60 (40.00%)	22 / 61 (36.07%)	26 / 60 (43.33%)
Investigations			
Blood creatine phosphokinase increased			
subjects affected / exposed	3 / 60 (5.00%)	1 / 61 (1.64%)	1 / 60 (1.67%)
occurrences (all)	3	2	1
Nervous system disorders			
Headache			
subjects affected / exposed	3 / 60 (5.00%)	5 / 61 (8.20%)	1 / 60 (1.67%)
occurrences (all)	9	5	2
Dizziness			
subjects affected / exposed	0 / 60 (0.00%)	0 / 61 (0.00%)	3 / 60 (5.00%)
occurrences (all)	0	0	3
Skin and subcutaneous tissue disorders			
Dermatitis atopic			
subjects affected / exposed	11 / 60 (18.33%)	12 / 61 (19.67%)	9 / 60 (15.00%)
occurrences (all)	20	15	11
Eczema			
subjects affected / exposed	0 / 60 (0.00%)	1 / 61 (1.64%)	5 / 60 (8.33%)
occurrences (all)	0	4	6
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	3 / 60 (5.00%)	0 / 61 (0.00%)	1 / 60 (1.67%)
occurrences (all)	3	0	1
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	4 / 60 (6.67%)	4 / 61 (6.56%)	6 / 60 (10.00%)
occurrences (all)	7	4	7
Upper respiratory tract infection			
subjects affected / exposed	3 / 60 (5.00%)	3 / 61 (4.92%)	3 / 60 (5.00%)
occurrences (all)	5	3	5
Oral herpes			
subjects affected / exposed	0 / 60 (0.00%)	0 / 61 (0.00%)	1 / 60 (1.67%)
occurrences (all)	0	0	1
Impetigo			

subjects affected / exposed	1 / 60 (1.67%)	0 / 61 (0.00%)	0 / 60 (0.00%)
occurrences (all)	1	0	0
Conjunctivitis			
subjects affected / exposed	3 / 60 (5.00%)	1 / 61 (1.64%)	0 / 60 (0.00%)
occurrences (all)	4	1	0

Non-serious adverse events	Etokimab 300 mg / 150 mg SC Q4W	Etokimab 300 mg / 150 mg SC Q8W	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	18 / 60 (30.00%)	23 / 59 (38.98%)	
Investigations			
Blood creatine phosphokinase increased			
subjects affected / exposed	1 / 60 (1.67%)	0 / 59 (0.00%)	
occurrences (all)	1	0	
Nervous system disorders			
Headache			
subjects affected / exposed	3 / 60 (5.00%)	3 / 59 (5.08%)	
occurrences (all)	5	4	
Dizziness			
subjects affected / exposed	0 / 60 (0.00%)	1 / 59 (1.69%)	
occurrences (all)	0	3	
Skin and subcutaneous tissue disorders			
Dermatitis atopic			
subjects affected / exposed	8 / 60 (13.33%)	6 / 59 (10.17%)	
occurrences (all)	11	12	
Eczema			
subjects affected / exposed	3 / 60 (5.00%)	2 / 59 (3.39%)	
occurrences (all)	4	2	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	2 / 60 (3.33%)	1 / 59 (1.69%)	
occurrences (all)	2	1	
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	5 / 60 (8.33%)	5 / 59 (8.47%)	
occurrences (all)	8	6	
Upper respiratory tract infection			

subjects affected / exposed	2 / 60 (3.33%)	1 / 59 (1.69%)	
occurrences (all)	4	2	
Oral herpes			
subjects affected / exposed	2 / 60 (3.33%)	3 / 59 (5.08%)	
occurrences (all)	2	4	
Impetigo			
subjects affected / exposed	0 / 60 (0.00%)	3 / 59 (5.08%)	
occurrences (all)	0	3	
Conjunctivitis			
subjects affected / exposed	0 / 60 (0.00%)	1 / 59 (1.69%)	
occurrences (all)	0	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
23 October 2018	Updates included: - Resolution of key comments and requests from respective Regulatory Agencies/Health Authorities; - Procedures were clarified; - Alignment with the Common Protocol Template; - Minor grammatical, editorial, formatting, and administrative changes not affecting the conduct of the study have been incorporated into this amendment for clarification and administrative purposes only.
02 July 2019	Updates to the statistical approach to data analysis included: - Secondary endpoints were reorganized; - Some previously secondary endpoints were reclassified as exploratory; - Some previously exploratory endpoints were reclassified as secondary; - Timepoints were clarified for some endpoints; - An interim analysis was introduced for analysis of efficacy data at Week 16 and safety data collected as of the date of the data cut-off.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported