Clinical trial results:
A PHASE 2, MULTICENTER, GLOBAL, RANDOMIZED, DOUBLE-BLIND, PLACEBO-ONTROLLED, PARALLEL-GROUP STUDY TO EVALUATE THE SAFETY AND EFFICACY OF CENDAKIMAB (CC-93538) IN ADULT SUBJECTS WITH MODERATE TO SEVERE ATOPIC DERMATITIS

Summary

EudraCT number	2020-005212-22
Trial protocol	CZ
Global end of trial date	09 November 2022

Results information

Result version number	v1 (current)
This version publication date	24 November 2023
First version publication date	24 November 2023

Trial information

Trial identification

Sponsor protocol code	CC-93538-AD-001

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Bristol-Myers Squibb
Sponsor organisation address	Chaussée de la Hulpe 185, Brussels, Belgium, 1170
Public contact	EU Study Start-Up Unit, Bristol-Myers Squibb International Corporation, Clinical.Trials@bms.com
Scientific contact	Bristol-Myers Squibb Study Director, Bristol-Myers Squibb, Clinical.Trials@bms.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	09 March 2023
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	09 November 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the clinical efficacy of 3 dosage regimens of CC-93538 compared with placebo on the change in the core clinical outcome measure, Eczema Area and Severity Index (EASI), in subjects with moderate to severe atopic dermatitis (AD)

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and in compliance with all International Conference on Harmonization Good Clinical Practice Guidelines. All the local regulatory requirements pertinent to safety of trial subjects were followed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	10 May 2021
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: 33
Country: Number of subjects enrolled	United States: 64
Country: Number of subjects enrolled	Czechia: 44
Country: Number of subjects enrolled	Poland: 43
Country: Number of subjects enrolled	Japan: 36
Worldwide total number of subjects	220
EEA total number of subjects	87

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)	208
From 65 to 84 years	12
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

221 participants Randomized, 220 Participants Treated

Period 1

Period 1 title	Randomization
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	Treatment 1

Arm description:

CC-93538 High Dose QW

Arm type	Experimental
Investigational medicinal product name	CC-93538
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

High Dose QW

Arm title	Treatment 2

Arm description:

CC-93538 High Dose Q2W

Arm type	Experimental
Investigational medicinal product name	CC-93538
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

High Dose Q2W

Arm title	Treatment 3

Arm description:

CC-93538 Low Dose Q2W

Arm type	Experimental
Investigational medicinal product name	CC-93538
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Low Dose Q2W

Arm title	Placebo
Arm description: Placebo	
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	

Number of subjects in period 1	Treatment 1	Treatment 2	Treatment 3
Started	55	55	55
Completed	54	55	55
Not completed	1	0	0
Did not receive study treatment	1	-	-

Number of subjects in period 1	Placebo
Started	56
Completed	56
Not completed	0
Did not receive study treatment	-

Period 2	
Period 2 title	Treatment Period
Is this the baseline period?	Yes[1]
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	Treatment 1
Arm description: CC-93538 High Dose QW	
Arm type	Experimental
Investigational medicinal product name	CC-93538
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details: High Dose QW	

Arm title	Treatment 2
Arm description: CC-93538 High Dose Q2W	
Arm type	Experimental
Investigational medicinal product name	CC-93538
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use
Dosage and administration details: High Dose Q2W	
Arm title	Treatment 3
Arm description: CC-93538 Low Dose Q2W	
Arm type	Experimental
Investigational medicinal product name	CC-93538
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use
Dosage and administration details: Low Dose Q2W	
Arm title	Placebo
Arm description: Placebo	
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	

Notes:
[1] - Period 1 is not the baseline period. It is expected that period 1 will be the baseline period.
Justification: Period 2 is the baseline period. mITT population

Number of subjects in period 2	Treatment 1	Treatment 2	Treatment 3
Started	54	55	55
Completed	49	50	52
Not completed	5	5	3
Adverse event, non-fatal	4	2	1
Other Reasons	-	2	-

Withdrawal by participant	-	-	-
Lost to follow-up	-	1	2
Lack of efficacy	1	-	-

Number of subjects in period 2	Placebo
Started	56
Completed	44
Not completed	12
Adverse event, non-fatal	2
Other Reasons	1
Withdrawal by participant	4
Lost to follow-up	2
Lack of efficacy	3

Baseline characteristics

Reporting groups	
Reporting group title	Treatment 1
Reporting group description: CC-93538 High Dose QW	
Reporting group title	Treatment 2
Reporting group description: CC-93538 High Dose Q2W	
Reporting group title	Treatment 3
Reporting group description: CC-93538 Low Dose Q2W	
Reporting group title	Placebo
Reporting group description: Placebo	

Reporting group values	Treatment 1	Treatment 2	Treatment 3
Number of subjects	54	55	55
Age Categorical Units: Participants			
Between 18 and 65 years	52	52	51
>=65 years	2	3	4
Age continuous Units: years			
arithmetic mean	36.3	34.5	40.3
standard deviation	± 13.0	± 13.76	± 14.18
Sex: Female, Male Units: Participants			
Female	19	26	29
Male	35	29	26
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	1	0	0
Asian	19	14	14
Black or African American	4	8	5
White	30	33	36
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	1	2	0
Not Hispanic or Latino	53	53	55
Unknown or Not Reported	0	0	0

Reporting group values	Placebo	Total	
Number of subjects	56	220	
Age Categorical Units: Participants			
Between 18 and 65 years	53	208	
>=65 years	3	12	

Age continuous Units: years			
arithmetic mean	39.5		
standard deviation	± 14.22	-	
Sex: Female, Male Units: Participants			
Female	21	95	
Male	35	125	
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	1	
Asian	13	60	
Black or African American	6	23	
White	37	136	
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	3	6	
Not Hispanic or Latino	53	214	
Unknown or Not Reported	0	0	

End points

End points reporting groups

Reporting group title	Treatment 1
Reporting group description: CC-93538 High Dose QW	
Reporting group title	Treatment 2
Reporting group description: CC-93538 High Dose Q2W	
Reporting group title	Treatment 3
Reporting group description: CC-93538 Low Dose Q2W	
Reporting group title	Placebo
Reporting group description: Placebo	
Reporting group title	Treatment 1
Reporting group description: CC-93538 High Dose QW	
Reporting group title	Treatment 2
Reporting group description: CC-93538 High Dose Q2W	
Reporting group title	Treatment 3
Reporting group description: CC-93538 Low Dose Q2W	
Reporting group title	Placebo
Reporting group description: Placebo	

Primary: Mean percentage change from baseline in EASI at week 16

End point title	Mean percentage change from baseline in EASI at week 16

End point description:

The Eczema Area and Severity Index (EASI) is a composite scoring system assessed by the Investigator based on the proportion of each of the 4 body regions (head and neck, upper limbs, lower limbs, and trunk) affected with Atopic Dermatitis (AD) and the intensity of each of 4 main signs of AD (eg, erythema, induration/papulation, excoriation, and lichenification) and is based on a 4-point scale of 0 (none), 1 (mild), 2 (moderate), and 3 (severe). The sum of the scores is totaled (0 to 72), the lower the score the better.

End point type	Primary

End point timeframe:

From initial EASI measurement to week 16

End point values	Treatment 1	Treatment 2	Treatment 3	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	54	55	55	56
Units: Percentage				
arithmetic mean (standard error)	-84.41 (± 5.07)	-76.03 (± 4.20)	-78.93 (± 4.53)	-62.65 (± 5.53)

Statistical analyses

Statistical analysis title	EASI - Statistical Analysis 1
Comparison groups	Treatment 1 v Placebo
Number of subjects included in analysis	110
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.003
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-21.76
Confidence interval	
level	95 %
sides	2-sided
lower limit	-35.81
upper limit	-7.7

Statistical analysis title	EASI - Statistical Analysis 3
Comparison groups	Treatment 3 v Placebo
Number of subjects included in analysis	111
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.029
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-16.28
Confidence interval	
level	95 %
sides	2-sided
lower limit	-30.88
upper limit	-1.68

Statistical analysis title	EASI - Statistical Analysis 2
Comparison groups	Treatment 2 v Placebo

Number of subjects included in analysis	111
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.057
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-13.38
Confidence interval	
level	95 %
sides	2-sided
lower limit	-27.19
upper limit	0.43

Secondary: Percent change from baseline in pruritus NRS at Week 16

End point title	Percent change from baseline in pruritus NRS at Week 16

End point description:

Pruritus will be assessed by the subject using the Pruritus NRS, which was developed and validated as a single item, patient reported outcome (PRO) of itch severity. Clinical response is indicated by a ≥ 2 to 4-point change from baseline in Peak Pruritus NRS score. The intensity of pruritus will be assessed based on last 24 hours using a validated 11-point NRS, ranging from 0 (“no pruritus”) to 10 (“the worst pruritus imaginable”).

End point type	Secondary

End point timeframe:

From initial NRS measurement to week 16

End point values	Treatment 1	Treatment 2	Treatment 3	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	54	55	55	56
Units: Mean Percentage Change from baseline				
arithmetic mean (standard error)	-55.48 (± 6.22)	-46.15 (± 5.32)	-49.30 (± 5.89)	-32.98 (± 7.46)

Statistical analyses

Statistical analysis title	Pruritis NRS - Statistical Analysis 2
Comparison groups	Treatment 2 v Placebo
Number of subjects included in analysis	111
Analysis specification	Pre-specified
Analysis type	
Method	ANCOVA
Parameter estimate	Adjusted Mean Difference VS Placebo
Point estimate	-13.17

Confidence interval	
level	95 %
sides	2-sided
lower limit	-30.67
upper limit	4.33

Statistical analysis title	Pruritis NRS - Statistical Analysis 3
Comparison groups	Treatment 3 v Placebo
Number of subjects included in analysis	111
Analysis specification	Pre-specified
Analysis type	
Method	ANCOVA
Parameter estimate	Adjusted Mean Difference VS Placebo
Point estimate	-16.32
Confidence interval	
level	95 %
sides	2-sided
lower limit	-36.4
upper limit	3.75

Statistical analysis title	Pruritis NRS - Statistical Analysis 1
Comparison groups	Treatment 1 v Placebo
Number of subjects included in analysis	110
Analysis specification	Pre-specified
Analysis type	
Method	ANCOVA
Parameter estimate	Adjusted Mean Difference VS Placebo
Point estimate	-22.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-41.46
upper limit	-3.54

Secondary: Time to achieve at least 4 points of improvement in the severity of pruritus NRS scale in the first 16 weeks of treatment

End point title	Time to achieve at least 4 points of improvement in the severity of pruritus NRS scale in the first 16 weeks of treatment

End point description:

Pruritus will be assessed by the subject using the Pruritus NRS, which was developed and validated as a single item, patient reported outcome (PRO) of itch severity. Clinical response is indicated by a ≥ 2 to 4-point change from baseline in Peak Pruritus NRS score. The intensity of pruritus will be assessed based on last 24 hours using a validated 11-point NRS, ranging from 0 (“no pruritus”) to 10 (“the worst pruritus imaginable”).

Here "99999" means NA

End point type	Secondary

End point timeframe:

From initial NRS assessment to week 16

End point values	Treatment 1	Treatment 2	Treatment 3	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	54	55	55	56
Units: Days				
median (confidence interval 95%)	54.0 (28.0 to 93.0)	76.0 (42.0 to 105.0)	50.0 (27.0 to 111.0)	123.0 (119.0 to 99999)

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with treatment emergent adverse events

End point title	Number of participants with treatment emergent adverse events

End point description:

Treatment emergent adverse events

End point type	Secondary

End point timeframe:

From first treatment to the end of follow up, approximately 32 weeks

End point values	Treatment 1	Treatment 2	Treatment 3	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	54	55	55	56
Units: Participants				
Any TEAE	40	41	38	41
Any TEAE leading to discontinuation	4	2	1	2
Any TEAE of special interest	9	10	8	10
Any TESAE	2	1	2	4

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with the presence of serum antibodies to CC-93538

End point title	Number of participants with the presence of serum antibodies

	to CC-93538

End point description:

End point type	Secondary

End point timeframe:

From first treatment to the end of follow up, approximately 32 weeks

End point values	Treatment 1	Treatment 2	Treatment 3	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	54	55	55	
Units: Participants				
Baseline ADA Positive	0	3	1	
Post Baseline Positive	22	35	28	
Post Baseline Negative	32	20	27	

Statistical analyses

No statistical analyses for this end point

Secondary: Serum trough concentration at week 16

End point title	Serum trough concentration at week 16

End point description:

End point type	Secondary

End point timeframe:

At week 16

End point values	Treatment 1	Treatment 2	Treatment 3	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	43	45	45	
Units: ng/mL				
geometric mean (geometric coefficient of variation)	274180.6 (± 88.0)	140413.6 (± 44.0)	57046.4 (± 106.8)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change in Mean SCORAD scores from baseline at week 16

End point title	Percent Change in Mean SCORAD scores from baseline at week 16

End point description:

The SCORAD is a validated scoring index for atopic dermatitis, which combines extent (0 to 100), severity (0 to 18), and subjective symptoms (0 to 20) based on pruritus and sleep loss, each scored (0 to 10). The subject will assess the subjective symptoms (itch and sleepless) part of the assessment.

SCORing Atopic Dermatitis Index (SCORAD) score ranges from 0 to 103, higher scores indicate more severe disease.

End point type	Secondary

End point timeframe:

From initial SCORAD measurement to week 16

End point values	Treatment 1	Treatment 2	Treatment 3	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	54	55	55	56
Units: Mean Percentage Change from baseline				
arithmetic mean (standard error)	-69.28 (± 4.64)	-55.47 (± 4.08)	-60.19 (± 4.38)	-41.11 (± 5.61)

Statistical analyses

Statistical analysis title	SCORAD - Statistical Analysis 1
Comparison groups	Treatment 1 v Placebo
Number of subjects included in analysis	110
Analysis specification	Pre-specified
Analysis type	
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-28.16
Confidence interval	
level	95 %
sides	2-sided
lower limit	-41.89
upper limit	-14.44

Statistical analysis title	SCORAD - Statistical Analysis 3
Comparison groups	Treatment 3 v Placebo
Number of subjects included in analysis	111
Analysis specification	Pre-specified
Analysis type	
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-19.07

Confidence interval	
level	95 %
sides	2-sided
lower limit	-33.53
upper limit	-4.62

Statistical analysis title	SCORAD - Statistical Analysis 2
Comparison groups	Treatment 2 v Placebo
Number of subjects included in analysis	111
Analysis specification	Pre-specified
Analysis type	
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-14.36
Confidence interval	
level	95 %
sides	2-sided
lower limit	-27.26
upper limit	-1.46

Secondary: Number of participants with clinically significant laboratory abnormalities

End point title	Number of participants with clinically significant laboratory abnormalities

End point description:

End point type	Secondary

End point timeframe:

From first treatment to the end of follow up, approximately 32 weeks

End point values	Treatment 1	Treatment 2	Treatment 3	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	54	55	55	56
Units: Number of Subjects	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of responders with an vIGA-AD score of 0 (clear) or 1 (almost clear) and a reduction ≥ 2 points from Baseline at Week 16

End point title	Percentage of responders with an vIGA-AD score of 0 (clear) or 1 (almost clear) and a reduction ≥ 2 points from Baseline at Week 16

End point description:

The Validated Investigator Global Assessment (vIGA-AD) is a validated 5-point assessment intended to assess the global severities of key acute clinical signs of AD, including erythema, induration/papulation, oozing/crusting (lichenification excluded). The rating of clear (0), almost clear (1), mild (2), moderate (3) and severe (4), will be assessed at scheduled visits. The vIGA-AD must be conducted before the EASI assessment. The vIGA-AD is a static evaluation conducted without regard to the score obtained at a previous visit.

End point type	Secondary

End point timeframe:

From initial vIGA-AD assessment to week 16

End point values	Treatment 1	Treatment 2	Treatment 3	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	54	55	55	56
Units: Percentage of Participants				
number (not applicable)	33.3	24.4	38.2	9.4

Statistical analyses

Statistical analysis title	vIGA-AD - Statistical Analysis 1
Comparison groups	Treatment 1 v Placebo
Number of subjects included in analysis	110
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.004
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk Difference VS Placebo
Point estimate	24
Confidence interval	
level	95 %
sides	2-sided
lower limit	8.8
upper limit	39.2

Statistical analysis title	vIGA-AD - Statistical Analysis 3
Comparison groups	Treatment 3 v Placebo

Number of subjects included in analysis	111
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk Difference VS Placebo
Point estimate	28.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	13.6
upper limit	44.2

Statistical analysis title	vIGA-AD - Statistical Analysis 2
Comparison groups	Treatment 2 v Placebo
Number of subjects included in analysis	111
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.061
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk Difference VS Placebo
Point estimate	15.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.8
upper limit	29.8

Secondary: Percentage of EASI-75 responders at week 16

End point title	Percentage of EASI-75 responders at week 16

End point description:

The EASI is a composite scoring system assessed by the Investigator based on the proportion of each of the 4 body regions (head and neck, upper limbs, lower limbs, and trunk) affected with AD and the intensity of each of 4 main signs of AD (eg, erythema, induration/papulation, excoriation, and lichenification) and is based on a 4-point scale of 0 (none), 1 (mild), 2 (moderate), and 3 (severe). The sum of the scores is totaled (0 to 72), the lower the score the better.

End point type	Secondary

End point timeframe:

From initial EASI measurement to week 16

End point values	Treatment 1	Treatment 2	Treatment 3	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	54	55	55	56
Units: Percentage of Participants				
number (not applicable)	50.0	48.2	52.7	26.3

Statistical analyses

Statistical analysis title	EASI75 - Statistical Analysis 1
Comparison groups	Treatment 1 v Placebo
Number of subjects included in analysis	110
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.018
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference VS Placebo
Point estimate	23.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	6.2
upper limit	41.2

Statistical analysis title	EASI75 - Statistical Analysis 2
Comparison groups	Treatment 2 v Placebo
Number of subjects included in analysis	111
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.033
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference VS Placebo
Point estimate	21.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	4.3
upper limit	39.3

Statistical analysis title	EASI75 - Statistical Analysis 3
Comparison groups	Treatment 3 v Placebo

Number of subjects included in analysis	111
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.006
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference VS Placebo
Point estimate	26.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	9.3
upper limit	44

Secondary: Percentage of EASI-90 responders at week 16

End point title	Percentage of EASI-90 responders at week 16

End point description:

The Eczema Area and Severity Index (EASI) is a composite scoring system assessed by the Investigator based on the proportion of each of the 4 body regions (head and neck, upper limbs, lower limbs, and trunk) affected with Atopic Dermatitis (AD) and the intensity of each of 4 main signs of AD (eg, erythema, induration/papulation, excoriation, and lichenification) and is based on a 4-point scale of 0 (none), 1 (mild), 2 (moderate), and 3 (severe). The sum of the scores is totaled (0 to 72), the lower the score the better.

End point type	Secondary

End point timeframe:

From initial EASI measurement to week 16

End point values	Treatment 1	Treatment 2	Treatment 3	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	54	55	55	56
Units: Percentage of participants				
number (not applicable)	31.5	24.0	29.1	13.4

Statistical analyses

Statistical analysis title	EASI90 - Statistical Analysis 1
Comparison groups	Treatment 1 v Placebo
Number of subjects included in analysis	110
Analysis specification	Pre-specified
Analysis type	
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk Difference
Point estimate	18.1

Confidence interval	
level	95 %
sides	2-sided
lower limit	2.3
upper limit	33.9

Statistical analysis title	EASI90 - Statistical Analysis 3
Comparison groups	Treatment 3 v Placebo
Number of subjects included in analysis	111
Analysis specification	Pre-specified
Analysis type	
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk Difference
Point estimate	15.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.4
upper limit	31.4

Statistical analysis title	EASI90 - Statistical Analysis 2
Comparison groups	Treatment 2 v Placebo
Number of subjects included in analysis	111
Analysis specification	Pre-specified
Analysis type	
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk Difference
Point estimate	10.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.6
upper limit	25.7

Secondary: Adjust mean percentage change in BSA in atopic dermatitis from Baseline at Week 16

End point title	Adjust mean percentage change in BSA in atopic dermatitis from Baseline at Week 16

End point description:

Body Surface Area involvement will be calculated from the sum of the number of handprints of skin afflicted with atopic dermatitis in a body region. The number of handprints of skin afflicted with atopic dermatitis in a body region can be used to determine the extent (%) to which a body region is involved with AD. When measuring, the handprint unit refers to the size of each individual subject’s hand with fingers in a closed position. BSA will be calculated by the Investigator or qualified designee using the 1% handprint rule, in which the area represented by the palm with all 5 digits adducted together is approximately 1% of the subject's BSA.

End point type	Secondary
End point timeframe:	
From initial BSA assessment to week 16	

End point values	Treatment 1	Treatment 2	Treatment 3	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	54	55	55	56
Units: mean percentage				
arithmetic mean (standard error)	-78.85 (± 6.13)	-64.01 (± 5.30)	-66.60 (± 6.03)	-55.73 (± 6.90)

Statistical analyses

Statistical analysis title	BSA - Statistical Analysis 1
Comparison groups	Treatment 1 v Placebo
Number of subjects included in analysis	110
Analysis specification	Pre-specified
Analysis type	
Method	ANCOVA
Parameter estimate	Adjusted mean difference VS Placebo
Point estimate	-23.12
Confidence interval	
level	95 %
sides	2-sided
lower limit	-41.48
upper limit	-4.76

Statistical analysis title	BSA - Statistical Analysis 3
Comparison groups	Treatment 3 v Placebo
Number of subjects included in analysis	111
Analysis specification	Pre-specified
Analysis type	
Method	ANCOVA
Parameter estimate	Adjusted mean difference VS Placebo
Point estimate	-10.87
Confidence interval	
level	95 %
sides	2-sided
lower limit	-29.39
upper limit	7.66

Statistical analysis title	BSA - Statistical Analysis 2
Comparison groups	Treatment 2 v Placebo
Number of subjects included in analysis	111
Analysis specification	Pre-specified
Analysis type	
Method	ANCOVA
Parameter estimate	Adjusted mean difference VS Placebo
Point estimate	-8.28
Confidence interval	
level	95 %
sides	2-sided
lower limit	-25.16
upper limit	8.59

Secondary: Percentage of participants with a response and pruritus NRS change of ≥ 4 points from Baseline at Week 16

End point title	Percentage of participants with a response and pruritus NRS change of ≥ 4 points from Baseline at Week 16

End point description:

Pruritus will be assessed by the subject using the Pruritus NRS, which was developed and validated as a single item, patient reported outcome (PRO) of itch severity. Clinical response is indicated by a ≥ 2 to 4-point change from baseline in Peak Pruritus NRS score. The intensity of pruritus will be assessed based on last 24 hours using a validated 11-point NRS, ranging from 0 (“no pruritus”) to 10 (“the worst pruritus imaginable”).

End point type	Secondary

End point timeframe:

From initial NRS assessment to week 16

End point values	Treatment 1	Treatment 2	Treatment 3	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	54	55	55	56
Units: Percentage of Participants				
number (not applicable)	33.3	34.5	32.7	14.8

Statistical analyses

Statistical analysis title	Pruritis - Statistical Analysis 1
Comparison groups	Treatment 1 v Placebo
Number of subjects included in analysis	110
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.042
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk Difference VS Placebo
Point estimate	18.5

Confidence interval	
level	95 %
sides	2-sided
lower limit	2.7
upper limit	34.3

Statistical analysis title	Pruritis - Statistical Analysis 3
Comparison groups	Treatment 3 v Placebo
Number of subjects included in analysis	111
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.052
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk Difference VS Placebo
Point estimate	18
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.3
upper limit	33.6

Statistical analysis title	Pruritis - Statistical Analysis 2
Comparison groups	Treatment 2 v Placebo
Number of subjects included in analysis	111
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.029
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk Difference VS Placebo
Point estimate	19.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	4.1
upper limit	35.7

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse Events and Serious Adverse Events (From first treatment to end of study): Approximately 32 Weeks

All-Cause mortality (From randomization to end of study): Approximately 33 Weeks

Adverse event reporting additional description:

The number at Risk for All-Cause Mortality represents all Randomized Participants. The number at Risk for Serious Adverse Events and Other (Not Including Serious) Adverse Events represents all participants that received at least 1 dose of study medication

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	25.1

Reporting groups

Reporting group title	Treatment 1
Reporting group description:	
High Dose QW	
Reporting group title	Placebo
Reporting group description:	
Placebo	
Reporting group title	Treatment 3
Reporting group description:	
Low Dose Q2W	
Reporting group title	Treatment 2
Reporting group description:	
High Dose Q2W	

Serious adverse events	Treatment 1	Placebo	Treatment 3
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 54 (3.70%)	4 / 56 (7.14%)	2 / 55 (3.64%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Road traffic accident			
subjects affected / exposed	0 / 54 (0.00%)	1 / 56 (1.79%)	0 / 55 (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
Vascular disorders			
Deep vein thrombosis			

subjects affected / exposed	1 / 54 (1.85%)	0 / 56 (0.00%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Large intestine polyp			
subjects affected / exposed	0 / 54 (0.00%)	1 / 56 (1.79%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Pulmonary hypertension			
subjects affected / exposed	1 / 54 (1.85%)	0 / 56 (0.00%)	0 / 55 (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			
Angioedema			
subjects affected / exposed	0 / 54 (0.00%)	0 / 56 (0.00%)	1 / 55 (1.82%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Mental status changes			
subjects affected / exposed	0 / 54 (0.00%)	1 / 56 (1.79%)	0 / 55 (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
Infections and infestations			
COVID-19			
subjects affected / exposed	0 / 54 (0.00%)	0 / 56 (0.00%)	0 / 55 (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
Cellulitis			
subjects affected / exposed	1 / 54 (1.85%)	1 / 56 (1.79%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Product issues			
Device dislocation			

subjects affected / exposed	0 / 54 (0.00%)	0 / 56 (0.00%)	1 / 55 (1.82%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Treatment 2		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 55 (1.82%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Road traffic accident			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Large intestine polyp			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Pulmonary hypertension			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Angioedema			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			

Mental status changes			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
COVID-19			
subjects affected / exposed	1 / 55 (1.82%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cellulitis			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Product issues			
Device dislocation			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Treatment 1	Placebo	Treatment 3
Total subjects affected by non-serious adverse events			
subjects affected / exposed	34 / 54 (62.96%)	34 / 56 (60.71%)	29 / 55 (52.73%)
Investigations			
Blood creatine phosphokinase increased			
subjects affected / exposed	3 / 54 (5.56%)	0 / 56 (0.00%)	1 / 55 (1.82%)
occurrences (all)	3	0	1
Alanine aminotransferase increased			
subjects affected / exposed	3 / 54 (5.56%)	0 / 56 (0.00%)	0 / 55 (0.00%)
occurrences (all)	3	0	0
Nervous system disorders			
Headache			
subjects affected / exposed	2 / 54 (3.70%)	2 / 56 (3.57%)	2 / 55 (3.64%)
occurrences (all)	2	2	2
General disorders and administration			

site conditions			
Injection site erythema			
subjects affected / exposed	1 / 54 (1.85%)	0 / 56 (0.00%)	3 / 55 (5.45%)
occurrences (all)	5	0	7
Fatigue			
subjects affected / exposed	3 / 54 (5.56%)	1 / 56 (1.79%)	0 / 55 (0.00%)
occurrences (all)	4	1	0
Pyrexia			
subjects affected / exposed	0 / 54 (0.00%)	5 / 56 (8.93%)	1 / 55 (1.82%)
occurrences (all)	0	5	1
Eye disorders			
Conjunctivitis allergic			
subjects affected / exposed	4 / 54 (7.41%)	2 / 56 (3.57%)	5 / 55 (9.09%)
occurrences (all)	4	2	6
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 54 (0.00%)	1 / 56 (1.79%)	1 / 55 (1.82%)
occurrences (all)	0	1	1
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	0 / 54 (0.00%)	0 / 56 (0.00%)	1 / 55 (1.82%)
occurrences (all)	0	0	1
Dermatitis atopic			
subjects affected / exposed	20 / 54 (37.04%)	20 / 56 (35.71%)	19 / 55 (34.55%)
occurrences (all)	27	41	27
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	2 / 54 (3.70%)	1 / 56 (1.79%)	3 / 55 (5.45%)
occurrences (all)	2	1	4
Infections and infestations			
Folliculitis			
subjects affected / exposed	3 / 54 (5.56%)	2 / 56 (3.57%)	1 / 55 (1.82%)
occurrences (all)	3	2	1
COVID-19			
subjects affected / exposed	4 / 54 (7.41%)	9 / 56 (16.07%)	3 / 55 (5.45%)
occurrences (all)	4	9	3
Upper respiratory tract infection			

subjects affected / exposed	4 / 54 (7.41%)	5 / 56 (8.93%)	5 / 55 (9.09%)
occurrences (all)	5	5	6
Nasopharyngitis			
subjects affected / exposed	2 / 54 (3.70%)	2 / 56 (3.57%)	3 / 55 (5.45%)
occurrences (all)	2	2	4
Respiratory tract infection			
subjects affected / exposed	1 / 54 (1.85%)	3 / 56 (5.36%)	0 / 55 (0.00%)
occurrences (all)	1	3	0

Non-serious adverse events	Treatment 2		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	35 / 55 (63.64%)		
Investigations			
Blood creatine phosphokinase increased			
subjects affected / exposed	3 / 55 (5.45%)		
occurrences (all)	4		
Alanine aminotransferase increased			
subjects affected / exposed	2 / 55 (3.64%)		
occurrences (all)	2		
Nervous system disorders			
Headache			
subjects affected / exposed	4 / 55 (7.27%)		
occurrences (all)	5		
General disorders and administration site conditions			
Injection site erythema			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences (all)	0		
Fatigue			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences (all)	0		
Pyrexia			
subjects affected / exposed	4 / 55 (7.27%)		
occurrences (all)	5		
Eye disorders			
Conjunctivitis allergic			

subjects affected / exposed	7 / 55 (12.73%)		
occurrences (all)	11		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	3 / 55 (5.45%)		
occurrences (all)	3		
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	3 / 55 (5.45%)		
occurrences (all)	6		
Dermatitis atopic			
subjects affected / exposed	15 / 55 (27.27%)		
occurrences (all)	15		
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	2 / 55 (3.64%)		
occurrences (all)	2		
Infections and infestations			
Folliculitis			
subjects affected / exposed	2 / 55 (3.64%)		
occurrences (all)	2		
COVID-19			
subjects affected / exposed	4 / 55 (7.27%)		
occurrences (all)	4		
Upper respiratory tract infection			
subjects affected / exposed	6 / 55 (10.91%)		
occurrences (all)	9		
Nasopharyngitis			
subjects affected / exposed	1 / 55 (1.82%)		
occurrences (all)	1		
Respiratory tract infection			
subjects affected / exposed	3 / 55 (5.45%)		
occurrences (all)	3		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
24 August 2021	This is a country specific amendment for the Czech Republic. As a result of questions raised by State Institute for Drug Control (SUKL), Ministry of Health in Czech Republic during the clinical trial application review process, changes have been incorporated in the protocol CC- 93538-AD-001. As requested by the Czech Republic Health Authority, significant changes included in this amendment are summarized below: Reduction in upper end age limit for inclusion into the study Increase in the required weight threshold for inclusion into the study Update to Criteria for Discontinuation of Dosing Update to Required Weight Assessments During the Treatment Phase Addition of Supplemental Laboratory Information

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported