Clinical trial results:
A Phase 2/3, Two-Part Study to Evaluate the Efficacy and Long-term Safety with Oral Etrasimod, 2 mg, Once Daily in Adult Participants with Moderate-to-Severe Atopic Dermatitis with a History of Prior Systemic Treatment Failure

Summary

EudraCT number	2022-003361-37
Trial protocol	CZ
Global end of trial date	29 April 2024

Results information

Result version number	v1 (current)
This version publication date	08 May 2025
First version publication date	08 May 2025

Trial information

Trial identification

Sponsor protocol code	C5041005

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05732454
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Pfizer Inc.
Sponsor organisation address	66 East Hudson boulevard, New York, United States, NY 10001
Public contact	Pfizer ClinicalTrials.gov Call Center, Pfizer Inc., 001 8007181021, ClinicalTrials.gov_Inquiries@pfizer.com
Scientific contact	Pfizer ClinicalTrials.gov Call Center, Pfizer Inc., 001 8007181021, ClinicalTrials.gov_Inquiries@pfizer.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	24 May 2024
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	29 April 2024
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

Etrasimod is a sphingosine 1-phosphate receptor modulator (S1PRM) and was being developed as an oral treatment for patients with moderate-to-severe AD. Part 1 of this study evaluated efficacy of etrasimod therapy QD and long-term safety in participants with moderate-to-severe AD with a history of a prior systemic therapy failure. Part 2 of this study were planned to evaluate the long-term safety of etrasimod therapy QD in participants with moderate-to-severe AD with a history of a prior systemic therapy failure.

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 Council for Harmonisation (ICH) Good Clinical Practice (GCP) Guidelines. All the local regulatory requirements pertinent to safety of trials participants were followed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	18 January 2023
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: 4
Country: Number of subjects enrolled	Czechia: 4
Country: Number of subjects enrolled	Poland: 30
Country: Number of subjects enrolled	United States: 20
Worldwide total number of subjects	58
EEA total number of subjects	34

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)	52
From 65 to 84 years	6
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study had 2 parts: Part 1 and Part 2. Part 2 was never initiated; hence no results are reported for it. All results are pertaining to Part 1 in the record. Part 1 of the study had 16-week double-blind (DB) treatment period and then 52-week part 1 open label extension (OLE) treatment period.

Pre-assignment

Screening details:

A total of 58 participants with moderate-to-severe atopic dermatitis (AD) were enrolled in Part 1- DB period and out of them 51 continued into the Part 1- OLE period.

Period 1

Period 1 title	Part 1: DB Period
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	DB Etrasimod 2 mg Then OLE Etrasimod 2 mg

Arm description:

Participants were randomized to receive etrasimod 2 milligram (mg) orally once daily for 16 weeks in DB period of Part 1. Eligible participants per investigator’s judgement then continued to receive etrasimod 2 mg orally once daily for maximum of another 52 weeks in OLE period of Part 1.

Arm type	Experimental
Investigational medicinal product name	Etrasimod 2 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Participants received etrasimod 2 mg QD

Arm title	DB Placebo Then OLE Etrasimod 2 mg

Arm description:

Participants were randomized to receive placebo matched to etrasimod 2 mg orally once daily for 16 weeks in DB period of Part 1. Eligible participants per investigator’s judgement then received etrasimod 2 mg orally once daily for maximum of another 52 weeks in OLE period of Part 1.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Participants received placebo QD

Number of subjects in period 1	DB Etrasimod 2 mg Then OLE Etrasimod 2 mg	DB Placebo Then OLE Etrasimod 2 mg
Started	30	28
Completed	27	25
Not completed	3	3
Consent withdrawn by subject	1	2
Adverse event, non-fatal	1	-
Lost to follow-up	1	-
Protocol deviation	-	1

Period 2

Period 2 title	Part 1: OLE Period
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	DB Etrasimod 2 mg Then OLE Etrasimod 2 mg

Arm description:

Participants were randomized to receive etrasimod 2 milligram (mg) orally once daily for 16 weeks in DB period of Part 1. Eligible participants per investigator's judgement then continued to receive etrasimod 2 mg orally once daily for maximum of another 52 weeks in OLE period of Part 1.

Arm type	Experimental
Investigational medicinal product name	Etrasimod 2 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Participants received etrasimod 2 mg QD

Arm title	DB Placebo Then OLE Etrasimod 2 mg

Arm description:

Participants were randomized to receive placebo matched to etrasimod 2 mg orally once daily for 16 weeks in DB period of Part 1. Eligible participants per investigator's judgement then received etrasimod 2 mg orally once daily for maximum of another 52 weeks in OLE period of Part 1.

Arm type	Experimental
Investigational medicinal product name	Etrasimod 2 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Participants received etrasimod 2 mg QD

Number of subjects in period 2[1]	DB Etrasimod 2 mg Then OLE Etrasimod 2 mg	DB Placebo Then OLE Etrasimod 2 mg
Started	27	24
Completed	0	0
Not completed	27	24
Consent withdrawn by subject	2	3
Adverse event, non-fatal	-	1
Study Terminated by Sponsor	25	19
Lack of efficacy	-	1

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.
Justification: The number of subjects starting is correct

Baseline characteristics

Reporting groups

Reporting group title	DB Etrasimod 2 mg Then OLE Etrasimod 2 mg

Reporting group description:

Participants were randomized to receive etrasimod 2 milligram (mg) orally once daily for 16 weeks in DB period of Part 1. Eligible participants per investigator's judgement then continued to receive etrasimod 2 mg orally once daily for maximum of another 52 weeks in OLE period of Part 1.

Reporting group title	DB Placebo Then OLE Etrasimod 2 mg

Reporting group description:

Participants were randomized to receive placebo matched to etrasimod 2 mg orally once daily for 16 weeks in DB period of Part 1. Eligible participants per investigator's judgement then received etrasimod 2 mg orally once daily for maximum of another 52 weeks in OLE period of Part 1.

Reporting group values	DB Etrasimod 2 mg Then OLE Etrasimod 2 mg	DB Placebo Then OLE Etrasimod 2 mg	Total
Number of subjects	30	28	58
Age Categorical Units: Subjects			
Age continuous Units: Years			
arithmetic mean	40.0	43.4	
standard deviation	± 14.78	± 18.18	-
Gender categorical Units: Participants			
Female (F)	21	9	30
Male (M)	9	19	28
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	3	0	3
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	3	1	4
White	24	27	51
More than one race	0	0	0
Unknown or Not Reported	0	0	0
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	5	5	10
Not Hispanic or Latino	25	23	48
Unknown or Not Reported	0	0	0

Subject analysis sets

Subject analysis set title	DB Period: Etrasimod 2 mg
Subject analysis set type	Full analysis

Subject analysis set description:

Participants who received etrasimod 2 mg orally once daily for 16 weeks in DB period of Part 1.

Subject analysis set title	DB Period: Placebo
Subject analysis set type	Full analysis

Subject analysis set description:

Participants who received placebo matched to etrasimod orally once daily for 16 weeks in DB period of Part 1.

Subject analysis set title	OLE Period: Etrasimod 2 mg (Etrasimod 2 mg in DB Period)
Subject analysis set type	Full analysis

Subject analysis set description:

Participants who received etrasimod in DB period continued to receive etrasimod 2 mg orally once daily in OLE period for maximum of another 52 weeks.

Subject analysis set title	OLE Period: Etrasimod 2 mg (Placebo in DB Period)
Subject analysis set type	Full analysis

Subject analysis set description:

Participants who received placebo matched to etrasimod in DB period and then received etrasimod 2 mg orally once daily in OLE period for maximum of another 52 weeks.

Reporting group values	DB Period: Etrasimod 2 mg	DB Period: Placebo	OLE Period: Etrasimod 2 mg (Etrasimod 2 mg in DB Period)
Number of subjects	30	28	30
Age Categorical Units: Subjects			
Age continuous Units: Years arithmetic mean standard deviation	±	±	±
Gender categorical Units: Participants			
Female (F)	0	0	0
Male (M)	0	0	0
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	0	0
White	0	0	0
More than one race	0	0	0
Unknown or Not Reported	0	0	0
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	0	0	0
Not Hispanic or Latino	0	0	0
Unknown or Not Reported	0	0	0

Reporting group values	OLE Period: Etrasimod 2 mg (Placebo in DB Period)		
Number of subjects	28		

Age Categorical Units: Subjects			

Age continuous Units: Years arithmetic mean standard deviation	 ±		
Gender categorical Units: Participants			
Female (F)	0		
Male (M)	0		
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0		
Asian	0		
Native Hawaiian or Other Pacific Islander	0		
Black or African American	0		
White	0		
More than one race	0		
Unknown or Not Reported	0		
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	0		
Not Hispanic or Latino	0		
Unknown or Not Reported	0		

End points reporting groups

Reporting group title	DB Etrasimod 2 mg Then OLE Etrasimod 2 mg
Reporting group description:	
Participants were randomized to receive etrasimod 2 milligram (mg) orally once daily for 16 weeks in DB period of Part 1. Eligible participants per investigator's judgement then continued to receive etrasimod 2 mg orally once daily for maximum of another 52 weeks in OLE period of Part 1.	
Reporting group title	DB Placebo Then OLE Etrasimod 2 mg
Reporting group description:	
Participants were randomized to receive placebo matched to etrasimod 2 mg orally once daily for 16 weeks in DB period of Part 1. Eligible participants per investigator's judgement then received etrasimod 2 mg orally once daily for maximum of another 52 weeks in OLE period of Part 1.	
Reporting group title	DB Etrasimod 2 mg Then OLE Etrasimod 2 mg
Reporting group description:	
Participants were randomized to receive etrasimod 2 milligram (mg) orally once daily for 16 weeks in DB period of Part 1. Eligible participants per investigator's judgement then continued to receive etrasimod 2 mg orally once daily for maximum of another 52 weeks in OLE period of Part 1.	
Reporting group title	DB Placebo Then OLE Etrasimod 2 mg
Reporting group description:	
Participants were randomized to receive placebo matched to etrasimod 2 mg orally once daily for 16 weeks in DB period of Part 1. Eligible participants per investigator's judgement then received etrasimod 2 mg orally once daily for maximum of another 52 weeks in OLE period of Part 1.	
Subject analysis set title	DB Period: Etrasimod 2 mg
Subject analysis set type	Full analysis
Subject analysis set description:	
Participants who received etrasimod 2 mg orally once daily for 16 weeks in DB period of Part 1.	
Subject analysis set title	DB Period: Placebo
Subject analysis set type	Full analysis
Subject analysis set description:	
Participants who received placebo matched to etrasimod orally once daily for 16 weeks in DB period of Part 1.	
Subject analysis set title	OLE Period: Etrasimod 2 mg (Etrasimod 2 mg in DB Period)
Subject analysis set type	Full analysis
Subject analysis set description:	
Participants who received etrasimod in DB period continued to receive etrasimod 2 mg orally once daily in OLE period for maximum of another 52 weeks.	
Subject analysis set title	OLE Period: Etrasimod 2 mg (Placebo in DB Period)
Subject analysis set type	Full analysis
Subject analysis set description:	
Participants who received placebo matched to etrasimod in DB period and then received etrasimod 2 mg orally once daily in OLE period for maximum of another 52 weeks.	

Primary: Part 1, DB Period: Percentage of Participants Achieving Investigator's Global Assessment (IGA) Response at Week 16

End point title	Part 1, DB Period: Percentage of Participants Achieving Investigator's Global Assessment (IGA) Response at Week 16
End point description:	
IGA measured AD severity, based on a 5-point scale (0-4); 0= AD is clear, 1= AD is almost clear, 2= mild AD, 3= moderate AD and 4= severe AD. IGA response was defined as participants achieving IGA 0 (clear) or 1 (almost clear) and a reduction of >=2 points from baseline. FAS included all participants who were randomized to the study irrespective of whether they received any dose of study intervention (i.e., etrasimod or placebo). Participants were analyzed in the treatment groups as they were randomized. Number of participants in FAS with baseline IGA>=2 was included in this analysis.	
End point type	Primary

End point timeframe:

DB Period: Week 16

End point values	DB Period: Etrasimod 2 mg	DB Period: Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	30	28		
Units: Percentage of Participants				
number (not applicable)	3.3	7.1		

Statistical analyses

Statistical analysis title	CMH Normal Approximation to IGA Response Rate

Statistical analysis description:

Normal approximation adjusting for the stratification factor (disease severity as measured by baseline IGA score 3 [moderate], 4 [severe]) derived from clinical database via Cochran-Mantel-Haenszel (CMH) approach was used.

Comparison groups	DB Period: Etrasimod 2 mg v DB Period: Placebo
Number of subjects included in analysis	58
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.558
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in percentage
Point estimate	-3.76
Confidence interval	
level	95 %
sides	2-sided
lower limit	-16.36
upper limit	8.83

Primary: Part 1, DB Period: Number of Participants With Treatment Emergent Serious Adverse Events (SAEs) (All Causality)

End point title	Part 1, DB Period: Number of Participants With Treatment Emergent Serious Adverse Events (SAEs) (All Causality)[1]

End point description:

An AE was any untoward medical occurrence in a participant, temporally associated with the use of study intervention, whether or not considered related to the study intervention. Treatment-emergent are events between first dose of study drug and up to last dose that were absent before treatment or that worsened relative to pretreatment state. SAE was an AE resulting in any of the following outcomes or deemed significant for any other reason: death; life-threatening experience (immediate risk of death); new or prolonged inpatient hospitalization; persistent or significant disability/incapacity; congenital anomaly/birth defect; suspected transmission via a Pfizer product of an infectious agent, pathogenic or non-pathogenic or other medical events judged by investigator. Safety analysis set in DB period included of all participants who were randomized and received at least 1 dose of study drug in DB period.

End point type	Primary

End point timeframe:

DB Period: From first dose of study drug up to 16 Weeks of treatment

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analyses was planned for this end point

End point values	DB Period: Etrasimod 2 mg	DB Period: Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	30	28		
Units: Participants	0	0		

Statistical analyses

No statistical analyses for this end point

Primary: Part 1, DB Period: Number of Participants With TEAEs (All Causality) Leading to Study Treatment Discontinuation

End point title	Part 1, DB Period: Number of Participants With TEAEs (All Causality) Leading to Study Treatment Discontinuation [2]

End point description:

An AE was any untoward medical occurrence in a participant, temporally associated with the use of study intervention, whether or not considered related to the study intervention. Treatment-emergent are events between first dose of study drug and up to last dose that were absent before treatment or that worsened relative to pretreatment state. Safety analysis set in DB period included of all participants who were randomized and received at least 1 dose of study drug in DB period.

End point type	Primary

End point timeframe:

DB Period: From first dose of study drug up to 16 Weeks of treatment

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analyses was planned for this end point

End point values	DB Period: Etrasimod 2 mg	DB Period: Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	30	28		
Units: Participants	1	0		

Statistical analyses

No statistical analyses for this end point

Primary: Part 1, DB Period: Number of Participants With Treatment Emergent Adverse Events (TEAEs) (All Causality)

End point title	Part 1, DB Period: Number of Participants With Treatment Emergent Adverse Events (TEAEs) (All Causality)[3]

End point description:

An adverse event (AE) was any untoward medical occurrence in a participant, temporally associated with the use of study intervention, whether or not considered related to the study intervention. Treatment-emergent are events between first dose of study drug and up to last dose that were absent before treatment or that worsened relative to pretreatment state. Safety analysis set in DB period included of all participants who were randomized and received at least 1 dose of study drug in DB period.

End point type	Primary

End point timeframe:

DB Period: From first dose of study drug up to 16 Weeks of treatment

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analyses was planned for this end point

End point values	DB Period: Etrasimod 2 mg	DB Period: Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	30	28		
Units: Participants	16	8		

Statistical analyses

No statistical analyses for this end point

Primary: Part 1, DB Period: Number of Participants With Treatment Emergent AEs of Special Interest (AESIs) (All Causality)

End point title	Part 1, DB Period: Number of Participants With Treatment Emergent AEs of Special Interest (AESIs) (All Causality)[4]

End point description:

An AE was any untoward medical occurrence in a participant, temporally associated with the use of study intervention, whether or not considered related to the study intervention. Treatment-emergent are events between first dose of study drug and up to last dose that were absent before treatment or that worsened relative to pretreatment state. AESIs included here were cardiovascular events (i.e., bradycardia, Atrioventricular (AV) conduction delay, and hypertension); macular edema, pulmonary events (airflow obstruction or decreased gas exchange); infections (severe infections, opportunistic infections [including progressive multifocal leukoencephalopathy (PML)], Herpes simplex and Herpes zoster); liver injury (liver transaminase elevation and bilirubin elevation); posterior reversible encephalopathy syndrome (PRES) and malignancies. Safety analysis set in DB period included of all participants who were randomized and received at least 1 dose of study drug in DB period.

End point type	Primary

End point timeframe:

DB Period: From first dose of study drug up to 16 Weeks of treatment

Notes:

[4] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analyses was planned for this end point

End point values	DB Period: Etrasimod 2 mg	DB Period: Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	30	28		
Units: Participants	2	1		

Statistical analyses

No statistical analyses for this end point

Primary: Part 1, DB Period: Number of Participants With Laboratory Test Abnormalities

End point title	Part 1, DB Period: Number of Participants With Laboratory Test Abnormalities[5]

End point description:

Laboratory assessments included hematology, clinical chemistry, urinalysis, other parameters and reflex tests. Number of participants with abnormalities in any of laboratory parameters is reported. Safety analysis set in DB period included of all participants who were randomized and received at least 1 dose of study drug in DB period. Here, "Overall Number of Participants Analyzed" signifies number of participants evaluable for this outcome measure.

End point type	Primary

End point timeframe:

DB Period: From first dose of study drug up to 16 Weeks of treatment

Notes:

[5] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analyses was planned for this end point

End point values	DB Period: Etrasimod 2 mg	DB Period: Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	29	27		
Units: Participants	22	13		

Statistical analyses

No statistical analyses for this end point

Primary: Part 1, DB Period: Number of Participants With Markedly Abnormal 12-Lead Electrocardiogram Measurements and Atrioventricular (AV) Blocks

End point title	Part 1, DB Period: Number of Participants With Markedly Abnormal 12-Lead Electrocardiogram Measurements and Atrioventricular (AV) Blocks [6]

End point description:

Standard 12-lead ECGs utilizing limb leads were used to measure PR interval, QT interval [increase (inc) or decrease (dec)], QTc corrected using Fridericia's formula (QTcF), and QRS complex. Number of participants with non-zero ECG abnormalities and AV blocks [AV conduction: First degree AV Block (AV C:1st-degree AV Block)] are reported in this outcome measure. Safety analysis set in DB period included of all participants who were randomized and received at least 1 dose of study drug in DB period. Here, "Number Analyzed" = number of participants evaluable for specified timepoints.

End point type	Primary

End point timeframe:

DB Period: Pre-dose and 4 hours (h) post-dose on Day 1/Week 0; Pre-dose and 4h post-dose on Day (D) 113/Week(W) 16

Notes:

[6] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analyses was planned for this end point

End point values	DB Period: Etrasimod 2 mg	DB Period: Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	30	28		
Units: Participants				
Predose/D1: AVC: 1st-degree AV Block(n=30,28)	1	0		
4h postdose/D1:QTCF,SB:>=450(M)/>=47	1	0		
4h postdose/D1: CFB in QT:>30 msec inc(30,28)	9	0		
4h postdose/D1:AVC:1st-degree AV Block(n=30,28)	3	0		
Predose/W16: CFB in QT: >30 msec inc(n=26, 24)	1	0		
Predose/W16:CFB in QT: >60 msec inc(n=26,24)	1	0		
Predose/W16: CFB in QTcF:>30 msec inc(n=26,24)	2	0		
4h postdose/W16:CFB in QTcF:>30 msec inc(n=25,24)	2	0		
4h postdose/W16:CFB in QT:>30 msec inc(n=25,24)	2	0		
4h postdose/W16:AVC:1st-degree AV Block(n=25,24)	2	0		

Statistical analyses

No statistical analyses for this end point

Primary: Part 1, DB Period: Number of Participants With Markedly Abnormal Vital Signs

End point title	Part 1, DB Period: Number of Participants With Markedly Abnormal Vital Signs[7]

End point description:

Vital signs evaluation included systolic blood pressure (SBP), diastolic blood pressure (DBP), pulse rate. Number of participants with non-zero vital signs abnormalities are reported in this outcome measure. Safety analysis set in DB period included of all participants who were randomized and received at least 1 dose of study drug in DB period. Here, "Number Analyzed"= number of participants evaluable for specified timepoints.

End point type	Primary

End point timeframe:

DB Period: Pre-dose and 1, 2, 3, 4 hours (hrs) post-dose on Day 1/Week 0; Day 29/Week 4; Day 57/Week 8; Day 85/Week 12; Pre-dose and 1, 2, 3, 4, 5 and 6 hrs post-dose on Day 113/Week 16

Notes:

[7] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analyses was planned for this end point

End point values	DB Period: Etrasimod 2 mg	DB Period: Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	30	28		
Units: Participants				
Predose/D1: DBP >90 mmHg (n=30,28)	0	1		
Predose/D1: Pulse rate: <60 bpm(n=30,28)	1	3		
Predose/D1: Pulse rate >100 bpm(n=30,28)	1	0		
1h postdose/D1: SBP:Chg >=30 mmHg dec(n=30,28)	0	1		
1h postdose/D1: DBP>90 mmHg(n=30,28)	2	2		
1h postdose/D1:Pulse rate: <50 bpm (n=30,28)	1	0		
1h postdose/D1: Pulse rate: <60 bpm(n=30,28)	7	3		
2h postdose/D1: SBP: >150 mmHg(n=30,28)	0	2		
2h postdose/D1: DBP >90 mmHg (n=30,28)	0	1		
2h postdose/D1: Pulse rate: <60 bpm(n=30, 28)	12	5		
3h post-dose/D1:SBP >150 mmHg(n=30,28)	0	1		
3h postdose/D1: SBP: Chg>=30 mmHg dec(n=30, 28)	1	0		
3h postdose/D1: DBP:>90 mmHg (n=30, 28)	0	1		
3h postdose/D1: DBP: Chg>=20 mmHg dec(n=30, 28)	2	0		
3h postdose/D1: Pulse rate: <60 bpm (n=30, 28)	11	6		
4h postdose/D1: DBP: >90 mmHg (n=30, 28)	1	1		
4h post-dose/D1: Pulse rate: <60 bpm(n=30, 28)	10	5		
4h postdose/D1: Pulse rate: >100 bpm (n=30, 28)	1	0		
W4: DBP:>90 mmHg (n=29, 27)	2	3		
W4: Pulse rate: <60 bpm (n=28, 27)	2	1		
W4: Pulse rate: >100 bpm (n=28, 27)	1	0		
W8: SBP: >150 mmHg (n=28, 25)	0	1		
W8: DBP:>90 mmHg (n=28, 25)	3	3		
W8: DBP:Chg >=20 mmHg dec (n=28, 25)	0	1		
W8: Pulse rate: <60 bpm (n=28, 25)	3	1		
W12: SBP: >150 mmHg (n=27, 25)	0	1		
W12: DBP:>90 mmHg (n=27, 25)	1	3		
W12:Pulse rate: <60 bpm(n=27,25)	1	0		
W12: Pulse rate: >100 bpm (n=27,25)	0	2		

Predose/W16: SBP: >150 mmHg(n=26, 24)	0	1		
Predose/W16: DBP: >90 mmHg(n=26, 24)	2	0		
Predose/W16: Pulse rate: <60 bpm (n=26, 24)	2	2		
1h postdose/W16: SBP: >150 mmHg (n=26, 24)	0	1		
1h postdose/W16: SBP:Chg>=30 mmHg dec(n=26,24)	0	1		
1h postdose/W16: DBP: >90 mmHg(n=26, 24)	2	1		
1h postdose/W16: Pulse rate: <50 bpm (n=26, 24)	1	1		
1h postdose/W16: Pulse rate: <60 bpm(n=26, 24)	3	4		
2h postdose/W16: SBP: >150 mmHg (n=26, 24)	0	1		
2h postdose/W16: SBP:Chg>=30 mmHg dec(n=26,24)	0	2		
2h postdose/W16: DBP: >90 mmHg(n=26,24)	2	2		
2h postdose/W16: Pulse rate: <50 bpm (n=26, 24)	0	1		
2h postdose/W16: Pulse rate: <60 bpm (n=26, 24)	3	10		
3h postdose/W16:DBP: >90 mmHg (n=26, 24)	2	0		
3h postdose/W16: Pulse rate: <50 bpm (n=26, 24)	0	1		
3h postdose/W16: Pulse rate: <60 bpm (n=26, 24)	3	9		
4hpostdose/W16: SBP: >150 mmHg(n=26, 24)	0	1		
4h postdose/W16: DBP:>90 mmHg (n=26, 24)	2	0		
4h postdose/W16: DBP:Chg>=20 mmHg dec(n=26,24)	0	1		
4h postdose/W16:Pulse rate: <50 bpm(n=26, 24)	0	1		
4h postdose/W16:Pulse rate:<60 bpm (n=26, 24)	1	6		
5h postdose/W16:Pulse rate:<50 bpm (n=0,1)	0	1		
5h postdose/W16:Pulse rate:<60 bpm (n=0,1)	0	1		
6h postdose/W16:Pulse rate:<50 bpm (n=0,1)	0	1		
6h postdose/W16: Pulse rate:<60 bpm (n=0,1)	0	1		

Statistical analyses

No statistical analyses for this end point

Primary: Part 1, OLE Period: Number of Participants With TEAEs (All Causality)

End point title	Part 1, OLE Period: Number of Participants With TEAEs (All Causality)[8]

End point description:

An AE was any untoward medical occurrence in a participant, temporally associated with the use of study intervention, whether or not considered related to the study intervention. Treatment-emergent are events between first dose of study drug and up to last dose that were absent before treatment or that worsened relative to pretreatment state. Safety analysis set included all participants who received at least 1 dose of study drug.

End point type	Primary

End point timeframe:

OLE Period: First dose of study drug in OLE period up to 4 weeks after last dose in OLE period (up to maximum of 56 Weeks)

Notes:

[8] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analyses was planned for this end point

End point values	OLE Period: Etrasimod 2 mg (Etrasimod 2 mg in DB Period)	OLE Period: Etrasimod 2 mg (Placebo in DB Period)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	30	28		
Units: Participants	9	5		

Statistical analyses

No statistical analyses for this end point

Primary: Part 1, OLE Period: Number of Participants With Treatment Emergent AEs (All Causality) Leading to Study Treatment Discontinuation

End point title	Part 1, OLE Period: Number of Participants With Treatment Emergent AEs (All Causality) Leading to Study Treatment Discontinuation[9]

End point description:

An AE was any untoward medical occurrence in a participant, temporally associated with the use of study intervention, whether or not considered related to the study intervention. Treatment-emergent are events between first dose of study drug and up to last dose that were absent before treatment or that worsened relative to pretreatment state. Safety analysis set included all participants who received at least 1 dose of study drug.

End point type	Primary

End point timeframe:

OLE Period: First dose of study drug in OLE period up to 4 weeks after last dose in OLE period (up to maximum of 56 Weeks)

Notes:

[9] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analyses was planned for this end point

End point values	OLE Period: Etrasimod 2 mg (Etrasimod 2 mg in DB Period)	OLE Period: Etrasimod 2 mg (Placebo in DB Period)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	30	28		
Units: Participants	0	1		

Statistical analyses

No statistical analyses for this end point

Primary: Part 1, OLE Period: Number of Participants With Treatment Emergent SAEs (All Causality)

End point title	Part 1, OLE Period: Number of Participants With Treatment Emergent SAEs (All Causality)[10]

End point description:

An AE was any untoward medical occurrence in a participant, temporally associated with the use of study intervention, whether or not considered related to the study intervention. Treatment-emergent are events between first dose of study drug and up to last dose that were absent before treatment or that worsened relative to pretreatment state. SAE was an AE resulting in any of the following outcomes or deemed significant for any other reason: death; life-threatening experience (immediate risk of death); new or prolonged inpatient hospitalization; persistent or significant disability/incapacity; congenital anomaly/birth defect; suspected transmission via a Pfizer product of an infectious agent, pathogenic or non-pathogenic or other medical events judged by investigator. Safety analysis set included all participants who received at least 1 dose of study drug.

End point type	Primary

End point timeframe:

OLE Period: First dose of study drug in OLE period up to 4 weeks after last dose in OLE period (up to maximum of 56 Weeks)

Notes:

[10] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analyses was planned for this end point

End point values	OLE Period: Etrasimod 2 mg (Etrasimod 2 mg in DB Period)	OLE Period: Etrasimod 2 mg (Placebo in DB Period)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	30	28		
Units: Participants	1	0		

Statistical analyses

No statistical analyses for this end point

Primary: Part 1, OLE Period: Number of Participants With Markedly Abnormal 12-Lead Electrocardiogram Measurements and Atrioventricular (AV) Blocks

End point title	Part 1, OLE Period: Number of Participants With Markedly Abnormal 12-Lead Electrocardiogram Measurements and Atrioventricular (AV) Blocks [11]

End point description:

Standard 12-lead ECGs utilizing limb leads were used to measure PR interval, QT interval, QTc corrected using Fridericia's formula (QTcF), and QRS complex. Number of participants with non-zero ECG

abnormalities and AV blocks are reported in this outcome measure. OLE period: Safety analysis set included all participants who received at least 1 dose of study drug in the OLE Period. Here, "Number Analyzed"= number of participants evaluable for specified timepoints.

End point type	Primary

End point timeframe:

OLE Period: Day 169/Week 24

Notes:

[11] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analyses was planned for this end point

End point values	OLE Period: Etrasimod 2 mg (Etrasimod 2 mg in DB Period)	OLE Period: Etrasimod 2 mg (Placebo in DB Period)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	30	28		
Units: Participants				
W24:QTCF,SB:>=450(M)/>=470(F) (n=14,11)	1	0		
Week 24:CFB in QTcF: >30 msec inc (n=14,11)	1	0		
Week 24:CFB in QT: >30 msec inc (n=14,11)	2	0		
Week 24:CFB in QT: >60 msec inc (n=14,11)	1	0		

Statistical analyses

No statistical analyses for this end point

Primary: Part 1, OLE Period: Number of Participants With Laboratory Test Abnormalities

End point title	Part 1, OLE Period: Number of Participants With Laboratory Test Abnormalities[12]

End point description:

Laboratory assessments included hematology, clinical chemistry, urinalysis, other parameters and reflex tests. Number of participants with abnormalities in any of laboratory parameters is reported. Safety analysis set included all participants who received at least 1 dose of study drug.

End point type	Primary

End point timeframe:

OLE Period: First dose of study drug in OLE period up to 4 weeks after last dose in OLE period (up to maximum of 56 Weeks)

Notes:

[12] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analyses was planned for this end point

End point values	OLE Period: Etrasimod 2 mg (Etrasimod 2 mg in DB Period)	OLE Period: Etrasimod 2 mg (Placebo in DB Period)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	28	25		
Units: Participants	20	18		

Statistical analyses

No statistical analyses for this end point

Primary: Part 1, OLE Period: Number of Participants With Treatment Emergent AESIs (All Causality)

End point title	Part 1, OLE Period: Number of Participants With Treatment Emergent AESIs (All Causality)[13]

End point description:

An AE was any untoward medical occurrence in a participant, temporally associated with the use of study intervention, whether or not considered related to the study intervention. Treatment-emergent are events between first dose of study drug and up to last dose that were absent before treatment or that worsened relative to pretreatment state. AESIs included here were cardiovascular events (i.e., bradycardia, AV conduction delay, and hypertension); macular edema, pulmonary events (airflow obstruction or decreased gas exchange); infections (severe infections, opportunistic infections [including PML], Herpes simplex and Herpes zoster); liver injury (liver transaminase elevation and/or bilirubin elevation); PRES and malignancies. Safety analysis set included all participants who received at least 1 dose of study drug.

End point type	Primary

End point timeframe:

OLE Period: First dose of study drug in OLE period up to 4 weeks after last dose in OLE period (up to maximum of 56 Weeks)

Notes:

[13] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analyses was planned for this end point

End point values	OLE Period: Etrasimod 2 mg (Etrasimod 2 mg in DB Period)	OLE Period: Etrasimod 2 mg (Placebo in DB Period)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	30	28		
Units: Participants	1	0		

Statistical analyses

No statistical analyses for this end point

Primary: Part 1, OLE Period: Number of Participants With Markedly Abnormal Vital Signs

End point title	Part 1, OLE Period: Number of Participants With Markedly Abnormal Vital Signs[14]

End point description:

Vital signs evaluation included systolic blood pressure (SBP), diastolic blood pressure (DBP), pulse rate. Number of participants with non-zero vital signs abnormalities are reported in this outcome measure. OLE period: Safety analysis set included all participants who received at least 1 dose of study drug in the OLE Period. Here, "Overall Number of Participants Analyzed" signifies number of participants evaluable for the specified endpoint.

End point type	Primary

End point timeframe:

OLE Period: Day 141/Week 20; Day 169/Week 24; Day 281/Week 40; Follow up 1 (FU1); Follow up 2 (FU2)

Notes:

[14] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analyses was planned for this end point

End point values	OLE Period: Etrasimod 2 mg (Etrasimod 2 mg in DB Period)	OLE Period: Etrasimod 2 mg (Placebo in DB Period)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	26	23		
Units: Participants				
W20:SBP:>150 mmHg(n=26,23)	1	1		
W20:SBP: Change:>=30 mmHg dec (n=26,23)	0	1		
W20:DBP:>90 mmHg(n=26,23)	2	1		
W20:Pulse rate: <60 bpm(n=26,23)	1	0		
W24:SBP:>150 mmHg(n=25,21)	0	1		
W24:SBP: CFB:>=30 mmHg dec(n=25,21)	0	1		
W24:DBP:>90 mmHg(n=25,21)	1	1		
W24:DBP: CFB>=20 mmHg dec(n=25, 21)	0	1		
W24: Pulse rate: <60 bpm (n=25, 21)	1	1		
W32: DBP: >90 mmHg (n=11, 9)	1	0		
W40: DBP: >90 mmHg (n=4, 3)	1	0		
FU1: DBP: >90 mmHg (n=21, 18)	2	0		
FU1: Pulse rate: <60 bpm (n=21, 18)	1	2		
FU2: DBP: >90 mmHg (n=21, 19)	2	0		
FU2: Pulse rate: <60 bpm (n=21, 19)	1	2		

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1, DB Period: Percentage of Participants Who Achieved >=75% Reduction From Baseline in Eczema Area and Severity Index (EASI) Score (EASI-75) at Week 16

End point title	Part 1, DB Period: Percentage of Participants Who Achieved >=75% Reduction From Baseline in Eczema Area and Severity Index (EASI) Score (EASI-75) at Week 16

End point description:

EASI-75 response was defined as a 75% reduction or greater in EASI score from Baseline to Week 16.

EASI quantified severity of AD based on severity of lesion clinical signs and percentage (%) of body surface area (BSA) affected. Severity of clinical signs of AD lesions (erythema [E], induration/papulation [I], excoriation [Ex] and lichenification [L]) were scored separately for each of 4 body regions (head and neck, upper limbs, trunk [including axillae and groin)] and lower limbs [including buttocks]) on a 4-point scale: 0= absent; 1= mild; 2= moderate; 3= severe. EASI area score was based on % BSA with AD in body region: 0 (0%), 1 (>0 to <10%), 2 (10 to <30%), 3 (30 to <50%), 4 (50 to <70%), 5 (70 to <90%) and 6 (90 to 100%). Total EASI score =0.1*Ah*(Eh+Ih+Exh+Lh) + 0.2*Au*(Eu+Iu+ExU+Lu) + 0.3*At*(Et+It+Ext+Lt) + 0.4*Al*(El+Il+Exl+Ll); A = EASI area score; h = head and neck; u = upper limbs; t = trunk; l = lower limbs. FAS population were analyzed for this endpoint.

End point type	Secondary

End point timeframe:

DB Period: Week 16

End point values	DB Period: Etrasimod 2 mg	DB Period: Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	30	28		
Units: Percentage of Participants				
number (not applicable)	23.3	14.3		

Statistical analyses

Statistical analysis title	CMH Normal Approximation to EASI-75 Response Rate

Statistical analysis description:

Normal approximation adjusting for the stratification factor (disease severity as measured by baseline IGA score 3 [moderate], 4 [severe]) derived from clinical database via Cochran-Mantel-Haenszel (CMH) approach was used.

Comparison groups	DB Period: Etrasimod 2 mg v DB Period: Placebo
Number of subjects included in analysis	58
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3685
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in percentage
Point estimate	9.07
Confidence interval	
level	95 %
sides	2-sided
lower limit	-10.7
upper limit	28.85

Secondary: Part 1, DB Period: Percent Change From Baseline in EASI Score at Week 16

End point title	Part 1, DB Period: Percent Change From Baseline in EASI Score at Week 16

End point description:

EASI quantified severity of AD based on severity of lesion clinical signs and percentage (%) of body

surface area (BSA) affected. Severity of clinical signs of AD lesions (erythema [E], induration/papulation [I], excoriation [Ex] and lichenification [L]) were scored separately for each of 4 body regions (head and neck, upper limbs, trunk [including axillae and groin)] and lower limbs [including buttocks]) on a 4-point scale: 0= absent; 1= mild; 2= moderate; 3= severe. EASI area score was based on % BSA with AD in body region: 0 (0%), 1 (>0 to <10%), 2 (10 to <30%), 3 (30 to <50%), 4 (50 to <70%), 5 (70 to <90%) and 6 (90 to 100%). Total EASI score =0.1*Ah*(Eh+Ih+Exh+Lh) + 0.2*Au*(Eu+Iu+ExU+Lu) + 0.3*At*(Et+It+Ext+Lt) + 0.4*Al*(El+Il+ExI+Ll); A = EASI area score; h = head and neck; u = upper limbs; t = trunk; l = lower limbs.FAS population were analyzed for this endpoint.

End point type	Secondary

End point timeframe:

DB Period: Baseline, Week 16

End point values	DB Period: Etrasimod 2 mg	DB Period: Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	30	28		
Units: Percent change				
least squares mean (standard error)	-53.87 (± 9.007)	-24.65 (± 9.533)		

Statistical analyses

Statistical analysis title	Percent Change from Baseline in EASI Score

Statistical analysis description:

Jump-to-Control (JTC) method was used for evaluation. A complete imputed dataset was analyzed using analysis of covariance model including effects of treatment group, actual stratification factor, and baseline value. Multiple results of the treatment comparison were combined using Rubin’s rules, reporting the combined treatment difference, its standard error, 95% CI and 2-sided p-value, across the visits.

Comparison groups	DB Period: Etrasimod 2 mg v DB Period: Placebo
Number of subjects included in analysis	58
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0303
Method	Rubin's rule
Parameter estimate	Difference in Mean
Point estimate	-29.22
Confidence interval	
level	95 %
sides	2-sided
lower limit	-55.53
upper limit	-2.9

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Part 1, DB Period: Day 1 to Week 16; Part 1, OLE Period: Week 20 to Week 68; Part 1, DB +OLE Period: Day 1 to Week 68

Adverse event reporting additional description:

The same all-causality treatment-emergent event may appear as both SAE & non-SAE.However, what is presented are distinct events.An event may be categorized as serious in one participant and as non-serious in another participant, or one participant may have experienced both serious & non-serious event during study. Safety analysis set was evaluated.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	27.0

Reporting groups

Reporting group title	DB Period: Etrasimod 2 mg

Reporting group description:

Participants who received etrasimod 2 mg orally once daily for 16 weeks in DB period of Part 1.

Reporting group title	DB Period: Placebo

Reporting group description:

Participants who received placebo matched to etrasimod orally once daily for 16 weeks in DB period of Part 1.

Reporting group title	OLE Period: Etrasimod 2 mg (Etrasimod 2 mg in DB Period)

Reporting group description:

Participants who received placebo matched to etrasimod in DB period and then received etrasimod 2 mg orally once daily in OLE period for maximum of another 52 weeks.

Reporting group title	OLE Period: Etrasimod 2 mg (Placebo in DB Period)

Reporting group description:

Participants who received placebo matched to etrasimod in DB period and then received etrasimod 2 mg orally once daily in OLE period for maximum of another 52 weeks.

Reporting group title	DB Etrasimod 2 mg Then OLE Etrasimod 2 mg

Reporting group description:

Participants were randomized to receive etrasimod 2 milligram (mg) orally once daily for 16 weeks in DB period of Part 1. Eligible participants per investigator’s judgement then continued to receive etrasimod 2 mg orally once daily for maximum of another 52 weeks in OLE period of Part 1.

Reporting group title	DB Placebo Then OLE Etrasimod 2 mg

Reporting group description:

Participants were randomized to receive placebo matched to etrasimod 2 mg orally once daily for 16 weeks in DB period of Part 1. Eligible participants per investigator’s judgement then received etrasimod 2 mg orally once daily for maximum of another 52 weeks in OLE period of Part 1.

Serious adverse events	DB Period: Etrasimod 2 mg	DB Period: Placebo	OLE Period: Etrasimod 2 mg (Etrasimod 2 mg in DB Period)
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 30 (0.00%)	0 / 28 (0.00%)	1 / 30 (3.33%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

Respiratory, thoracic and mediastinal disorders			
Pneumothorax spontaneous			
subjects affected / exposed	0 / 30 (0.00%)	0 / 28 (0.00%)	1 / 30 (3.33%)
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	OLE Period: Etrasimod 2 mg (Placebo in DB Period)	DB Etrasimod 2 mg Then OLE Etrasimod 2 mg	DB Placebo Then OLE Etrasimod 2 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 28 (0.00%)	1 / 30 (3.33%)	0 / 28 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Respiratory, thoracic and mediastinal disorders			
Pneumothorax spontaneous			
subjects affected / exposed	0 / 28 (0.00%)	1 / 30 (3.33%)	0 / 28 (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

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

Non-serious adverse events	DB Period: Etrasimod 2 mg	DB Period: Placebo	OLE Period: Etrasimod 2 mg (Etrasimod 2 mg in DB Period)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 30 (20.00%)	4 / 28 (14.29%)	4 / 30 (13.33%)
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 30 (3.33%)	2 / 28 (7.14%)	2 / 30 (6.67%)
occurrences (all)	1	2	4
Skin and subcutaneous tissue disorders			
Dermatitis atopic			
subjects affected / exposed	2 / 30 (6.67%)	1 / 28 (3.57%)	0 / 30 (0.00%)
occurrences (all)	2	2	0
Infections and infestations			
COVID-19			
subjects affected / exposed	2 / 30 (6.67%)	0 / 28 (0.00%)	0 / 30 (0.00%)
occurrences (all)	2	0	0

Nasopharyngitis			
subjects affected / exposed	2 / 30 (6.67%)	1 / 28 (3.57%)	0 / 30 (0.00%)
occurrences (all)	2	1	0
Respiratory tract infection			
subjects affected / exposed	0 / 30 (0.00%)	0 / 28 (0.00%)	2 / 30 (6.67%)
occurrences (all)	0	0	2

Non-serious adverse events	OLE Period: Etrasimod 2 mg (Placebo in DB Period)	DB Etrasimod 2 mg Then OLE Etrasimod 2 mg	DB Placebo Then OLE Etrasimod 2 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 28 (3.57%)	9 / 30 (30.00%)	5 / 28 (17.86%)
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 28 (0.00%)	3 / 30 (10.00%)	2 / 28 (7.14%)
occurrences (all)	0	5	2
Skin and subcutaneous tissue disorders			
Dermatitis atopic			
subjects affected / exposed	1 / 28 (3.57%)	2 / 30 (6.67%)	2 / 28 (7.14%)
occurrences (all)	1	2	3
Infections and infestations			
COVID-19			
subjects affected / exposed	0 / 28 (0.00%)	2 / 30 (6.67%)	0 / 28 (0.00%)
occurrences (all)	0	2	0
Nasopharyngitis			
subjects affected / exposed	0 / 28 (0.00%)	2 / 30 (6.67%)	1 / 28 (3.57%)
occurrences (all)	0	2	1
Respiratory tract infection			
subjects affected / exposed	0 / 28 (0.00%)	2 / 30 (6.67%)	0 / 28 (0.00%)
occurrences (all)	0	2	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
17 May 2023	Protocol Amendment 1: Updated Section 1.3. Schedule of Activities, Updated Section 7.1 Discontinuation of Study Intervention and Participant Discontinuation/Withdrawal, Updated Section 7.1.1 Discontinuation after Part 1 DB (Week 16) due to a Clinically Significant Safety Concern, Updated Section 7.1.3 ECG Changes, Updated Section 8.4.8 Adverse Events of Special Interest, Section 10.10.2 Serious Infections Monitoring, Updated Section 10.10.3.2 Study Treatment Discontinuation Related to Post Dose Cardiac Monitoring, Updated Section 10.10.4 Pulmonary Function Monitoring, Updated Section 10.10.5 Ophthalmic Symptom Monitoring; Section 5.3.1 Contraception, Updated Section 10.4 Appendix 4: Contraceptive and Barrier Guidance-Contraception guidance regarding abstinence and pregnancy risk; Updated Section 10.10.1 Monitoring of Lymphocyte, Neutrophil, and White Blood Cell Counts- The safety follow-up approach for participants with lymphocyte declines; Updated Section 8.3.3. Electrocardiograms- Expanded section to emphasize ECG values of potential concern at Screening and Day 1, and further detailed investigator responsibility and process of ECG evaluation; Updated Section 1.1 Synopsis, Section 4.1 Overall Design, Section 7.1.1. Discontinuation after Part 1 DB (Week 16) due to a Clinically Significant Safety Concern; Updated Section 1.1 Synopsis and Section 3 – Objectives, Endpoints, and Estimands- Removed the detailed bullet of change from baseline in laboratory values for the listed parameters

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported