Clinical trial results:
A Phase 2 Randomized, Double-Blind, Placebo-Controlled Study to Assess the Safety and Efficacy of Etrasimod in Adult Subjects With Eosinophilic Esophagitis

Summary

EudraCT number	2020-003226-23
Trial protocol	BE NL DE
Global end of trial date	30 June 2023

Results information

Result version number	v1 (current)
This version publication date	18 May 2024
First version publication date	18 May 2024

Trial information

Trial identification

Sponsor protocol code	C5041009

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04682639
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Pfizer Inc.
Sponsor organisation address	235E 42nd Street, New York, United States, NY 10017
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	05 December 2023
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	30 June 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the effects of Etrasimod on esophageal eosinophilia in adult subjects with active eosinophilic esophagitis (EoE).
To evaluate the dose-response relationship of 2 doses of Etrasimod versus placebo in adult subjects with active EoE.
To select an Etrasimod dose based on efficacy and safety for continued development.

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 Harmonization (ICH) Good Clinical Practice (GCP) Guidelines. All the local regulatory requirements pertinent to safety of trials subjects were followed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	15 December 2020
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United States: 80
Country: Number of subjects enrolled	Belgium: 6
Country: Number of subjects enrolled	Spain: 4
Country: Number of subjects enrolled	Switzerland: 4
Country: Number of subjects enrolled	Australia: 14
Worldwide total number of subjects	108
EEA total number of subjects	10

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)	108
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study consisted of a Double-Blind treatment period (24 weeks) and an Open Label Extension (OLE) period (28 weeks). Subjects who were in the placebo group during the Double-Blind treatment period were re-randomized to Etrasimod 1 milligram (mg) or Etrasimod 2 mg at entry into the Open Label Extension period.

Pre-assignment

Screening details:

A total of 262 subjects were screened in the study. Out of 262, 154 subjects were screen failures and 108 subjects were randomised and treated.

Period 1

Period 1 title	Double-Blind Treatment Period (24 weeks)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Investigator, Monitor, Subject

Arms

Are arms mutually exclusive?	Yes
Arm title	Experimental: Etrasimod 2 mg

Arm description:

Subjects received Etrasimod 2 mg tablet orally, once daily for 24 weeks in Double-blind treatment and for 28 weeks in OLE period. Subjects were then followed up for safety for up to 4 weeks.

Arm type	Experimental
Investigational medicinal product name	Etrasimod
Investigational medicinal product code	
Other name	APD334
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received Etrasimod 2 mg tablet orally, once daily for 24 weeks in Double-blind treatment and for 28 weeks in OLE period.

Arm title	Experimental: Etrasimod 1 mg

Arm description:

Subjects received Etrasimod 1 mg tablet orally, once daily for 24 weeks in Double-blind treatment and for 28 weeks in OLE period. Subjects were then followed up for safety for up to 4 weeks.

Arm type	Experimental
Investigational medicinal product name	Etrasimod
Investigational medicinal product code	
Other name	APD334
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received Etrasimod 1 mg tablet orally, once daily for 24 weeks in Double-blind treatment and for 28 weeks in OLE period.

Arm title	Placebo Then Etrasimod Any Dose

Arm description:

Subjects received Etrasimod matching placebo orally, once daily for 24 weeks in Double-blind treatment and re-randomized to receive Etrasimod tablet 1 or 2 mg orally, once daily for 28 weeks in OLE period. Subjects were then followed up for safety for up to 4 weeks.

Arm type	Placebo
Investigational medicinal product name	Etrasimod
Investigational medicinal product code	
Other name	APD334
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received Etrasimod orally, once daily for 24 weeks in Double-blind treatment and re-randomized to receive Etrasimod tablet 1 or 2 mg orally, once daily for 28 weeks in OLE period.

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

Dosage and administration details:

Subjects received Etrasimod matching placebo orally, once daily for 24 weeks in Double-blind treatment and re-randomized to receive Etrasimod tablet 1 or 2 mg orally, once daily for 28 weeks in OLE period.

Number of subjects in period 1	Experimental: Etrasimod 2 mg	Experimental: Etrasimod 1 mg	Placebo Then Etrasimod Any Dose
Started	41	39	28
Completed	30	31	24
Not completed	11	8	4
Consent withdrawn by subject	5	5	2
Adverse event, non-fatal	1	-	1
Pregnancy	-	1	-
Non-compliance	2	-	-
Lost to follow-up	2	1	-
Lack of efficacy	1	1	1

Period 2

Period 2 title	OLE Period (28 weeks)
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes

Arm title	Experimental: Etrasimod 2 mg

Arm description:

Subjects received Etrasimod 2 mg tablet orally, once daily for 24 weeks in Double-blind treatment and for 28 weeks in OLE period. Subjects were then followed up for safety for up to 4 weeks.

Arm type	Experimental
Investigational medicinal product name	Etrasimod
Investigational medicinal product code	
Other name	APD334
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received Etrasimod 2 mg tablet orally, once daily for 24 weeks in Double-blind treatment and for 28 weeks in OLE period.

Arm title	Experimental: Etrasimod 1 mg

Arm description:

Subjects received Etrasimod 1 mg tablet orally, once daily for 24 weeks in Double-blind treatment and for 28 weeks in OLE period. Subjects were then followed up for safety for up to 4 weeks.

Arm type	Experimental
Investigational medicinal product name	Etrasimod
Investigational medicinal product code	
Other name	APD334
Pharmaceutical forms	Tablet
Routes of administration	Oromucosal use, Oral use

Dosage and administration details:

Subjects received Etrasimod 1 mg tablet orally, once daily for 24 weeks in Double-blind treatment and for 28 weeks in OLE period.

Arm title	OLE: Placebo then Etrasimod 2 mg

Arm description:

Subjects received Etrasimod matching placebo orally, once daily for 24 weeks in Double-blind treatment and re-randomized to receive Etrasimod tablet 2 mg orally, once daily for 28 weeks in OLE period. Subjects were then followed up for safety for up to 4 weeks.

Arm type	Experimental
Investigational medicinal product name	Etrasimod
Investigational medicinal product code	
Other name	APD334
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received Etrasimod matching placebo orally, once daily for 24 weeks in Double-blind treatment and re-randomized to receive Etrasimod tablet 2 mg orally, once daily for 28 weeks in OLE period.

Arm title	OLE: Placebo then Etrasimod 1 mg

Arm description:

Subjects received Etrasimod matching placebo orally, once daily for 24 weeks in Double-blind treatment and re-randomized to receive Etrasimod tablet 1 mg orally, once daily for 28 weeks in OLE period. Subjects were then followed up for safety for up to 4 weeks.

Arm type	Experimental
Investigational medicinal product name	Etrasimod
Investigational medicinal product code	
Other name	APD334
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received Etrasimod matching placebo orally, once daily for 24 weeks in Double-blind treatment

and re-randomized to receive Etrasimod tablet 1 mg orally, once daily for 28 weeks in OLE period.

Number of subjects in period 2	Experimental: Etrasimod 2 mg	Experimental: Etrasimod 1 mg	OLE: Placebo then Etrasimod 2 mg
Started	30	31	12
Completed	22	28	11
Not completed	8	3	1
Consent withdrawn by subject	1	1	-
Adverse event, non-fatal	3	-	1
Non-compliance	1	-	-
Unspecified	-	-	-
Lost to follow-up	1	-	-
Lack of efficacy	2	2	-

Number of subjects in period 2	OLE: Placebo then Etrasimod 1 mg
Started	12
Completed	10
Not completed	2
Consent withdrawn by subject	-
Adverse event, non-fatal	-
Non-compliance	1
Unspecified	1
Lost to follow-up	-
Lack of efficacy	-

Baseline characteristics

Reporting groups	
Reporting group title	Experimental: Etrasimod 2 mg
Reporting group description:	
Subjects received Etrasimod 2 mg tablet orally, once daily for 24 weeks in Double-blind treatment and for 28 weeks in OLE period. Subjects were then followed up for safety for up to 4 weeks.	
Reporting group title	Experimental: Etrasimod 1 mg
Reporting group description:	
Subjects received Etrasimod 1 mg tablet orally, once daily for 24 weeks in Double-blind treatment and for 28 weeks in OLE period. Subjects were then followed up for safety for up to 4 weeks.	
Reporting group title	Placebo Then Etrasimod Any Dose
Reporting group description:	
Subjects received Etrasimod matching placebo orally, once daily for 24 weeks in Double-blind treatment and re-randomized to receive Etrasimod tablet 1 or 2 mg orally, once daily for 28 weeks in OLE period. Subjects were then followed up for safety for up to 4 weeks.	

Reporting group values	Experimental: Etrasimod 2 mg	Experimental: Etrasimod 1 mg	Placebo Then Etrasimod Any Dose
Number of subjects	41	39	28
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	41	39	28
From 65-84 years	0	0	0
85 years and over	0	0	0
Age Continuous Units: Years			
arithmetic mean	35.6	39.9	39.1
standard deviation	± 9.80	± 12.87	± 11.65
Sex: Female, Male Units: Subjects			
Female	20	17	14
Male	21	22	14
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	1	0	0
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	1	1	0
White	39	38	28
More than one race	0	0	0
Unknown or Not Reported	0	0	0
Ethnicity (NIH/OMB)			

Units: Subjects			
Hispanic or Latino	4	5	0
Not Hispanic or Latino	36	34	28
Unknown or Not Reported	1	0	0

Reporting group values	Total		
Number of subjects	108		
Age categorical Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	0		
Newborns (0-27 days)	0		
Infants and toddlers (28 days-23 months)	0		
Children (2-11 years)	0		
Adolescents (12-17 years)	0		
Adults (18-64 years)	108		
From 65-84 years	0		
85 years and over	0		
Age Continuous Units: Years			
arithmetic mean			
standard deviation	-		
Sex: Female, Male Units: Subjects			
Female	51		
Male	57		
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0		
Asian	1		
Native Hawaiian or Other Pacific Islander	0		
Black or African American	2		
White	105		
More than one race	0		
Unknown or Not Reported	0		
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	9		
Not Hispanic or Latino	98		
Unknown or Not Reported	1		

End points

End points reporting groups

Reporting group title	Experimental: Etrasimod 2 mg
Reporting group description:	
Subjects received Etrasimod 2 mg tablet orally, once daily for 24 weeks in Double-blind treatment and for 28 weeks in OLE period. Subjects were then followed up for safety for up to 4 weeks.	
Reporting group title	Experimental: Etrasimod 1 mg
Reporting group description:	
Subjects received Etrasimod 1 mg tablet orally, once daily for 24 weeks in Double-blind treatment and for 28 weeks in OLE period. Subjects were then followed up for safety for up to 4 weeks.	
Reporting group title	Placebo Then Etrasimod Any Dose
Reporting group description:	
Subjects received Etrasimod matching placebo orally, once daily for 24 weeks in Double-blind treatment and re-randomized to receive Etrasimod tablet 1 or 2 mg orally, once daily for 28 weeks in OLE period. Subjects were then followed up for safety for up to 4 weeks.	
Reporting group title	Experimental: Etrasimod 2 mg
Reporting group description:	
Subjects received Etrasimod 2 mg tablet orally, once daily for 24 weeks in Double-blind treatment and for 28 weeks in OLE period. Subjects were then followed up for safety for up to 4 weeks.	
Reporting group title	Experimental: Etrasimod 1 mg
Reporting group description:	
Subjects received Etrasimod 1 mg tablet orally, once daily for 24 weeks in Double-blind treatment and for 28 weeks in OLE period. Subjects were then followed up for safety for up to 4 weeks.	
Reporting group title	OLE: Placebo then Etrasimod 2 mg
Reporting group description:	
Subjects received Etrasimod matching placebo orally, once daily for 24 weeks in Double-blind treatment and re-randomized to receive Etrasimod tablet 2 mg orally, once daily for 28 weeks in OLE period. Subjects were then followed up for safety for up to 4 weeks.	
Reporting group title	OLE: Placebo then Etrasimod 1 mg
Reporting group description:	
Subjects received Etrasimod matching placebo orally, once daily for 24 weeks in Double-blind treatment and re-randomized to receive Etrasimod tablet 1 mg orally, once daily for 28 weeks in OLE period. Subjects were then followed up for safety for up to 4 weeks.	

Primary: Percent Change From Baseline in Esophageal Peak Eosinophil Count (PEC) at Week 16

End point title	Percent Change From Baseline in Esophageal Peak Eosinophil Count (PEC) at Week 16
End point description:	
Eosinophils was counted in the areas of greatest eosinophil density. Counts were reported as the number of eosinophils/high power field (eos/hpf) and multiple hpfs analysed until the PEC was clearly identified after taking into account all biopsies from all esophageal levels. The Full Analysis Set (FAS) included all randomised subjects in the double-blind treatment period who received at least 1 dose of study treatment. Here, "Number of Subjects Analysed" signifies number of subjects evaluable for this endpoint.	
End point type	Primary
End point timeframe:	
Baseline, Week 16	

End point values	Experimental: Etrasimod 2 mg	Experimental: Etrasimod 1 mg	Placebo Then Etrasimod Any Dose	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	33	35	20	
Units: Percent change				
median (inter-quartile range (Q1-Q3))	-58.4 (-86.21 to -26.25)	-39.4 (-71.08 to 78.95)	-21.5 (-57.20 to 55.42)	

Statistical analyses

Statistical analysis title	Etrasimod 2 mg versus placebo
Comparison groups	Experimental: Etrasimod 2 mg v Placebo Then Etrasimod Any Dose
Number of subjects included in analysis	53
Analysis specification	Pre-specified
Analysis type	other[1]
P-value	= 0.0103
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	-18.54
Confidence interval	
level	95 %
sides	2-sided
lower limit	-32.6
upper limit	-4.49

Notes:

[1] - Estimates were from ANCOVA model for rank score of percent change from baseline in esophageal PEC.

Statistical analysis title	Etrasimod 1 mg versus placebo
Comparison groups	Experimental: Etrasimod 1 mg v Placebo Then Etrasimod Any Dose
Number of subjects included in analysis	55
Analysis specification	Pre-specified
Analysis type	other[2]
P-value	= 0.2861
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	-7.53
Confidence interval	
level	95 %
sides	2-sided
lower limit	-21.48
upper limit	6.42

Notes:

[2] - Estimates were from ANCOVA model for rank score of percent change from baseline in esophageal PEC.

Secondary: Absolute Change From Baseline in Dysphagia Symptom Questionnaire (DSQ) Score at Week 16

End point title	Absolute Change From Baseline in Dysphagia Symptom

	Questionnaire (DSQ) Score at Week 16

End point description:

The DSQ was used to measure the frequency and intensity of dysphagia to solid food. DSQ consisted of 4 questions, all subjects used a diary, and responded to Questions 1 (did you eat solid food) and 2 (did food pass slowly or get stuck). If the subject's answer to Question 2 was 'No', the diary ended for that day. If a subject answered 'Yes', he/she advanced to Questions 3 (did you have to do anything to make the food go down or get relief) and 4 (extent to which the subject experienced pain while swallowing). DSQ score = (Sum of points from questions 2+3 in the daily DSQ)×14 days/(Number of diaries reported with non-missing data). DSQ scores can range from 0 to 84, with a higher score indicating worse dysphagia. The FAS included all randomised subjects in the double-blind treatment period who received at least 1 dose of study treatment. Here, "Number of Subjects Analysed" signifies number of subjects evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Baseline, Week 16

End point values	Experimental: Etrasimod 2 mg	Experimental: Etrasimod 1 mg	Placebo Then Etrasimod Any Dose	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	32	36	24	
Units: Units on a scale				
least squares mean (standard error)	-17.11 (± 2.247)	-14.78 (± 2.166)	-19.49 (± 2.602)	

Statistical analyses

Statistical analysis title	Etrasimod 1 mg versus placebo
Comparison groups	Experimental: Etrasimod 1 mg v Placebo Then Etrasimod Any Dose
Number of subjects included in analysis	60
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.1671
Method	Linear mixed effects model
Parameter estimate	LS mean difference
Point estimate	4.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2
upper limit	11.41

Statistical analysis title	Etrasimod 2 mg versus placebo
Comparison groups	Experimental: Etrasimod 2 mg v Placebo Then Etrasimod Any Dose

Number of subjects included in analysis	56
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.4894
Method	Linear mixed effects model
Parameter estimate	LS mean difference
Point estimate	2.38
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.43
upper limit	9.19

Secondary: Absolute Change From Baseline in Esophageal Peak Eosinophil Count (PEC) at Week 16

End point title	Absolute Change From Baseline in Esophageal Peak Eosinophil Count (PEC) at Week 16

End point description:

Eosinophils was counted in the areas of greatest eosinophil density. Counts were reported as the number of eos/hpf and multiple hpfs analysed until the PEC was clearly identified after taking into account all biopsies from all esophageal levels.The FAS included all randomised subjects in the double-blind treatment period who received at least 1 dose of study treatment. Here, "Number of Subjects Analysed" signifies number of subjects evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Baseline, Week 16

End point values	Experimental: Etrasimod 2 mg	Experimental: Etrasimod 1 mg	Placebo Then Etrasimod Any Dose	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	33	35	20	
Units: eos/hpf				
least squares mean (standard error)	-46.3 (± 17.46)	-5.7 (± 16.99)	8.3 (± 22.37)	

Statistical analyses

Statistical analysis title	Etrasimod 1 mg versus placebo
Comparison groups	Experimental: Etrasimod 1 mg v Placebo Then Etrasimod Any Dose

Number of subjects included in analysis	55
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.6193
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	-13.95
Confidence interval	
level	95 %
sides	2-sided
lower limit	-69.61
upper limit	41.71

Statistical analysis title	Etrasimod 2 mg versus placebo
Comparison groups	Experimental: Etrasimod 2 mg v Placebo Then Etrasimod Any Dose
Number of subjects included in analysis	53
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0565
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	-54.53
Confidence interval	
level	95 %
sides	2-sided
lower limit	-110.59
upper limit	1.54

Secondary: Percentage of Subjects with Esophageal PEC Less Than or Equal to (<=) 6 eos/hpf at Week 16

End point title	Percentage of Subjects with Esophageal PEC Less Than or Equal to (<=) 6 eos/hpf at Week 16

End point description:

The FAS included all randomised subjects in the double-blind treatment period who received at least 1 dose of study treatment.

End point type	Secondary

End point timeframe:

Week 16

End point values	Experimental: Etrasimod 2 mg	Experimental: Etrasimod 1 mg	Placebo Then Etrasimod Any Dose	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	41	39	28	
Units: Percentage of subjects				
number (not applicable)	12.2	7.7	0	

Statistical analyses

Statistical analysis title	Etrasimod 1 mg versus placebo
Comparison groups	Experimental: Etrasimod 1 mg v Placebo Then Etrasimod Any Dose
Number of subjects included in analysis	67
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.059
Method	Mantel-Haenszel
Parameter estimate	Adjusted difference from placebo
Point estimate	8.37
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.32
upper limit	17.07

Statistical analysis title	Etrasimod 2 mg versus placebo
Comparison groups	Experimental: Etrasimod 2 mg v Placebo Then Etrasimod Any Dose
Number of subjects included in analysis	69
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0173
Method	Mantel-Haenszel
Parameter estimate	Adjusted difference from placebo
Point estimate	12.15
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.15
upper limit	22.16

Secondary: Percentage Of Subjects With Esophageal PEC Less Than (<) 15 eos/hpf at Week 16

End point title	Percentage Of Subjects With Esophageal PEC Less Than (<) 15 eos/hpf at Week 16

End point description:

The FAS included all randomised subjects in the double-blind treatment period who received at least 1 dose of study treatment.

End point type	Secondary

End point timeframe:

Week 16

End point values	Experimental: Etrasimod 2 mg	Experimental: Etrasimod 1 mg	Placebo Then Etrasimod Any Dose	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	41	39	28	
Units: Percentage of subjects				
number (not applicable)	22.0	12.8	0	

Statistical analyses

Statistical analysis title	Etrasimod 1 mg versus placebo
Comparison groups	Experimental: Etrasimod 1 mg v Placebo Then Etrasimod Any Dose
Number of subjects included in analysis	67
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0121
Method	Mantel-Haenszel
Parameter estimate	Adjusted difference from placebo
Point estimate	13.85
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.03
upper limit	24.66

Statistical analysis title	Etrasimod 2 mg versus placebo
Comparison groups	Experimental: Etrasimod 2 mg v Placebo Then Etrasimod Any Dose
Number of subjects included in analysis	69
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0007
Method	Mantel-Haenszel
Parameter estimate	Adjusted difference from placebo
Point estimate	21.9

Confidence interval	
level	95 %
sides	2-sided
lower limit	9.23
upper limit	34.57

Other pre-specified: Number of Subjects With Serious TEAEs, TEAEs Leading to Study Treatment Discontinuation, TEAEs Leading to Death and TEAEs of Special Interest During 24 Week Double Blind Treatment Period

End point title	Number of Subjects With Serious TEAEs, TEAEs Leading to Study Treatment Discontinuation, TEAEs Leading to Death and TEAEs of Special Interest During 24 Week Double Blind Treatment Period

End point description:

An AE was any untoward medical occurrence in a subject who received study drug without regard to possibility of causal relationship. Serious adverse event (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. Treatment-emergent are events between first dose of study drug and up to 24 weeks after last dose that were absent before treatment or that worsened relative to pretreatment state. Relatedness to Etrasimod was assessed by the investigator (Yes/No). Subjects with multiple occurrences of an AE within a category were counted once within the category. The safety set included all randomised subjects who received at least 1 dose of study treatment during the specified treatment period.

End point type	Other pre-specified

End point timeframe:

Baseline up to Week 24

End point values	Experimental: Etrasimod 2 mg	Experimental: Etrasimod 1 mg	Placebo Then Etrasimod Any Dose	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	41	39	28	
Units: Subjects				
Serious TEAEs	0	0	0	
TEAEs leading to study treatment discontinuation	1	0	1	
TEAEs leading to death	0	0	0	

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Number of Subjects With Treatment Emergent Adverse Events (TEAEs) by Maximum Severity During 24 Week Double Blind Treatment Period

End point title	Number of Subjects With Treatment Emergent Adverse Events (TEAEs) by Maximum Severity During 24 Week Double Blind Treatment Period

End point description:

An adverse event (AE) was any untoward medical occurrence in a subject who received study drug without regard to possibility of causal relationship. Treatment-emergent AE was defined as an AE that started or worsened in severity on or after the first dose of study treatment. Severity of AE was graded according to Common Terminology Criteria for Adverse Events (CTCAE) as Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe or medically significant but not immediately life-threatening hospitalization or prolongation of hospitalization indicated; disabling, limiting self-care activities of daily living (ADL), Grade 4: Life-Threatening consequences, urgent intervention indicated, Grade 5: Death Related to AE. The safety set included all randomised subjects who received at least 1 dose of study treatment during the specified treatment period. Here, "Number of Subjects Analysed" signifies number of subjects evaluable for this endpoint.

End point type	Other pre-specified

End point timeframe:

Baseline, up to Week 24

End point values	Experimental: Etrasimod 2 mg	Experimental: Etrasimod 1 mg	Placebo Then Etrasimod Any Dose	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	29	27	21	
Units: Subjects				
TEAE: Grade 1	19	15	8	
TEAE: Grade 2	9	12	11	
TEAE: Grade 3	1	0	2	
TEAE: Grade 4	0	0	0	
TEAE: Grade 5	0	0	0	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Baseline up to a maximum of 61 weeks (35 days screening period, 24 weeks of double-blind treatment period, 28 weeks of active extended treatment, and 4 weeks of follow-up period)

Adverse event reporting additional description:

Same event may appear as both non-SAE and a serious AE. However, what is presented are distinct events. An event may be categorised as serious in one subject and as non-serious in another subject, or one subject may have experienced both a serious and non-serious event during the study. Safety set was evaluated.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	25.1

Reporting groups

Reporting group title	Experimental: Etrasimod 1 mg

Reporting group description:

Subjects received Etrasimod 1 mg tablet orally, once daily for 24 weeks in Double-blind treatment and for 28 weeks in OLE period. Subjects were then followed up for safety for up to 4 weeks.

Reporting group title	Placebo Then Etrasimod Any Dose

Reporting group description:

Subjects received Etrasimod matching placebo orally, once daily for 24 weeks in Double-blind treatment and re-randomized to receive Etrasimod tablet 1 or 2 mg orally, once daily for 28 weeks in OLE period. Subjects were then followed up for safety for up to 4 weeks.

Reporting group title	OLE: Placebo then Etrasimod 2 mg

Reporting group description:

Subjects received Etrasimod matching placebo orally, once daily for 24 weeks in Double-blind treatment and re-randomized to receive Etrasimod tablet 2 mg orally, once daily for 28 weeks in OLE period. Subjects were then followed up for safety for up to 4 weeks.

Reporting group title	OLE: Etrasimod 1 mg

Reporting group description:

Subjects received Etrasimod 1 mg tablet orally, once daily for 28 weeks in OLE period. Subjects were then followed up for safety for up to 4 weeks.

Reporting group title	Experimental: Etrasimod 2 mg

Reporting group description:

Subjects received Etrasimod 2 mg tablet orally, once daily for 24 weeks in Double-blind treatment and for 28 weeks in OLE period. Subjects were then followed up for safety for up to 4 weeks.

Reporting group title	OLE: Etrasimod 2 mg

Reporting group description:

Subjects received Etrasimod 2 mg tablet orally, once daily for 28 weeks in OLE period. Subjects were then followed up for safety for up to 4 weeks.

Reporting group title	OLE: Placebo then Etrasimod 1 mg

Reporting group description:

Subjects received Etrasimod matching placebo orally, once daily for 24 weeks in Double-blind treatment and re-randomized to receive Etrasimod tablet 1 mg orally, once daily for 28 weeks in OLE period. Subjects were then followed up for safety for up to 4 weeks.

Serious adverse events	Experimental: Etrasimod 1 mg	Placebo Then Etrasimod Any Dose	OLE: Placebo then Etrasimod 2 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 39 (0.00%)	0 / 28 (0.00%)	0 / 12 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Craniocerebral injury			
subjects affected / exposed	0 / 39 (0.00%)	0 / 28 (0.00%)	0 / 12 (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
Fall			
subjects affected / exposed	0 / 39 (0.00%)	0 / 28 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	OLE: Etrasimod 1 mg	Experimental: Etrasimod 2 mg	OLE: Etrasimod 2 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 31 (0.00%)	0 / 41 (0.00%)	0 / 30 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Craniocerebral injury			
subjects affected / exposed	0 / 31 (0.00%)	0 / 41 (0.00%)	0 / 30 (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
Fall			
subjects affected / exposed	0 / 31 (0.00%)	0 / 41 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	OLE: Placebo then Etrasimod 1 mg		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 12 (8.33%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

Injury, poisoning and procedural complications			
Craniocerebral injury			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Fall			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Experimental: Etrasimod 1 mg	Placebo Then Etrasimod Any Dose	OLE: Placebo then Etrasimod 2 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	27 / 39 (69.23%)	23 / 28 (82.14%)	11 / 12 (91.67%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Lipoma			
subjects affected / exposed	0 / 39 (0.00%)	0 / 28 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 39 (0.00%)	2 / 28 (7.14%)	1 / 12 (8.33%)
occurrences (all)	0	2	1
Influenza like illness			
subjects affected / exposed	1 / 39 (2.56%)	0 / 28 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Fatigue			
subjects affected / exposed	1 / 39 (2.56%)	0 / 28 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Pain			
subjects affected / exposed	0 / 39 (0.00%)	0 / 28 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Chills			

subjects affected / exposed	0 / 39 (0.00%)	0 / 28 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Chest pain			
subjects affected / exposed	1 / 39 (2.56%)	0 / 28 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Chest discomfort			
subjects affected / exposed	1 / 39 (2.56%)	2 / 28 (7.14%)	0 / 12 (0.00%)
occurrences (all)	2	2	0
Immune system disorders			
Seasonal allergy			
subjects affected / exposed	1 / 39 (2.56%)	0 / 28 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Hypersensitivity			
subjects affected / exposed	0 / 39 (0.00%)	0 / 28 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			
Vulvovaginal discomfort			
subjects affected / exposed	0 / 39 (0.00%)	0 / 28 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Breast discomfort			
subjects affected / exposed	1 / 39 (2.56%)	0 / 28 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 39 (2.56%)	2 / 28 (7.14%)	0 / 12 (0.00%)
occurrences (all)	1	2	0
Oropharyngeal pain			
subjects affected / exposed	2 / 39 (5.13%)	2 / 28 (7.14%)	0 / 12 (0.00%)
occurrences (all)	2	2	0
Rhinorrhoea			
subjects affected / exposed	0 / 39 (0.00%)	1 / 28 (3.57%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Dyspnoea			
subjects affected / exposed	1 / 39 (2.56%)	1 / 28 (3.57%)	1 / 12 (8.33%)
occurrences (all)	1	2	1
Nasal congestion			

subjects affected / exposed	1 / 39 (2.56%)	0 / 28 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Obstructive airways disorder			
subjects affected / exposed	1 / 39 (2.56%)	0 / 28 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Oropharyngeal spasm			
subjects affected / exposed	0 / 39 (0.00%)	0 / 28 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Throat tightness			
subjects affected / exposed	1 / 39 (2.56%)	0 / 28 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Sleep apnoea syndrome			
subjects affected / exposed	0 / 39 (0.00%)	1 / 28 (3.57%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Psychiatric disorders			
Insomnia			
subjects affected / exposed	1 / 39 (2.56%)	0 / 28 (0.00%)	1 / 12 (8.33%)
occurrences (all)	1	0	1
Anxiety			
subjects affected / exposed	1 / 39 (2.56%)	0 / 28 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Attention deficit hyperactivity disorder			
subjects affected / exposed	1 / 39 (2.56%)	0 / 28 (0.00%)	1 / 12 (8.33%)
occurrences (all)	1	0	1
Panic attack			
subjects affected / exposed	0 / 39 (0.00%)	0 / 28 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Stress			
subjects affected / exposed	0 / 39 (0.00%)	0 / 28 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Investigations			
Heart rate decreased			
subjects affected / exposed	1 / 39 (2.56%)	0 / 28 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
C-reactive protein increased			

subjects affected / exposed	1 / 39 (2.56%)	0 / 28 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Blood pressure increased			
subjects affected / exposed	0 / 39 (0.00%)	0 / 28 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Blood bilirubin increased			
subjects affected / exposed	1 / 39 (2.56%)	0 / 28 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Liver function test increased			
subjects affected / exposed	1 / 39 (2.56%)	0 / 28 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Alanine aminotransferase increased			
subjects affected / exposed	2 / 39 (5.13%)	0 / 28 (0.00%)	0 / 12 (0.00%)
occurrences (all)	2	0	0
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 39 (0.00%)	0 / 28 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Helicobacter test positive			
subjects affected / exposed	0 / 39 (0.00%)	0 / 28 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
White blood cell count decreased			
subjects affected / exposed	0 / 39 (0.00%)	0 / 28 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Transaminases increased			
subjects affected / exposed	1 / 39 (2.56%)	0 / 28 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
SARS-CoV-2 test positive			
subjects affected / exposed	1 / 39 (2.56%)	0 / 28 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Lymphocyte count decreased			
subjects affected / exposed	0 / 39 (0.00%)	0 / 28 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Pulmonary function test decreased			
subjects affected / exposed	0 / 39 (0.00%)	1 / 28 (3.57%)	0 / 12 (0.00%)
occurrences (all)	0	1	0

Pulmonary function test abnormal			
subjects affected / exposed	0 / 39 (0.00%)	0 / 28 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Procedural pain			
subjects affected / exposed	1 / 39 (2.56%)	0 / 28 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Contusion			
subjects affected / exposed	0 / 39 (0.00%)	0 / 28 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Skin laceration			
subjects affected / exposed	1 / 39 (2.56%)	0 / 28 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Procedural nausea			
subjects affected / exposed	1 / 39 (2.56%)	0 / 28 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Ligament sprain			
subjects affected / exposed	0 / 39 (0.00%)	0 / 28 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Hand fracture			
subjects affected / exposed	1 / 39 (2.56%)	0 / 28 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Stress fracture			
subjects affected / exposed	0 / 39 (0.00%)	0 / 28 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Procedural complication			
subjects affected / exposed	0 / 39 (0.00%)	1 / 28 (3.57%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Limb fracture			
subjects affected / exposed	0 / 39 (0.00%)	0 / 28 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Joint injury			
subjects affected / exposed	0 / 39 (0.00%)	0 / 28 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Clavicle fracture			

subjects affected / exposed	0 / 39 (0.00%)	0 / 28 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Wound dehiscence			
subjects affected / exposed	0 / 39 (0.00%)	0 / 28 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Cardiac disorders			
Sinus bradycardia			
subjects affected / exposed	0 / 39 (0.00%)	1 / 28 (3.57%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Bradycardia			
subjects affected / exposed	0 / 39 (0.00%)	0 / 28 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Hypoaesthesia			
subjects affected / exposed	0 / 39 (0.00%)	0 / 28 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Balance disorder			
subjects affected / exposed	0 / 39 (0.00%)	0 / 28 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Headache			
subjects affected / exposed	2 / 39 (5.13%)	1 / 28 (3.57%)	2 / 12 (16.67%)
occurrences (all)	4	1	2
Dizziness			
subjects affected / exposed	4 / 39 (10.26%)	1 / 28 (3.57%)	1 / 12 (8.33%)
occurrences (all)	5	1	1
Hypoglossal nerve paralysis			
subjects affected / exposed	0 / 39 (0.00%)	0 / 28 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Somnolence			
subjects affected / exposed	1 / 39 (2.56%)	1 / 28 (3.57%)	0 / 12 (0.00%)
occurrences (all)	1	1	0
Sciatica			
subjects affected / exposed	1 / 39 (2.56%)	0 / 28 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Paraesthesia			

subjects affected / exposed	1 / 39 (2.56%)	0 / 28 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Migraine			
subjects affected / exposed	0 / 39 (0.00%)	1 / 28 (3.57%)	1 / 12 (8.33%)
occurrences (all)	0	2	1
Blood and lymphatic system disorders			
Lymphadenopathy			
subjects affected / exposed	0 / 39 (0.00%)	0 / 28 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	1 / 39 (2.56%)	0 / 28 (0.00%)	1 / 12 (8.33%)
occurrences (all)	1	0	1
Tinnitus			
subjects affected / exposed	0 / 39 (0.00%)	0 / 28 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Ear pain			
subjects affected / exposed	1 / 39 (2.56%)	0 / 28 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Eye disorders			
Eye irritation			
subjects affected / exposed	0 / 39 (0.00%)	0 / 28 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Dry eye			
subjects affected / exposed	1 / 39 (2.56%)	0 / 28 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Cataract			
subjects affected / exposed	0 / 39 (0.00%)	0 / 28 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Blepharospasm			
subjects affected / exposed	0 / 39 (0.00%)	0 / 28 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Blepharitis			
subjects affected / exposed	1 / 39 (2.56%)	0 / 28 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Conjunctivitis allergic			

subjects affected / exposed	1 / 39 (2.56%)	0 / 28 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Meibomian gland dysfunction			
subjects affected / exposed	0 / 39 (0.00%)	0 / 28 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Vitreous floaters			
subjects affected / exposed	0 / 39 (0.00%)	0 / 28 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Hypermetropia			
subjects affected / exposed	0 / 39 (0.00%)	0 / 28 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Visual field defect			
subjects affected / exposed	1 / 39 (2.56%)	0 / 28 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Retinal degeneration			
subjects affected / exposed	0 / 39 (0.00%)	0 / 28 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Photopsia			
subjects affected / exposed	0 / 39 (0.00%)	0 / 28 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Ocular discomfort			
subjects affected / exposed	1 / 39 (2.56%)	0 / 28 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Visual impairment			
subjects affected / exposed	0 / 39 (0.00%)	0 / 28 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	3 / 39 (7.69%)	3 / 28 (10.71%)	0 / 12 (0.00%)
occurrences (all)	3	3	0
Gastritis			
subjects affected / exposed	1 / 39 (2.56%)	0 / 28 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Eosinophilic oesophagitis			
subjects affected / exposed	1 / 39 (2.56%)	3 / 28 (10.71%)	0 / 12 (0.00%)
occurrences (all)	1	6	0

Dysphagia			
subjects affected / exposed	0 / 39 (0.00%)	1 / 28 (3.57%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Abdominal pain			
subjects affected / exposed	1 / 39 (2.56%)	1 / 28 (3.57%)	1 / 12 (8.33%)
occurrences (all)	1	2	1
Abdominal distension			
subjects affected / exposed	1 / 39 (2.56%)	0 / 28 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Oesophageal food impaction			
subjects affected / exposed	1 / 39 (2.56%)	5 / 28 (17.86%)	4 / 12 (33.33%)
occurrences (all)	2	6	5
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 39 (2.56%)	0 / 28 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Abdominal pain upper			
subjects affected / exposed	2 / 39 (5.13%)	1 / 28 (3.57%)	0 / 12 (0.00%)
occurrences (all)	2	1	0
Diarrhoea			
subjects affected / exposed	1 / 39 (2.56%)	1 / 28 (3.57%)	1 / 12 (8.33%)
occurrences (all)	1	1	1
Odynophagia			
subjects affected / exposed	0 / 39 (0.00%)	0 / 28 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Inguinal hernia			
subjects affected / exposed	1 / 39 (2.56%)	0 / 28 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Frequent bowel movements			
subjects affected / exposed	1 / 39 (2.56%)	0 / 28 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Food poisoning			
subjects affected / exposed	0 / 39 (0.00%)	0 / 28 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Dyspepsia			
subjects affected / exposed	0 / 39 (0.00%)	1 / 28 (3.57%)	0 / 12 (0.00%)
occurrences (all)	0	1	0

Duodenal ulcer			
subjects affected / exposed	1 / 39 (2.56%)	0 / 28 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Dry mouth			
subjects affected / exposed	1 / 39 (2.56%)	0 / 28 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Dental caries			
subjects affected / exposed	0 / 39 (0.00%)	1 / 28 (3.57%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Constipation			
subjects affected / exposed	0 / 39 (0.00%)	0 / 28 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Colitis microscopic			
subjects affected / exposed	1 / 39 (2.56%)	0 / 28 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Oesophageal pain			
subjects affected / exposed	0 / 39 (0.00%)	0 / 28 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Abdominal discomfort			
subjects affected / exposed	0 / 39 (0.00%)	0 / 28 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Swollen tongue			
subjects affected / exposed	0 / 39 (0.00%)	0 / 28 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Regurgitation			
subjects affected / exposed	0 / 39 (0.00%)	1 / 28 (3.57%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Oesophageal rupture			
subjects affected / exposed	0 / 39 (0.00%)	1 / 28 (3.57%)	0 / 12 (0.00%)
occurrences (all)	0	2	0
Hiatus hernia			
subjects affected / exposed	0 / 39 (0.00%)	1 / 28 (3.57%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Haemorrhoids			
subjects affected / exposed	0 / 39 (0.00%)	1 / 28 (3.57%)	1 / 12 (8.33%)
occurrences (all)	0	1	1

Bile acid malabsorption			
subjects affected / exposed	0 / 39 (0.00%)	0 / 28 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Vomiting			
subjects affected / exposed	1 / 39 (2.56%)	0 / 28 (0.00%)	1 / 12 (8.33%)
occurrences (all)	1	0	1
Erosive oesophagitis			
subjects affected / exposed	0 / 39 (0.00%)	0 / 28 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Acquired oesophageal web			
subjects affected / exposed	0 / 39 (0.00%)	0 / 28 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Oesophageal obstruction			
subjects affected / exposed	0 / 39 (0.00%)	0 / 28 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Gastric ulcer			
subjects affected / exposed	0 / 39 (0.00%)	0 / 28 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Hepatobiliary disorders			
Hepatic steatosis			
subjects affected / exposed	0 / 39 (0.00%)	0 / 28 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Excessive granulation tissue			
subjects affected / exposed	0 / 39 (0.00%)	1 / 28 (3.57%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Skin lesion			
subjects affected / exposed	0 / 39 (0.00%)	0 / 28 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Petechiae			
subjects affected / exposed	1 / 39 (2.56%)	0 / 28 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Acne			
subjects affected / exposed	0 / 39 (0.00%)	0 / 28 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Skin odour abnormal			

subjects affected / exposed	0 / 39 (0.00%)	0 / 28 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Rash			
subjects affected / exposed	0 / 39 (0.00%)	1 / 28 (3.57%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	1 / 39 (2.56%)	0 / 28 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Urinary hesitation			
subjects affected / exposed	0 / 39 (0.00%)	0 / 28 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	1 / 39 (2.56%)	0 / 28 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 39 (0.00%)	1 / 28 (3.57%)	1 / 12 (8.33%)
occurrences (all)	0	1	1
Femoroacetabular impingement			
subjects affected / exposed	1 / 39 (2.56%)	0 / 28 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Joint effusion			
subjects affected / exposed	0 / 39 (0.00%)	0 / 28 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Muscle contracture			
subjects affected / exposed	1 / 39 (2.56%)	0 / 28 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Myalgia			
subjects affected / exposed	0 / 39 (0.00%)	0 / 28 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Pain in extremity			
subjects affected / exposed	0 / 39 (0.00%)	0 / 28 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Arthralgia			

subjects affected / exposed	2 / 39 (5.13%)	0 / 28 (0.00%)	0 / 12 (0.00%)
occurrences (all)	2	0	0
Tendonitis			
subjects affected / exposed	0 / 39 (0.00%)	0 / 28 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Bursitis			
subjects affected / exposed	0 / 39 (0.00%)	0 / 28 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Osteochondrosis			
subjects affected / exposed	0 / 39 (0.00%)	1 / 28 (3.57%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	2 / 39 (5.13%)	0 / 28 (0.00%)	0 / 12 (0.00%)
occurrences (all)	2	0	0
Upper respiratory tract infection			
subjects affected / exposed	2 / 39 (5.13%)	0 / 28 (0.00%)	0 / 12 (0.00%)
occurrences (all)	2	0	0
Nasopharyngitis			
subjects affected / exposed	2 / 39 (5.13%)	0 / 28 (0.00%)	0 / 12 (0.00%)
occurrences (all)	2	0	0
COVID-19			
subjects affected / exposed	4 / 39 (10.26%)	6 / 28 (21.43%)	1 / 12 (8.33%)
occurrences (all)	4	6	1
Gastroenteritis viral			
subjects affected / exposed	1 / 39 (2.56%)	0 / 28 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Pharyngitis streptococcal			
subjects affected / exposed	0 / 39 (0.00%)	0 / 28 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Pharyngitis			
subjects affected / exposed	1 / 39 (2.56%)	0 / 28 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Fungal skin infection			
subjects affected / exposed	1 / 39 (2.56%)	0 / 28 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0

Folliculitis			
subjects affected / exposed	0 / 39 (0.00%)	0 / 28 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Sinusitis			
subjects affected / exposed	0 / 39 (0.00%)	0 / 28 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Ear infection			
subjects affected / exposed	1 / 39 (2.56%)	0 / 28 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Diarrhoea infectious			
subjects affected / exposed	0 / 39 (0.00%)	0 / 28 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Cellulitis			
subjects affected / exposed	0 / 39 (0.00%)	0 / 28 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Bronchitis			
subjects affected / exposed	0 / 39 (0.00%)	0 / 28 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Influenza			
subjects affected / exposed	1 / 39 (2.56%)	0 / 28 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Epstein-Barr virus infection			
subjects affected / exposed	1 / 39 (2.56%)	0 / 28 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 39 (0.00%)	0 / 28 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Viral infection			
subjects affected / exposed	1 / 39 (2.56%)	0 / 28 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Pneumonia			
subjects affected / exposed	0 / 39 (0.00%)	1 / 28 (3.57%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Vulvovaginal mycotic infection			
subjects affected / exposed	0 / 39 (0.00%)	0 / 28 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0

Vulvovaginal candidiasis			
subjects affected / exposed	0 / 39 (0.00%)	0 / 28 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Tonsillitis			
subjects affected / exposed	1 / 39 (2.56%)	0 / 28 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Tooth abscess			
subjects affected / exposed	1 / 39 (2.56%)	0 / 28 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Tooth infection			
subjects affected / exposed	1 / 39 (2.56%)	0 / 28 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Hordeolum			
subjects affected / exposed	0 / 39 (0.00%)	0 / 28 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Vitamin D deficiency			
subjects affected / exposed	1 / 39 (2.56%)	0 / 28 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Hypophosphataemia			
subjects affected / exposed	0 / 39 (0.00%)	0 / 28 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Decreased appetite			
subjects affected / exposed	2 / 39 (5.13%)	0 / 28 (0.00%)	0 / 12 (0.00%)
occurrences (all)	2	0	0
Hyperkalaemia			
subjects affected / exposed	0 / 39 (0.00%)	0 / 28 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	OLE: Etrasimod 1 mg	Experimental: Etrasimod 2 mg	OLE: Etrasimod 2 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	19 / 31 (61.29%)	30 / 41 (73.17%)	16 / 30 (53.33%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Lipoma			
subjects affected / exposed	1 / 31 (3.23%)	0 / 41 (0.00%)	0 / 30 (0.00%)
occurrences (all)	1	0	0

General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 31 (0.00%)	2 / 41 (4.88%)	1 / 30 (3.33%)
occurrences (all)	0	3	1
Influenza like illness			
subjects affected / exposed	0 / 31 (0.00%)	1 / 41 (2.44%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
Fatigue			
subjects affected / exposed	1 / 31 (3.23%)	0 / 41 (0.00%)	1 / 30 (3.33%)
occurrences (all)	1	0	1
Pain			
subjects affected / exposed	0 / 31 (0.00%)	0 / 41 (0.00%)	1 / 30 (3.33%)
occurrences (all)	0	0	1
Chills			
subjects affected / exposed	0 / 31 (0.00%)	0 / 41 (0.00%)	1 / 30 (3.33%)
occurrences (all)	0	0	1
Chest pain			
subjects affected / exposed	0 / 31 (0.00%)	0 / 41 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Chest discomfort			
subjects affected / exposed	0 / 31 (0.00%)	0 / 41 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Immune system disorders			
Seasonal allergy			
subjects affected / exposed	1 / 31 (3.23%)	0 / 41 (0.00%)	0 / 30 (0.00%)
occurrences (all)	1	0	0
Hypersensitivity			
subjects affected / exposed	1 / 31 (3.23%)	0 / 41 (0.00%)	0 / 30 (0.00%)
occurrences (all)	1	0	0
Reproductive system and breast disorders			
Vulvovaginal discomfort			
subjects affected / exposed	0 / 31 (0.00%)	1 / 41 (2.44%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
Breast discomfort			
subjects affected / exposed	0 / 31 (0.00%)	0 / 41 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0

Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 31 (0.00%)	2 / 41 (4.88%)	2 / 30 (6.67%)
occurrences (all)	0	2	2
Oropharyngeal pain			
subjects affected / exposed	0 / 31 (0.00%)	1 / 41 (2.44%)	1 / 30 (3.33%)
occurrences (all)	0	1	1
Rhinorrhoea			
subjects affected / exposed	0 / 31 (0.00%)	2 / 41 (4.88%)	1 / 30 (3.33%)
occurrences (all)	0	2	1
Dyspnoea			
subjects affected / exposed	1 / 31 (3.23%)	0 / 41 (0.00%)	0 / 30 (0.00%)
occurrences (all)	2	0	0
Nasal congestion			
subjects affected / exposed	0 / 31 (0.00%)	0 / 41 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Obstructive airways disorder			
subjects affected / exposed	0 / 31 (0.00%)	0 / 41 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Oropharyngeal spasm			
subjects affected / exposed	1 / 31 (3.23%)	0 / 41 (0.00%)	0 / 30 (0.00%)
occurrences (all)	1	0	0
Throat tightness			
subjects affected / exposed	0 / 31 (0.00%)	0 / 41 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Sleep apnoea syndrome			
subjects affected / exposed	0 / 31 (0.00%)	0 / 41 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Insomnia			
subjects affected / exposed	0 / 31 (0.00%)	1 / 41 (2.44%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
Anxiety			
subjects affected / exposed	1 / 31 (3.23%)	0 / 41 (0.00%)	1 / 30 (3.33%)
occurrences (all)	1	0	1
Attention deficit hyperactivity disorder			

subjects affected / exposed	1 / 31 (3.23%)	0 / 41 (0.00%)	0 / 30 (0.00%)
occurrences (all)	1	0	0
Panic attack			
subjects affected / exposed	1 / 31 (3.23%)	0 / 41 (0.00%)	0 / 30 (0.00%)
occurrences (all)	1	0	0
Stress			
subjects affected / exposed	1 / 31 (3.23%)	0 / 41 (0.00%)	0 / 30 (0.00%)
occurrences (all)	1	0	0
Investigations			
Heart rate decreased			
subjects affected / exposed	0 / 31 (0.00%)	0 / 41 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
C-reactive protein increased			
subjects affected / exposed	0 / 31 (0.00%)	0 / 41 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Blood pressure increased			
subjects affected / exposed	0 / 31 (0.00%)	1 / 41 (2.44%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
Blood bilirubin increased			
subjects affected / exposed	0 / 31 (0.00%)	0 / 41 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Liver function test increased			
subjects affected / exposed	0 / 31 (0.00%)	0 / 41 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Alanine aminotransferase increased			
subjects affected / exposed	0 / 31 (0.00%)	3 / 41 (7.32%)	4 / 30 (13.33%)
occurrences (all)	0	3	6
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 31 (0.00%)	1 / 41 (2.44%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
Helicobacter test positive			
subjects affected / exposed	0 / 31 (0.00%)	0 / 41 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
White blood cell count decreased			

subjects affected / exposed	0 / 31 (0.00%)	1 / 41 (2.44%)	0 / 30 (0.00%)
occurrences (all)	0	2	0
Transaminases increased			
subjects affected / exposed	0 / 31 (0.00%)	0 / 41 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
SARS-CoV-2 test positive			
subjects affected / exposed	0 / 31 (0.00%)	0 / 41 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Lymphocyte count decreased			
subjects affected / exposed	0 / 31 (0.00%)	1 / 41 (2.44%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
Pulmonary function test decreased			
subjects affected / exposed	0 / 31 (0.00%)	0 / 41 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Pulmonary function test abnormal			
subjects affected / exposed	0 / 31 (0.00%)	0 / 41 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Procedural pain			
subjects affected / exposed	0 / 31 (0.00%)	1 / 41 (2.44%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
Contusion			
subjects affected / exposed	0 / 31 (0.00%)	1 / 41 (2.44%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
Skin laceration			
subjects affected / exposed	0 / 31 (0.00%)	0 / 41 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Procedural nausea			
subjects affected / exposed	0 / 31 (0.00%)	0 / 41 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Ligament sprain			
subjects affected / exposed	0 / 31 (0.00%)	1 / 41 (2.44%)	0 / 30 (0.00%)
occurrences (all)	0	2	0
Hand fracture			

subjects affected / exposed	0 / 31 (0.00%)	0 / 41 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Stress fracture			
subjects affected / exposed	0 / 31 (0.00%)	0 / 41 (0.00%)	1 / 30 (3.33%)
occurrences (all)	0	0	1
Procedural complication			
subjects affected / exposed	0 / 31 (0.00%)	0 / 41 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Limb fracture			
subjects affected / exposed	0 / 31 (0.00%)	0 / 41 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Joint injury			
subjects affected / exposed	0 / 31 (0.00%)	0 / 41 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Clavicle fracture			
subjects affected / exposed	0 / 31 (0.00%)	0 / 41 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Wound dehiscence			
subjects affected / exposed	0 / 31 (0.00%)	0 / 41 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Sinus bradycardia			
subjects affected / exposed	0 / 31 (0.00%)	0 / 41 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Bradycardia			
subjects affected / exposed	0 / 31 (0.00%)	2 / 41 (4.88%)	0 / 30 (0.00%)
occurrences (all)	0	2	0
Nervous system disorders			
Hypoaesthesia			
subjects affected / exposed	1 / 31 (3.23%)	0 / 41 (0.00%)	0 / 30 (0.00%)
occurrences (all)	1	0	0
Balance disorder			
subjects affected / exposed	0 / 31 (0.00%)	1 / 41 (2.44%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
Headache			

subjects affected / exposed	1 / 31 (3.23%)	3 / 41 (7.32%)	1 / 30 (3.33%)
occurrences (all)	1	4	2
Dizziness			
subjects affected / exposed	1 / 31 (3.23%)	4 / 41 (9.76%)	0 / 30 (0.00%)
occurrences (all)	1	4	0
Hypoglossal nerve paralysis			
subjects affected / exposed	0 / 31 (0.00%)	0 / 41 (0.00%)	1 / 30 (3.33%)
occurrences (all)	0	0	1
Somnolence			
subjects affected / exposed	0 / 31 (0.00%)	0 / 41 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Sciatica			
subjects affected / exposed	0 / 31 (0.00%)	0 / 41 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Paraesthesia			
subjects affected / exposed	0 / 31 (0.00%)	0 / 41 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Migraine			
subjects affected / exposed	0 / 31 (0.00%)	1 / 41 (2.44%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
Blood and lymphatic system disorders			
Lymphadenopathy			
subjects affected / exposed	0 / 31 (0.00%)	1 / 41 (2.44%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 31 (0.00%)	0 / 41 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Tinnitus			
subjects affected / exposed	1 / 31 (3.23%)	0 / 41 (0.00%)	0 / 30 (0.00%)
occurrences (all)	1	0	0
Ear pain			
subjects affected / exposed	0 / 31 (0.00%)	0 / 41 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Eye disorders			

Eye irritation			
subjects affected / exposed	0 / 31 (0.00%)	0 / 41 (0.00%)	1 / 30 (3.33%)
occurrences (all)	0	0	1
Dry eye			
subjects affected / exposed	1 / 31 (3.23%)	0 / 41 (0.00%)	0 / 30 (0.00%)
occurrences (all)	2	0	0
Cataract			
subjects affected / exposed	0 / 31 (0.00%)	0 / 41 (0.00%)	1 / 30 (3.33%)
occurrences (all)	0	0	1
Blepharospasm			
subjects affected / exposed	0 / 31 (0.00%)	0 / 41 (0.00%)	1 / 30 (3.33%)
occurrences (all)	0	0	1
Blepharitis			
subjects affected / exposed	0 / 31 (0.00%)	0 / 41 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Conjunctivitis allergic			
subjects affected / exposed	1 / 31 (3.23%)	0 / 41 (0.00%)	0 / 30 (0.00%)
occurrences (all)	1	0	0
Meibomian gland dysfunction			
subjects affected / exposed	0 / 31 (0.00%)	0 / 41 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Vitreous floaters			
subjects affected / exposed	2 / 31 (6.45%)	0 / 41 (0.00%)	0 / 30 (0.00%)
occurrences (all)	2	0	0
Hypermetropia			
subjects affected / exposed	0 / 31 (0.00%)	1 / 41 (2.44%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
Visual field defect			
subjects affected / exposed	0 / 31 (0.00%)	0 / 41 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Retinal degeneration			
subjects affected / exposed	1 / 31 (3.23%)	0 / 41 (0.00%)	0 / 30 (0.00%)
occurrences (all)	1	0	0
Photopsia			
subjects affected / exposed	0 / 31 (0.00%)	1 / 41 (2.44%)	0 / 30 (0.00%)
occurrences (all)	0	3	0

Ocular discomfort			
subjects affected / exposed	0 / 31 (0.00%)	0 / 41 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Visual impairment			
subjects affected / exposed	0 / 31 (0.00%)	1 / 41 (2.44%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	1 / 31 (3.23%)	6 / 41 (14.63%)	2 / 30 (6.67%)
occurrences (all)	1	6	2
Gastritis			
subjects affected / exposed	1 / 31 (3.23%)	1 / 41 (2.44%)	0 / 30 (0.00%)
occurrences (all)	1	1	0
Eosinophilic oesophagitis			
subjects affected / exposed	0 / 31 (0.00%)	0 / 41 (0.00%)	1 / 30 (3.33%)
occurrences (all)	0	0	1
Dysphagia			
subjects affected / exposed	0 / 31 (0.00%)	0 / 41 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Abdominal pain			
subjects affected / exposed	0 / 31 (0.00%)	2 / 41 (4.88%)	1 / 30 (3.33%)
occurrences (all)	0	2	1
Abdominal distension			
subjects affected / exposed	1 / 31 (3.23%)	1 / 41 (2.44%)	0 / 30 (0.00%)
occurrences (all)	1	1	0
Oesophageal food impaction			
subjects affected / exposed	1 / 31 (3.23%)	1 / 41 (2.44%)	0 / 30 (0.00%)
occurrences (all)	1	1	0
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 31 (3.23%)	0 / 41 (0.00%)	1 / 30 (3.33%)
occurrences (all)	1	0	1
Abdominal pain upper			
subjects affected / exposed	0 / 31 (0.00%)	1 / 41 (2.44%)	1 / 30 (3.33%)
occurrences (all)	0	1	1
Diarrhoea			

subjects affected / exposed	0 / 31 (0.00%)	0 / 41 (0.00%)	1 / 30 (3.33%)
occurrences (all)	0	0	1
Odynophagia			
subjects affected / exposed	0 / 31 (0.00%)	1 / 41 (2.44%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
Inguinal hernia			
subjects affected / exposed	0 / 31 (0.00%)	0 / 41 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Frequent bowel movements			
subjects affected / exposed	0 / 31 (0.00%)	0 / 41 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Food poisoning			
subjects affected / exposed	0 / 31 (0.00%)	1 / 41 (2.44%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
Dyspepsia			
subjects affected / exposed	1 / 31 (3.23%)	0 / 41 (0.00%)	0 / 30 (0.00%)
occurrences (all)	1	0	0
Duodenal ulcer			
subjects affected / exposed	0 / 31 (0.00%)	0 / 41 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Dry mouth			
subjects affected / exposed	0 / 31 (0.00%)	0 / 41 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Dental caries			
subjects affected / exposed	0 / 31 (0.00%)	0 / 41 (0.00%)	1 / 30 (3.33%)
occurrences (all)	0	0	1
Constipation			
subjects affected / exposed	1 / 31 (3.23%)	0 / 41 (0.00%)	0 / 30 (0.00%)
occurrences (all)	1	0	0
Colitis microscopic			
subjects affected / exposed	0 / 31 (0.00%)	0 / 41 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Oesophageal pain			
subjects affected / exposed	1 / 31 (3.23%)	0 / 41 (0.00%)	0 / 30 (0.00%)
occurrences (all)	2	0	0
Abdominal discomfort			

subjects affected / exposed	0 / 31 (0.00%)	1 / 41 (2.44%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
Swollen tongue			
subjects affected / exposed	0 / 31 (0.00%)	1 / 41 (2.44%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
Regurgitation			
subjects affected / exposed	0 / 31 (0.00%)	0 / 41 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Oesophageal rupture			
subjects affected / exposed	0 / 31 (0.00%)	0 / 41 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Hiatus hernia			
subjects affected / exposed	0 / 31 (0.00%)	0 / 41 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Haemorrhoids			
subjects affected / exposed	0 / 31 (0.00%)	0 / 41 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Bile acid malabsorption			
subjects affected / exposed	0 / 31 (0.00%)	0 / 41 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Vomiting			
subjects affected / exposed	0 / 31 (0.00%)	0 / 41 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Erosive oesophagitis			
subjects affected / exposed	0 / 31 (0.00%)	1 / 41 (2.44%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
Acquired oesophageal web			
subjects affected / exposed	0 / 31 (0.00%)	0 / 41 (0.00%)	1 / 30 (3.33%)
occurrences (all)	0	0	1
Oesophageal obstruction			
subjects affected / exposed	0 / 31 (0.00%)	0 / 41 (0.00%)	1 / 30 (3.33%)
occurrences (all)	0	0	1
Gastric ulcer			
subjects affected / exposed	0 / 31 (0.00%)	0 / 41 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Hepatobiliary disorders			

Hepatic steatosis			
subjects affected / exposed	0 / 31 (0.00%)	0 / 41 (0.00%)	1 / 30 (3.33%)
occurrences (all)	0	0	1
Skin and subcutaneous tissue disorders			
Excessive granulation tissue			
subjects affected / exposed	0 / 31 (0.00%)	0 / 41 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Skin lesion			
subjects affected / exposed	1 / 31 (3.23%)	0 / 41 (0.00%)	0 / 30 (0.00%)
occurrences (all)	1	0	0
Petechiae			
subjects affected / exposed	0 / 31 (0.00%)	0 / 41 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Acne			
subjects affected / exposed	0 / 31 (0.00%)	1 / 41 (2.44%)	1 / 30 (3.33%)
occurrences (all)	0	1	1
Skin odour abnormal			
subjects affected / exposed	0 / 31 (0.00%)	0 / 41 (0.00%)	1 / 30 (3.33%)
occurrences (all)	0	0	1
Rash			
subjects affected / exposed	0 / 31 (0.00%)	0 / 41 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	0 / 31 (0.00%)	0 / 41 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Urinary hesitation			
subjects affected / exposed	0 / 31 (0.00%)	1 / 41 (2.44%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	0 / 31 (0.00%)	0 / 41 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Back pain			

subjects affected / exposed	1 / 31 (3.23%)	0 / 41 (0.00%)	1 / 30 (3.33%)
occurrences (all)	1	0	1
Femoroacetabular impingement			
subjects affected / exposed	0 / 31 (0.00%)	0 / 41 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Joint effusion			
subjects affected / exposed	0 / 31 (0.00%)	1 / 41 (2.44%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
Muscle contracture			
subjects affected / exposed	0 / 31 (0.00%)	0 / 41 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Myalgia			
subjects affected / exposed	0 / 31 (0.00%)	0 / 41 (0.00%)	1 / 30 (3.33%)
occurrences (all)	0	0	1
Pain in extremity			
subjects affected / exposed	0 / 31 (0.00%)	1 / 41 (2.44%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
Arthralgia			
subjects affected / exposed	1 / 31 (3.23%)	0 / 41 (0.00%)	1 / 30 (3.33%)
occurrences (all)	1	0	1
Tendonitis			
subjects affected / exposed	1 / 31 (3.23%)	0 / 41 (0.00%)	0 / 30 (0.00%)
occurrences (all)	1	0	0
Bursitis			
subjects affected / exposed	0 / 31 (0.00%)	0 / 41 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Osteochondrosis			
subjects affected / exposed	0 / 31 (0.00%)	0 / 41 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	0 / 31 (0.00%)	0 / 41 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract infection			
subjects affected / exposed	0 / 31 (0.00%)	0 / 41 (0.00%)	2 / 30 (6.67%)
occurrences (all)	0	0	2

Nasopharyngitis			
subjects affected / exposed	1 / 31 (3.23%)	3 / 41 (7.32%)	1 / 30 (3.33%)
occurrences (all)	1	3	1
COVID-19			
subjects affected / exposed	5 / 31 (16.13%)	4 / 41 (9.76%)	2 / 30 (6.67%)
occurrences (all)	5	4	2
Gastroenteritis viral			
subjects affected / exposed	0 / 31 (0.00%)	1 / 41 (2.44%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
Pharyngitis streptococcal			
subjects affected / exposed	1 / 31 (3.23%)	0 / 41 (0.00%)	0 / 30 (0.00%)
occurrences (all)	1	0	0
Pharyngitis			
subjects affected / exposed	0 / 31 (0.00%)	0 / 41 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Fungal skin infection			
subjects affected / exposed	0 / 31 (0.00%)	0 / 41 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Folliculitis			
subjects affected / exposed	0 / 31 (0.00%)	1 / 41 (2.44%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
Sinusitis			
subjects affected / exposed	0 / 31 (0.00%)	1 / 41 (2.44%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
Ear infection			
subjects affected / exposed	0 / 31 (0.00%)	0 / 41 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Diarrhoea infectious			
subjects affected / exposed	0 / 31 (0.00%)	1 / 41 (2.44%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
Cellulitis			
subjects affected / exposed	0 / 31 (0.00%)	1 / 41 (2.44%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
Bronchitis			
subjects affected / exposed	0 / 31 (0.00%)	0 / 41 (0.00%)	1 / 30 (3.33%)
occurrences (all)	0	0	1

Influenza			
subjects affected / exposed	0 / 31 (0.00%)	1 / 41 (2.44%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
Epstein-Barr virus infection			
subjects affected / exposed	0 / 31 (0.00%)	0 / 41 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 31 (0.00%)	0 / 41 (0.00%)	1 / 30 (3.33%)
occurrences (all)	0	0	1
Viral infection			
subjects affected / exposed	0 / 31 (0.00%)	0 / 41 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Pneumonia			
subjects affected / exposed	1 / 31 (3.23%)	0 / 41 (0.00%)	0 / 30 (0.00%)
occurrences (all)	1	0	0
Vulvovaginal mycotic infection			
subjects affected / exposed	0 / 31 (0.00%)	1 / 41 (2.44%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
Vulvovaginal candidiasis			
subjects affected / exposed	0 / 31 (0.00%)	1 / 41 (2.44%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
Tonsillitis			
subjects affected / exposed	0 / 31 (0.00%)	0 / 41 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Tooth abscess			
subjects affected / exposed	0 / 31 (0.00%)	0 / 41 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Tooth infection			
subjects affected / exposed	0 / 31 (0.00%)	0 / 41 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Hordeolum			
subjects affected / exposed	0 / 31 (0.00%)	0 / 41 (0.00%)	1 / 30 (3.33%)
occurrences (all)	0	0	1
Metabolism and nutrition disorders			
Vitamin D deficiency			

subjects affected / exposed	0 / 31 (0.00%)	0 / 41 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Hypophosphataemia			
subjects affected / exposed	0 / 31 (0.00%)	1 / 41 (2.44%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
Decreased appetite			
subjects affected / exposed	0 / 31 (0.00%)	0 / 41 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Hyperkalaemia			
subjects affected / exposed	1 / 31 (3.23%)	0 / 41 (0.00%)	0 / 30 (0.00%)
occurrences (all)	1	0	0

Non-serious adverse events	OLE: Placebo then Etrasimod 1 mg		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	7 / 12 (58.33%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Lipoma			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Influenza like illness			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Fatigue			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Pain			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Chills			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Chest pain			

subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Chest discomfort			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Immune system disorders			
Seasonal allergy			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Hypersensitivity			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Reproductive system and breast disorders			
Vulvovaginal discomfort			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Breast discomfort			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Oropharyngeal pain			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Rhinorrhoea			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Dyspnoea			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Nasal congestion			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Obstructive airways disorder			

subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Oropharyngeal spasm			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Throat tightness			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Sleep apnoea syndrome			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Psychiatric disorders			
Insomnia			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Anxiety			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Attention deficit hyperactivity disorder			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Panic attack			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Stress			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Investigations			
Heart rate decreased			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
C-reactive protein increased			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Blood pressure increased			

subjects affected / exposed	0 / 12 (0.00%)			
occurrences (all)	0			
Blood bilirubin increased				
subjects affected / exposed	0 / 12 (0.00%)			
occurrences (all)	0			
Liver function test increased				
subjects affected / exposed	0 / 12 (0.00%)			
occurrences (all)	0			
Alanine aminotransferase increased				
subjects affected / exposed	2 / 12 (16.67%)			
occurrences (all)	2			
Aspartate aminotransferase increased				
subjects affected / exposed	2 / 12 (16.67%)			
occurrences (all)	2			
Helicobacter test positive				
subjects affected / exposed	1 / 12 (8.33%)			
occurrences (all)	1			
White blood cell count decreased				
subjects affected / exposed	0 / 12 (0.00%)			
occurrences (all)	0			
Transaminases increased				
subjects affected / exposed	0 / 12 (0.00%)			
occurrences (all)	0			
SARS-CoV-2 test positive				
subjects affected / exposed	0 / 12 (0.00%)			
occurrences (all)	0			
Lymphocyte count decreased				
subjects affected / exposed	0 / 12 (0.00%)			
occurrences (all)	0			
Pulmonary function test decreased				
subjects affected / exposed	0 / 12 (0.00%)			
occurrences (all)	0			
Pulmonary function test abnormal				
subjects affected / exposed	1 / 12 (8.33%)			
occurrences (all)	1			

Injury, poisoning and procedural complications			
Procedural pain			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Contusion			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Skin laceration			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Procedural nausea			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Ligament sprain			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Hand fracture			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Stress fracture			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Procedural complication			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Limb fracture			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Joint injury			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Clavicle fracture			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Wound dehiscence			

subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Cardiac disorders			
Sinus bradycardia			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Bradycardia			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Nervous system disorders			
Hypoaesthesia			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Balance disorder			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Headache			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Dizziness			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Hypoglossal nerve paralysis			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Somnolence			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Sciatica			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Paraesthesia			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Migraine			

subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1		
Blood and lymphatic system disorders Lymphadenopathy subjects affected / exposed occurrences (all)	 0 / 12 (0.00%) 0		
Ear and labyrinth disorders Vertigo subjects affected / exposed occurrences (all) Tinnitus subjects affected / exposed occurrences (all) Ear pain subjects affected / exposed occurrences (all)	 0 / 12 (0.00%) 0 0 / 12 (0.00%) 0 0 / 12 (0.00%) 0		
Eye disorders Eye irritation subjects affected / exposed occurrences (all) Dry eye subjects affected / exposed occurrences (all) Cataract subjects affected / exposed occurrences (all) Blepharospasm subjects affected / exposed occurrences (all) Blepharitis subjects affected / exposed occurrences (all) Conjunctivitis allergic subjects affected / exposed occurrences (all) Meibomian gland dysfunction	 0 / 12 (0.00%) 0 0 / 12 (0.00%) 0 0 / 12 (0.00%) 0 0 / 12 (0.00%) 0 0 / 12 (0.00%) 0 0 / 12 (0.00%) 0		

subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Vitreous floaters			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Hypermetropia			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Visual field defect			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Retinal degeneration			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Photopsia			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Ocular discomfort			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Visual impairment			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Gastritis			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Eosinophilic oesophagitis			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Dysphagia			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		

Abdominal pain				
subjects affected / exposed	0 / 12 (0.00%)			
occurrences (all)	0			
Abdominal distension				
subjects affected / exposed	0 / 12 (0.00%)			
occurrences (all)	0			
Oesophageal food impaction				
subjects affected / exposed	0 / 12 (0.00%)			
occurrences (all)	0			
Gastrooesophageal reflux disease				
subjects affected / exposed	0 / 12 (0.00%)			
occurrences (all)	0			
Abdominal pain upper				
subjects affected / exposed	0 / 12 (0.00%)			
occurrences (all)	0			
Diarrhoea				
subjects affected / exposed	0 / 12 (0.00%)			
occurrences (all)	0			
Odynophagia				
subjects affected / exposed	0 / 12 (0.00%)			
occurrences (all)	0			
Inguinal hernia				
subjects affected / exposed	0 / 12 (0.00%)			
occurrences (all)	0			
Frequent bowel movements				
subjects affected / exposed	0 / 12 (0.00%)			
occurrences (all)	0			
Food poisoning				
subjects affected / exposed	0 / 12 (0.00%)			
occurrences (all)	0			
Dyspepsia				
subjects affected / exposed	0 / 12 (0.00%)			
occurrences (all)	0			
Duodenal ulcer				
subjects affected / exposed	0 / 12 (0.00%)			
occurrences (all)	0			

Dry mouth				
subjects affected / exposed	0 / 12 (0.00%)			
occurrences (all)	0			
Dental caries				
subjects affected / exposed	0 / 12 (0.00%)			
occurrences (all)	0			
Constipation				
subjects affected / exposed	0 / 12 (0.00%)			
occurrences (all)	0			
Colitis microscopic				
subjects affected / exposed	0 / 12 (0.00%)			
occurrences (all)	0			
Oesophageal pain				
subjects affected / exposed	0 / 12 (0.00%)			
occurrences (all)	0			
Abdominal discomfort				
subjects affected / exposed	0 / 12 (0.00%)			
occurrences (all)	0			
Swollen tongue				
subjects affected / exposed	0 / 12 (0.00%)			
occurrences (all)	0			
Regurgitation				
subjects affected / exposed	0 / 12 (0.00%)			
occurrences (all)	0			
Oesophageal rupture				
subjects affected / exposed	0 / 12 (0.00%)			
occurrences (all)	0			
Hiatus hernia				
subjects affected / exposed	2 / 12 (16.67%)			
occurrences (all)	2			
Haemorrhoids				
subjects affected / exposed	0 / 12 (0.00%)			
occurrences (all)	0			
Bile acid malabsorption				
subjects affected / exposed	0 / 12 (0.00%)			
occurrences (all)	0			

Vomiting			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Erosive oesophagitis			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Acquired oesophageal web			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Oesophageal obstruction			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Gastric ulcer			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Hepatobiliary disorders			
Hepatic steatosis			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Skin and subcutaneous tissue disorders			
Excessive granulation tissue			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Skin lesion			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Petechiae			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Acne			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Skin odour abnormal			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Rash			

subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0		
Renal and urinary disorders Nephrolithiasis subjects affected / exposed occurrences (all) Urinary hesitation subjects affected / exposed occurrences (all)	 0 / 12 (0.00%) 0 0 / 12 (0.00%) 0		
Endocrine disorders Hypothyroidism subjects affected / exposed occurrences (all)	 0 / 12 (0.00%) 0		
Musculoskeletal and connective tissue disorders Back pain subjects affected / exposed occurrences (all) Femoroacetabular impingement subjects affected / exposed occurrences (all) Joint effusion subjects affected / exposed occurrences (all) Muscle contracture subjects affected / exposed occurrences (all) Myalgia subjects affected / exposed occurrences (all) Pain in extremity subjects affected / exposed occurrences (all) Arthralgia subjects affected / exposed occurrences (all) Tendonitis	 0 / 12 (0.00%) 0 0 / 12 (0.00%) 0 0 / 12 (0.00%) 0 0 / 12 (0.00%) 0 0 / 12 (0.00%) 0 0 / 12 (0.00%) 0 0 / 12 (0.00%) 0		

subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Bursitis			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	2		
Osteochondrosis			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Upper respiratory tract infection			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Nasopharyngitis			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
COVID-19			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Gastroenteritis viral			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Pharyngitis streptococcal			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Pharyngitis			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Fungal skin infection			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Folliculitis			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		

Sinusitis				
subjects affected / exposed	0 / 12 (0.00%)			
occurrences (all)	0			
Ear infection				
subjects affected / exposed	0 / 12 (0.00%)			
occurrences (all)	0			
Diarrhoea infectious				
subjects affected / exposed	0 / 12 (0.00%)			
occurrences (all)	0			
Cellulitis				
subjects affected / exposed	0 / 12 (0.00%)			
occurrences (all)	0			
Bronchitis				
subjects affected / exposed	0 / 12 (0.00%)			
occurrences (all)	0			
Influenza				
subjects affected / exposed	0 / 12 (0.00%)			
occurrences (all)	0			
Epstein-Barr virus infection				
subjects affected / exposed	0 / 12 (0.00%)			
occurrences (all)	0			
Viral upper respiratory tract infection				
subjects affected / exposed	0 / 12 (0.00%)			
occurrences (all)	0			
Viral infection				
subjects affected / exposed	0 / 12 (0.00%)			
occurrences (all)	0			
Pneumonia				
subjects affected / exposed	0 / 12 (0.00%)			
occurrences (all)	0			
Vulvovaginal mycotic infection				
subjects affected / exposed	0 / 12 (0.00%)			
occurrences (all)	0			
Vulvovaginal candidiasis				
subjects affected / exposed	0 / 12 (0.00%)			
occurrences (all)	0			

Tonsillitis subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0		
Tooth abscess subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0		
Tooth infection subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0		
Hordeolum subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0		
Metabolism and nutrition disorders Vitamin D deficiency subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0		
Hypophosphataemia subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0		
Decreased appetite subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0		
Hyperkalaemia subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported