



Clinical trial results:

A Phase 2b, multicenter, randomized, double-blind, placebo-controlled, parallel-group study to evaluate the efficacy, safety, and tolerability of cenerimod in subjects with moderate to severe systemic lupus erythematosus (SLE)

Summary

EudraCT number	2018-001808-11
Trial protocol	FR GB DE ES HU BG PL GR IT RO
Global end of trial date	25 August 2022

Results information

Result version number	v1 (current)
This version publication date	23 August 2023
First version publication date	23 August 2023

Trial information

Trial identification

Sponsor protocol code	ID-064A202
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03742037
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Idorsia Pharmaceuticals Ltd
Sponsor organisation address	Hegenheimermattweg 91, Allschwil, Switzerland, 4123
Public contact	Idorsia Clinical Trial Information, Idorsia Pharmaceuticals Ltd, +41 58 844 1977, idorsiaclinicaltrials@idorsia.com
Scientific contact	Idorsia Clinical Trial Information, Idorsia Pharmaceuticals Ltd, +41 58 844 1977, idorsiaclinicaltrials@idorsia.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	25 August 2022
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	25 August 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the efficacy of 6 months' cenerimod treatment given at 4 different dose levels (0.5, 1, 2, and 4 mg once daily) on disease activity in adult subjects with moderate to severe SLE concurrently receiving background therapy.

Protection of trial subjects:

Prior to the start of the study, each study site consulted an Independent Ethics Committee (IEC) or Institutional Review Board (IRB), i.e., a review panel that was responsible for ensuring the protection of the rights, safety, and well-being of human subjects involved in a clinical investigation. The protocol and any materials provided to the subject (such as a subject information sheet or description of the study used to obtain informed consent) were reviewed and approved by the appropriate IEC or IRB before the study was started. Sponsor personnel and the investigators were required to conduct the study in full compliance with ICH-GCP Guidelines, the principles of the Declaration of Helsinki, and with the laws and regulations in the country in which the study is conducted. The sponsor had the right to terminate the study at any time globally or locally. The investigators had the right to terminate the participation of their site in the study at any time. The investigator was responsible for protecting the subject's best interests. Study-specific criteria for discontinuation were described in the protocol. The investigators were responsible for maintaining the subjects' identities in strictest confidence. Written informed consent was required to be obtained from each individual participating in the study prior to any study procedure and after adequate explanation of the aims, methods, objectives, and potential hazards of the study. It was made clear to each subject that he or she was completely free to refuse to enter the study, or to withdraw from the study at any time for any reason.

Background therapy:

To be eligible for this study, subjects must have been on stable doses of one or more of the following systemic lupus erythematosus (SLE) background medications:

- Non-steroidal anti-inflammatory drugs,
- Anti-malarials,
- Mycophenolate mofetil,
- Mycophenolic acid,
- Azathioprine,
- Methotrexate,
- Corticosteroids,
- Belimumab.

Treatment with anti-malarials, mycophenolate mofetil, mycophenolic acid, azathioprine, methotrexate or belimumab must have been started at least 90 days prior to Screening. All other background SLE therapies must have been started at least 30 days prior to Screening.

Background SLE therapy doses must be stable for at least 30 days prior to Randomization. For corticosteroids, doses must be stable for at least 15 days prior to Randomization

Evidence for comparator: -

Actual start date of recruitment	21 December 2018
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Poland: 21
Country: Number of subjects enrolled	Spain: 7
Country: Number of subjects enrolled	United Kingdom: 3
Country: Number of subjects enrolled	Bulgaria: 13
Country: Number of subjects enrolled	Czech Republic: 7
Country: Number of subjects enrolled	France: 1
Country: Number of subjects enrolled	Greece: 1
Country: Number of subjects enrolled	Italy: 4
Country: Number of subjects enrolled	Romania: 2
Country: Number of subjects enrolled	Chile: 18
Country: Number of subjects enrolled	Georgia: 15
Country: Number of subjects enrolled	Israel: 2
Country: Number of subjects enrolled	Mexico: 39
Country: Number of subjects enrolled	Philippines: 27
Country: Number of subjects enrolled	Russian Federation: 24
Country: Number of subjects enrolled	Taiwan: 2
Country: Number of subjects enrolled	Thailand: 2
Country: Number of subjects enrolled	Turkey: 1
Country: Number of subjects enrolled	Ukraine: 150
Country: Number of subjects enrolled	United States: 88
Worldwide total number of subjects	427
EEA total number of subjects	59

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)	415
From 65 to 84 years	12
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was done from 21 December 2018 to 25 August 2022.

Pre-assignment

Screening details:

427 participants are considered to be enrolled in the study and were randomized to study treatment.

Period 1

Period 1 title	Treatment period 1 (TP1)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Cenerimod 0.5 mg

Arm description:

Subjects received cenerimod 0.5 mg once daily in addition to background SLE therapy for up to 6 months in treatment period 1.

Arm type	Experimental
Investigational medicinal product name	Cenerimod
Investigational medicinal product code	ACT-334441
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

One tablet of cenerimod was taken once daily, preferably in the morning.

Arm title	Cenerimod 1 mg
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Arm description:

Subjects received cenerimod 1 mg once daily in addition to background SLE therapy for up to 6 months in treatment period 1.

Arm type	Experimental
Investigational medicinal product name	Cenerimod
Investigational medicinal product code	ACT-334441
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

One tablet of cenerimod was taken once daily, preferably in the morning.

Arm title	Cenerimod 2 mg
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Arm description:

Subjects received cenerimod 2 mg once daily in addition to background SLE therapy for up to 6 months in treatment period 1.

Arm type	Experimental
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Investigational medicinal product name	Cenerimod
Investigational medicinal product code	ACT-334441
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use
Dosage and administration details:	
One tablet of cenerimod was taken once daily, preferably in the morning.	
Arm title	Cenerimod 4 mg

Arm description:

Subjects received cenerimod 4 mg once daily in addition to background SLE therapy for up to 6 months in treatment period 1.

Arm type	Experimental
Investigational medicinal product name	Cenerimod
Investigational medicinal product code	ACT-334441
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use
Dosage and administration details:	
One tablet of cenerimod was taken once daily, preferably in the morning.	
Arm title	Placebo

Arm description:

Subjects were randomized to receive placebo once daily in addition to background SLE therapy for up to 6 months.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use
Dosage and administration details:	
Subjects received placebo, with the same excipients but without the active ingredient cenerimod, tablets once daily preferably in the morning.	

Number of subjects in period 1	Cenerimod 0.5 mg	Cenerimod 1 mg	Cenerimod 2 mg
Started	85	85	86
Completed	78	78	71
Not completed	7	7	15
Adverse event, serious fatal	-	1	-
Consent withdrawn by subject	4	1	2
pre-specified criteria	1	3	7
Adverse event, non-fatal	-	1	4
No study treatment administered	-	-	-
Other reasons	2	-	2
Lost to follow-up	-	1	-
Lack of efficacy	-	-	-

Number of subjects in period 1	Cenerimod 4 mg	Placebo
Started	85	86
Completed	70	77
Not completed	15	9
Adverse event, serious fatal	-	-
Consent withdrawn by subject	2	4
pre-specified criteria	6	1
Adverse event, non-fatal	3	2
No study treatment administered	1	-
Other reasons	2	1
Lost to follow-up	1	-
Lack of efficacy	-	1

Period 2

Period 2 title	Treatment period 2 (TP2)
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Cenerimod 0.5 mg

Arm description:

Subjects completing treatment period 1 continued to receive cenerimod 0.5 mg once daily in addition to background SLE therapy during treatment period 2 for up to an additional 6 months.

Arm type	Experimental
Investigational medicinal product name	Cenerimod
Investigational medicinal product code	ACT-334441
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

One tablet of cenerimod was taken once daily, preferably in the morning.

Arm title	Cenerimod 1 mg
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Arm description:

Subjects completing treatment period 1 continued to receive cenerimod 1 mg once daily in addition to background SLE therapy during treatment period 2 for up to an additional 6 months.

Arm type	Experimental
Investigational medicinal product name	Cenerimod
Investigational medicinal product code	ACT-334441
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

One tablet of cenerimod was taken once daily, preferably in the morning.

Arm title	Cenerimod 2 mg
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Arm description:

Subjects completing treatment period 1 continued to receive cenerimod 2 mg once daily in addition to background SLE therapy during treatment period 2 for up to an additional 6 months.

Arm type	Experimental
Investigational medicinal product name	Cenerimod
Investigational medicinal product code	ACT-334441
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

One tablet of cenerimod was taken once daily, preferably in the morning.

Arm title	Cenerimod 2 mg (Ex 4 mg)
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Arm description:

Half the subjects completing treatment with cenerimod 4 mg in treatment period 1 were re-randomized to cenerimod 2 mg once daily in addition to background SLE therapy during treatment period 2. Subjects received cenerimod 2 mg for up to 6 months.

Arm type	Experimental
Investigational medicinal product name	Cenerimod
Investigational medicinal product code	ACT-334441
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

One tablet of cenerimod was taken once daily, preferably in the morning.

Arm title	Placebo (Ex 4 mg)
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Arm description:

Half the subjects completing treatment with cenerimod 4 mg in treatment period 1 were re-randomized to placebo once daily in addition to background SLE therapy during treatment period 2. Subjects received placebo for up to 6 months.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Matching placebo identical to the cenerimod tablet was taken once daily, preferably in the morning.

Arm title	Placebo
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Arm description:

Subjects completing treatment period 1 continued to receive placebo once daily in addition to background SLE therapy during treatment period 2 for up to an additional 6 months.

Arm type	Placebo
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Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Matching placebo identical to the cenerimod tablet was taken once daily, preferably in the morning.

Number of subjects in period 2	Cenerimod 0.5 mg	Cenerimod 1 mg	Cenerimod 2 mg
Started	78	78	71
Completed	74	74	59
Not completed	4	4	12
Consent withdrawn by subject	-	-	2
pre-specified criteria	-	1	3
Adverse event, non-fatal	1	2	3
Other reasons	2	-	2
Lost to follow-up	-	1	2
Lack of efficacy	1	-	-

Number of subjects in period 2	Cenerimod 2 mg (Ex 4 mg)	Placebo (Ex 4 mg)	Placebo
Started	35	35	77
Completed	30	35	68
Not completed	5	0	9
Consent withdrawn by subject	2	-	1
pre-specified criteria	2	-	2
Adverse event, non-fatal	1	-	4
Other reasons	-	-	1
Lost to follow-up	-	-	-
Lack of efficacy	-	-	1

Baseline characteristics

Reporting groups

Reporting group title	Cenerimod 0.5 mg
Reporting group description: Subjects received cenerimod 0.5 mg once daily in addition to background SLE therapy for up to 6 months in treatment period 1.	
Reporting group title	Cenerimod 1 mg
Reporting group description: Subjects received cenerimod 1 mg once daily in addition to background SLE therapy for up to 6 months in treatment period 1.	
Reporting group title	Cenerimod 2 mg
Reporting group description: Subjects received cenerimod 2 mg once daily in addition to background SLE therapy for up to 6 months in treatment period 1.	
Reporting group title	Cenerimod 4 mg
Reporting group description: Subjects received cenerimod 4 mg once daily in addition to background SLE therapy for up to 6 months in treatment period 1.	
Reporting group title	Placebo
Reporting group description: Subjects were randomized to receive placebo once daily in addition to background SLE therapy for up to 6 months.	

Reporting group values	Cenerimod 0.5 mg	Cenerimod 1 mg	Cenerimod 2 mg
Number of subjects	85	85	86
Age categorical Units: Subjects			
Between 18 and 45 years	49	54	49
Between 45 and 64 years	31	29	36
Between 64 and 75 years	5	2	1
Age continuous Units: years			
arithmetic mean	42.8	40.0	42.2
standard deviation	± 12.41	± 12.77	± 12.06
Gender categorical Units: Subjects			
Female	79	83	80
Male	6	2	6
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	5	3	6
Asian	5	9	7
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	3	6	8
White	72	67	65
Unknown or Not Reported	0	0	0
Ethnicity Units: Subjects			
Hispanic or Latino	16	17	18

Not Hispanic or Latino	69	68	68
Unknown or Not Reported	0	0	0

Body Mass Index			
Units: kilogram(s)/square metre			
arithmetic mean	25.67	25.55	26.16
standard deviation	± 5.67	± 5.95	± 6.6
modified SLEDAI-2K at baseline			
The SLEDAI-2K is a weighted, cumulative index of lupus disease activity scored by the physician. It is calculated from 24 individual descriptors across 9 organ systems, 0 indicates inactive disease and the maximum theoretical score is 105 (Gladman D et al. J Rheumatol 2002;29;288-291). In this study the SLEDAI-2K was modified, to exclude leucopenia (1 point), due to the mechanism of action of cenerimod. A score of 6 or greater is clinically relevant and associated with requiring lupus-directed therapy (Nuttall A et al. Best Pract Res Clin Rheumatol. 2013 Jun; 27(3):309-18).			
Units: Units of a scale			
arithmetic mean	9.8	10.1	9.5
standard deviation	± 2.69	± 3.71	± 2.88

Reporting group values	Cenerimod 4 mg	Placebo	Total
Number of subjects	85	86	427
Age categorical			
Units: Subjects			
Between 18 and 45 years	50	57	259
Between 45 and 64 years	33	27	156
Between 64 and 75 years	2	2	12
Age continuous			
Units: years			
arithmetic mean	42.1	41.0	-
standard deviation	± 10.44	± 11.94	-
Gender categorical			
Units: Subjects			
Female	82	82	406
Male	3	4	21
Race (NIH/OMB)			
Units: Subjects			
American Indian or Alaska Native	1	3	18
Asian	6	6	33
Native Hawaiian or Other Pacific Islander	0	1	1
Black or African American	10	6	33
White	65	68	337
Unknown or Not Reported	3	2	5
Ethnicity			
Units: Subjects			
Hispanic or Latino	19	19	89
Not Hispanic or Latino	65	66	336
Unknown or Not Reported	1	1	2
Body Mass Index			
Units: kilogram(s)/square metre			
arithmetic mean	26.82	26.49	-
standard deviation	± 7.15	± 6.24	-
modified SLEDAI-2K at baseline			
The SLEDAI-2K is a weighted, cumulative index of lupus disease activity scored by the physician. It is			

calculated from 24 individual descriptors across 9 organ systems, 0 indicates inactive disease and the maximum theoretical score is 105 (Gladman D et al. J Rheumatol 2002;29;288-291). In this study the SLEDAI-2K was modified, to exclude leucopenia (1 point), due to the mechanism of action of cenerimod. A score of 6 or greater is clinically relevant and associated with requiring lupus-directed therapy (Nuttall A et al. Best Pract Res Clin Rheumatol. 2013 Jun; 27(3):309-18).

Units: Units of a scale			
arithmetic mean	10.0	10.2	
standard deviation	± 2.50	± 3.05	-

End points

End points reporting groups

Reporting group title	Cenerimod 0.5 mg
Reporting group description: Subjects received cenerimod 0.5 mg once daily in addition to background SLE therapy for up to 6 months in treatment period 1.	
Reporting group title	Cenerimod 1 mg
Reporting group description: Subjects received cenerimod 1 mg once daily in addition to background SLE therapy for up to 6 months in treatment period 1.	
Reporting group title	Cenerimod 2 mg
Reporting group description: Subjects received cenerimod 2 mg once daily in addition to background SLE therapy for up to 6 months in treatment period 1.	
Reporting group title	Cenerimod 4 mg
Reporting group description: Subjects received cenerimod 4 mg once daily in addition to background SLE therapy for up to 6 months in treatment period 1.	
Reporting group title	Placebo
Reporting group description: Subjects were randomized to receive placebo once daily in addition to background SLE therapy for up to 6 months.	
Reporting group title	Cenerimod 0.5 mg
Reporting group description: Subjects completing treatment period 1 continued to receive cenerimod 0.5 mg once daily in addition to background SLE therapy during treatment period 2 for up to an additional 6 months.	
Reporting group title	Cenerimod 1 mg
Reporting group description: Subjects completing treatment period 1 continued to receive cenerimod 1 mg once daily in addition to background SLE therapy during treatment period 2 for up to an additional 6 months.	
Reporting group title	Cenerimod 2 mg
Reporting group description: Subjects completing treatment period 1 continued to receive cenerimod 2 mg once daily in addition to background SLE therapy during treatment period 2 for up to an additional 6 months.	
Reporting group title	Cenerimod 2 mg (Ex 4 mg)
Reporting group description: Half the subjects completing treatment with cenerimod 4 mg in treatment period 1 were re-randomized to cenerimod 2 mg once daily in addition to background SLE therapy during treatment period 2. Subjects received cenerimod 2 mg for up to 6 months.	
Reporting group title	Placebo (Ex 4 mg)
Reporting group description: Half the subjects completing treatment with cenerimod 4 mg in treatment period 1 were re-randomized to placebo once daily in addition to background SLE therapy during treatment period 2. Subjects received placebo for up to 6 months.	
Reporting group title	Placebo
Reporting group description: Subjects completing treatment period 1 continued to receive placebo once daily in addition to background SLE therapy during treatment period 2 for up to an additional 6 months.	

Primary: Change From Baseline to Month 6 in the Modified Systemic Lupus Erythematosus Activity Index 2000 (mSLEDAI-2K) Score

End point title	Change From Baseline to Month 6 in the Modified Systemic Lupus Erythematosus Activity Index 2000 (mSLEDAI-2K) Score
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End point description:

The primary endpoint is the absolute change from baseline in the modified Systemic Lupus Erythematosus Activity Index 2000 (mSLEDAI-2K) score. The SLEDAI-2K is a weighted, cumulative index of lupus disease activity scored by the physician and is calculated from 24 individual descriptors and measures disease activity within the last 10 days. In this study the SLEDAI-2K was modified, to exclude leucopenia, due to the mechanism of action of cenerimod. Improvement in systemic lupus erythematosus disease activity is defined as a reduction in SLEDAI-2K score of greater than or equal to 4. A decreased score, i.e., a negative change indicates an improvement in systemic lupus erythematosus disease activity from baseline to month 6.

End point type	Primary
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End point timeframe:

Baseline (Day 1) and Month 6.

End point values	Cenerimod 0.5 mg	Cenerimod 1 mg	Cenerimod 2 mg	Cenerimod 4 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	85	85	86	85
Units: score on a scale				
least squares mean (confidence interval 95%)	-3.24 (-3.98 to -2.49)	-3.41 (-4.16 to -2.67)	-2.84 (-3.58 to -2.09)	-4.04 (-4.79 to -3.28)

End point values	Placebo			
Subject group type	Reporting group			
Number of subjects analysed	86			
Units: score on a scale				
least squares mean (confidence interval 95%)	-2.85 (-3.60 to -2.10)			

Statistical analyses

Statistical analysis title	mSLEDAI analysis: TP1 cenerimod 0.5 mg and placebo
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Statistical analysis description:

The analysis was performed on the Full Analysis Set (FAS). The FAS included all participants who were randomized. Baseline was defined as the last measurement before randomization.

Comparison groups	Cenerimod 0.5 mg v Placebo
Number of subjects included in analysis	171
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4749
Method	Mixed models analysis
Parameter estimate	LS mean difference to placebo
Point estimate	-0.39

Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.45
upper limit	0.68
Variability estimate	Standard error of the mean
Dispersion value	0.54

Statistical analysis title	mSLEDAI analysis: TP1 cenerimod 1 mg and placebo
Comparison groups	Cenerimod 1 mg v Placebo
Number of subjects included in analysis	171
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2941
Method	Mixed models analysis
Parameter estimate	LS Mean difference to placebo
Point estimate	-0.57
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.62
upper limit	0.49
Variability estimate	Standard error of the mean
Dispersion value	0.54

Statistical analysis title	mSLEDAI analysis: TP1 cenerimod 2 mg and placebo
Comparison groups	Cenerimod 2 mg v Placebo
Number of subjects included in analysis	172
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9802
Method	Mixed models analysis
Parameter estimate	LS mean difference to placebo
Point estimate	0.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.05
upper limit	1.08
Variability estimate	Standard error of the mean
Dispersion value	0.54

Statistical analysis title	mSLEDAI analysis: TP1 cenerimod 4 mg and placebo
Comparison groups	Cenerimod 4 mg v Placebo

Number of subjects included in analysis	171
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0291
Method	Mixed models analysis
Parameter estimate	LS Mean difference to placebo
Point estimate	-1.19
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.25
upper limit	-0.12
Variability estimate	Standard error of the mean
Dispersion value	0.54

Secondary: Response on Systemic Lupus Erythematosus Responder Index 4 (SRI-4) at Month 6 as Compared to Baseline

End point title	Response on Systemic Lupus Erythematosus Responder Index 4 (SRI-4) at Month 6 as Compared to Baseline
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End point description:

A responder could only be assessed if the full information of all body systems was available. A participant was defined as a responder based on the Systemic Lupus Erythematosus Responder Index 4 (SRI-4) was a composite, binary endpoint based on three variables:

- mSLEDAI-2K score had to have a reduction from baseline greater than or equal to 4,
- Physician Global Assessment (PGA) had to have an increase from baseline less than or equal to 0.3. The PGA is a 100 mm visual analog scale used by the physician to assess disease activity ranging for 0 to 3. The scale is anchored with values from 0 = "none" and 3 = "severe"), and
- BILAG-2004 (no new BILAG A organ domain score and at most one new BILAG B organ domain score) compared with baseline.

If one of the SRI-4 mSLEDAI-2K, PGA and BILAG variables were not met the subject was scored a non-responder.

Subjects that did not fit at least one of the above criteria were assigned to the missing group.

End point type	Secondary
End point timeframe:	
Baseline (Day 1) and Month 6	

End point values	Cenerimod 0.5 mg	Cenerimod 1 mg	Cenerimod 2 mg	Cenerimod 4 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	85	85	86	85
Units: number of subjects				
Responder	36	41	38	41
Non-responder	45	38	41	36
Missing	4	6	7	8

End point values	Placebo			
Subject group type	Reporting group			
Number of subjects analysed	86			
Units: number of subjects				
Responder	34			
Non-responder	43			
Missing	9			

Statistical analyses

Statistical analysis title	SRI-4 analysis: TP1 cenerimod 0.5 mg and placebo
Statistical analysis description:	
A generalized mixed effects model for repeated measures was applied to the SRI-4 response from Month 1 through 6 with treatment group, month, treatment group by month interaction, and stratification factors (oral corticosteroids dose and mSLEDAI-2K) as fixed effects and subject as random effect.	
Comparison groups	Cenerimod 0.5 mg v Placebo
Number of subjects included in analysis	171
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.974
Method	Mixed models analysis
Parameter estimate	Odds ratio (OR)
Point estimate	1.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.54
upper limit	1.9

Statistical analysis title	SRI-4 analysis: TP1 cenerimod 1 mg and placebo
Statistical analysis description:	
A generalized mixed effects model for repeated measures was applied to the SRI-4 response from Month 1 through 6 with treatment group, month, treatment group by month interaction, and stratification factors (oral corticosteroids dose and mSLEDAI-2K) as fixed effects and subject as random effect..	
Comparison groups	Cenerimod 1 mg v Placebo
Number of subjects included in analysis	171
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2845
Method	Mixed models analysis
Parameter estimate	Odds ratio (OR)
Point estimate	1.41
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.75
upper limit	2.65

Statistical analysis title	SRI-4 analysis: TP1 cenerimod 2 mg and placebo
Statistical analysis description: A generalized mixed effects model for repeated measures was applied to the SRI-4 response from Month 1 through 6 with treatment group, month, treatment group by month interaction, and stratification factors (oral corticosteroids dose and mSLEDAI-2K) as fixed effects and subject as random effect.	
Comparison groups	Cenerimod 2 mg v Placebo
Number of subjects included in analysis	172
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5115
Method	Mixed models analysis
Parameter estimate	Odds ratio (OR)
Point estimate	1.23
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.66
upper limit	2.32

Statistical analysis title	SRI-4 analysis: TP1 cenerimod 4 mg and placebo
Statistical analysis description: A generalized mixed effects model for repeated measures was applied to the SRI-4 response from Month 1 through 6 with treatment group, month, treatment group by month interaction, and stratification factors (oral corticosteroids dose and mSLEDAI-2K) as fixed effects and subject as random effect.	
Comparison groups	Cenerimod 4 mg v Placebo
Number of subjects included in analysis	171
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2408
Method	Mixed models analysis
Parameter estimate	Odds ratio (OR)
Point estimate	1.46
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.77
upper limit	2.76

Secondary: British Isles Lupus Assessment Group-2004 (BILAG) disease activity index response at Month 6

End point title	British Isles Lupus Assessment Group-2004 (BILAG) disease activity index response at Month 6
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End point description:

The British Isles Lupus Assessment Group-2004 (BILAG) is a comprehensive tool used by the physician to assess disease activity and is sensitive to small changes over time.

Response (no worsening) at Month 6 on BILAG-2004 disease activity index was defined as no new BILAG A organ domain score and no more than one new BILAG B organ domain score compared with baseline.

No analysis is reported because the model did not meet the convergence criteria.

End point type	Secondary
End point timeframe:	
Baseline (Day 1) and Month 6	

End point values	Cenerimod 0.5 mg	Cenerimod 1 mg	Cenerimod 2 mg	Cenerimod 4 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	81	79	79	77
Units: Percentage of subjects				
number (not applicable)	98.8	98.7	97.5	98.7

End point values	Placebo			
Subject group type	Reporting group			
Number of subjects analysed	77			
Units: Percentage of subjects				
number (not applicable)	97.4			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to 18 months after first intake of medication after randomization. Adverse Events (AEs) were defined as those AEs with onset on or after the first day, treatment-emergent, to the last day of double-blind study treatment intake plus 6 months.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
Dictionary version	25.0

Reporting groups

Reporting group title	Cenerimod 0.5 mg
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Reporting group description:

Subjects received cenerimod 0.5 mg once daily in addition to background SLE therapy for up to 6 months in treatment period 1. Subjects completing treatment period 1 continued with cenerimod 0.5 mg once daily in addition to background SLE therapy during treatment period 2 for up to an additional 6 months.

Reporting group title	Cenerimod 1 mg
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Reporting group description:

Subjects received cenerimod 1 mg once daily in addition to background SLE therapy for up to 6 months in treatment period 1. Subjects completing treatment period 1 continued to receive cenerimod 1 mg once daily in addition to background SLE therapy during treatment period 2 for up to an additional 6 months.

Reporting group title	Cenerimod 2 mg
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Reporting group description:

Subjects received cenerimod 2 mg once daily in addition to background SLE therapy for up to 6 months in treatment period 1. Subjects completing treatment period 1 continued to receive cenerimod 2 mg once daily in addition to background SLE therapy during treatment period 2 for up to an additional 6 months.

Reporting group title	Placebo
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Reporting group description:

Subjects received placebo once daily in addition to background SLE therapy for up to 6 months in treatment period 1. Subjects completing treatment period 1 continued with placebo once daily in addition to background SLE therapy during treatment period 2 for up to an additional 6 months.

Reporting group title	Placebo / Ex-4 mg
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Reporting group description:

Subjects received placebo once daily in addition to background SLE therapy for up to 6 months in treatment period 2. (These participants previously received cenerimod 4 mg once daily in addition to background SLE therapy for 6 months in treatment period 1).

Reporting group title	Not re-randomized / Ex-4 mg
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Reporting group description:

Subjects were not re-randomized and did not receive treatment in treatment period 2. (These subjects previously received cenerimod 4 mg once daily in addition to background SLE therapy for 6 months in treatment period 1).

Reporting group title	Cenerimod 2 mg / Ex-4 mg
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Reporting group description:

Subjects received cenerimod 2 mg once daily in addition to background SLE therapy for up to 6 months in treatment period 2. (These subjects previously received cenerimod 4 mg once daily in addition to background SLE therapy for 6 months in treatment period 1).

Serious adverse events	Cenerimod 0.5 mg	Cenerimod 1 mg	Cenerimod 2 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 84 (4.76%)	12 / 85 (14.12%)	4 / 87 (4.60%)
number of deaths (all causes)	0	2	0
number of deaths resulting from adverse events	0	2	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Benign ovarian tumour			
subjects affected / exposed	0 / 84 (0.00%)	1 / 85 (1.18%)	0 / 87 (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
Meningioma			
subjects affected / exposed	0 / 84 (0.00%)	1 / 85 (1.18%)	0 / 87 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metastases to liver			
subjects affected / exposed	0 / 84 (0.00%)	0 / 85 (0.00%)	0 / 87 (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
Ovarian cancer			
subjects affected / exposed	0 / 84 (0.00%)	0 / 85 (0.00%)	0 / 87 (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
Papillary thyroid cancer			
subjects affected / exposed	0 / 84 (0.00%)	0 / 85 (0.00%)	0 / 87 (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
Vascular disorders			
Hypertensive emergency			
subjects affected / exposed	0 / 84 (0.00%)	0 / 85 (0.00%)	0 / 87 (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
Reproductive system and breast disorders			
Ovarian cyst			

subjects affected / exposed	0 / 84 (0.00%)	0 / 85 (0.00%)	0 / 87 (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
Respiratory, thoracic and mediastinal disorders			
Pleural effusion			
subjects affected / exposed	0 / 84 (0.00%)	1 / 85 (1.18%)	0 / 87 (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
Pulmonary embolism			
subjects affected / exposed	0 / 84 (0.00%)	0 / 85 (0.00%)	1 / 87 (1.15%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Femoral neck fracture			
subjects affected / exposed	0 / 84 (0.00%)	1 / 85 (1.18%)	0 / 87 (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
Cardiac disorders			
Acute coronary syndrome			
subjects affected / exposed	0 / 84 (0.00%)	2 / 85 (2.35%)	0 / 87 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Angina pectoris			
subjects affected / exposed	0 / 84 (0.00%)	1 / 85 (1.18%)	0 / 87 (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
Nervous system disorders			
Loss of consciousness			
subjects affected / exposed	0 / 84 (0.00%)	0 / 85 (0.00%)	1 / 87 (1.15%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Duodenal perforation			

subjects affected / exposed	0 / 84 (0.00%)	1 / 85 (1.18%)	0 / 87 (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
Gastric haemorrhage			
subjects affected / exposed	0 / 84 (0.00%)	0 / 85 (0.00%)	1 / 87 (1.15%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 84 (0.00%)	1 / 85 (1.18%)	0 / 87 (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
Haematemesis			
subjects affected / exposed	0 / 84 (0.00%)	0 / 85 (0.00%)	1 / 87 (1.15%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper gastrointestinal haemorrhage			
subjects affected / exposed	1 / 84 (1.19%)	1 / 85 (1.18%)	0 / 87 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Hepatobiliary disorders			
Hepatic mass			
subjects affected / exposed	0 / 84 (0.00%)	1 / 85 (1.18%)	0 / 87 (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
Skin and subcutaneous tissue disorders			
Systemic lupus erythematosus rash			
subjects affected / exposed	0 / 84 (0.00%)	1 / 85 (1.18%)	0 / 87 (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
Cutaneous vasculitis			
subjects affected / exposed	0 / 84 (0.00%)	0 / 85 (0.00%)	0 / 87 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue			

disorders			
Systemic lupus erythematosus			
subjects affected / exposed	0 / 84 (0.00%)	2 / 85 (2.35%)	0 / 87 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
COVID-19 pneumonia			
subjects affected / exposed	1 / 84 (1.19%)	2 / 85 (2.35%)	0 / 87 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COVID-19			
subjects affected / exposed	0 / 84 (0.00%)	2 / 85 (2.35%)	0 / 87 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Herpes zoster			
subjects affected / exposed	0 / 84 (0.00%)	0 / 85 (0.00%)	1 / 87 (1.15%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebral toxoplasmosis			
subjects affected / exposed	0 / 84 (0.00%)	0 / 85 (0.00%)	0 / 87 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	0 / 84 (0.00%)	0 / 85 (0.00%)	0 / 87 (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
Pneumonia			
subjects affected / exposed	1 / 84 (1.19%)	1 / 85 (1.18%)	0 / 87 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis			
subjects affected / exposed	0 / 84 (0.00%)	0 / 85 (0.00%)	1 / 87 (1.15%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Metabolism and nutrition disorders			
Hypoglycaemia			
subjects affected / exposed	1 / 84 (1.19%)	0 / 85 (0.00%)	0 / 87 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Placebo	Placebo / Ex-4 mg	Not re-randomized / Ex-4 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 86 (6.98%)	0 / 35 (0.00%)	2 / 14 (14.29%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Benign ovarian tumour			
subjects affected / exposed	0 / 86 (0.00%)	0 / 35 (0.00%)	0 / 14 (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
Meningioma			
subjects affected / exposed	0 / 86 (0.00%)	0 / 35 (0.00%)	0 / 14 (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
Metastases to liver			
subjects affected / exposed	1 / 86 (1.16%)	0 / 35 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ovarian cancer			
subjects affected / exposed	1 / 86 (1.16%)	0 / 35 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Papillary thyroid cancer			
subjects affected / exposed	1 / 86 (1.16%)	0 / 35 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Hypertensive emergency			

subjects affected / exposed	0 / 86 (0.00%)	0 / 35 (0.00%)	0 / 14 (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
Reproductive system and breast disorders			
Ovarian cyst			
subjects affected / exposed	0 / 86 (0.00%)	0 / 35 (0.00%)	1 / 14 (7.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Pleural effusion			
subjects affected / exposed	0 / 86 (0.00%)	0 / 35 (0.00%)	0 / 14 (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
Pulmonary embolism			
subjects affected / exposed	0 / 86 (0.00%)	0 / 35 (0.00%)	0 / 14 (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
Injury, poisoning and procedural complications			
Femoral neck fracture			
subjects affected / exposed	0 / 86 (0.00%)	0 / 35 (0.00%)	0 / 14 (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
Cardiac disorders			
Acute coronary syndrome			
subjects affected / exposed	0 / 86 (0.00%)	0 / 35 (0.00%)	0 / 14 (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
Angina pectoris			
subjects affected / exposed	0 / 86 (0.00%)	0 / 35 (0.00%)	0 / 14 (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
Nervous system disorders			
Loss of consciousness			

subjects affected / exposed	0 / 86 (0.00%)	0 / 35 (0.00%)	0 / 14 (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
Gastrointestinal disorders			
Duodenal perforation			
subjects affected / exposed	0 / 86 (0.00%)	0 / 35 (0.00%)	0 / 14 (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
Gastric haemorrhage			
subjects affected / exposed	0 / 86 (0.00%)	0 / 35 (0.00%)	0 / 14 (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
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 86 (0.00%)	0 / 35 (0.00%)	0 / 14 (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
Haematemesis			
subjects affected / exposed	0 / 86 (0.00%)	0 / 35 (0.00%)	0 / 14 (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
Upper gastrointestinal haemorrhage			
subjects affected / exposed	0 / 86 (0.00%)	0 / 35 (0.00%)	0 / 14 (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
Hepatobiliary disorders			
Hepatic mass			
subjects affected / exposed	0 / 86 (0.00%)	0 / 35 (0.00%)	0 / 14 (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
Skin and subcutaneous tissue disorders			
Systemic lupus erythematosus rash			
subjects affected / exposed	0 / 86 (0.00%)	0 / 35 (0.00%)	0 / 14 (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

Cutaneous vasculitis			
subjects affected / exposed	1 / 86 (1.16%)	0 / 35 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Systemic lupus erythematosus			
subjects affected / exposed	1 / 86 (1.16%)	0 / 35 (0.00%)	1 / 14 (7.14%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
COVID-19 pneumonia			
subjects affected / exposed	1 / 86 (1.16%)	0 / 35 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COVID-19			
subjects affected / exposed	0 / 86 (0.00%)	0 / 35 (0.00%)	0 / 14 (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
Herpes zoster			
subjects affected / exposed	0 / 86 (0.00%)	0 / 35 (0.00%)	0 / 14 (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
Cerebral toxoplasmosis			
subjects affected / exposed	1 / 86 (1.16%)	0 / 35 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	0 / 86 (0.00%)	0 / 35 (0.00%)	1 / 14 (7.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 86 (0.00%)	0 / 35 (0.00%)	0 / 14 (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

Pyelonephritis			
subjects affected / exposed	0 / 86 (0.00%)	0 / 35 (0.00%)	0 / 14 (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
Metabolism and nutrition disorders			
Hypoglycaemia			
subjects affected / exposed	0 / 86 (0.00%)	0 / 35 (0.00%)	0 / 14 (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	Cenerimod 2 mg / Ex-4 mg		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 35 (2.86%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Benign ovarian tumour			
subjects affected / exposed	0 / 35 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Meningioma			
subjects affected / exposed	0 / 35 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Metastases to liver			
subjects affected / exposed	0 / 35 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Ovarian cancer			
subjects affected / exposed	0 / 35 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Papillary thyroid cancer			

subjects affected / exposed	0 / 35 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Hypertensive emergency			
subjects affected / exposed	1 / 35 (2.86%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Reproductive system and breast disorders			
Ovarian cyst			
subjects affected / exposed	0 / 35 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Pleural effusion			
subjects affected / exposed	0 / 35 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pulmonary embolism			
subjects affected / exposed	0 / 35 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Femoral neck fracture			
subjects affected / exposed	0 / 35 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Acute coronary syndrome			
subjects affected / exposed	0 / 35 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Angina pectoris			

subjects affected / exposed	0 / 35 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Loss of consciousness			
subjects affected / exposed	0 / 35 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Duodenal perforation			
subjects affected / exposed	0 / 35 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastric haemorrhage			
subjects affected / exposed	0 / 35 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 35 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Haematemesis			
subjects affected / exposed	0 / 35 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Upper gastrointestinal haemorrhage			
subjects affected / exposed	0 / 35 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Hepatic mass			
subjects affected / exposed	0 / 35 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Skin and subcutaneous tissue disorders Systemic lupus erythematosus rash	subjects affected / exposed	0 / 35 (0.00%)		
	occurrences causally related to treatment / all	0 / 0		
	deaths causally related to treatment / all	0 / 0		
Cutaneous vasculitis	subjects affected / exposed	0 / 35 (0.00%)		
	occurrences causally related to treatment / all	0 / 0		
	deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders	subjects affected / exposed	0 / 35 (0.00%)		
	occurrences causally related to treatment / all	0 / 0		
	deaths causally related to treatment / all	0 / 0		
Infections and infestations COVID-19 pneumonia	subjects affected / exposed	0 / 35 (0.00%)		
	occurrences causally related to treatment / all	0 / 0		
	deaths causally related to treatment / all	0 / 0		
COVID-19	subjects affected / exposed	0 / 35 (0.00%)		
	occurrences causally related to treatment / all	0 / 0		
	deaths causally related to treatment / all	0 / 0		
Herpes zoster	subjects affected / exposed	0 / 35 (0.00%)		
	occurrences causally related to treatment / all	0 / 0		
	deaths causally related to treatment / all	0 / 0		
Cerebral toxoplasmosis	subjects affected / exposed	0 / 35 (0.00%)		
	occurrences causally related to treatment / all	0 / 0		
	deaths causally related to treatment / all	0 / 0		
Cellulitis				

subjects affected / exposed	0 / 35 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pneumonia			
subjects affected / exposed	0 / 35 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pyelonephritis			
subjects affected / exposed	0 / 35 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Hypoglycaemia			
subjects affected / exposed	0 / 35 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Cenerimod 0.5 mg	Cenerimod 1 mg	Cenerimod 2 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	37 / 84 (44.05%)	54 / 85 (63.53%)	53 / 87 (60.92%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Haemangioma of liver			
subjects affected / exposed	0 / 84 (0.00%)	0 / 85 (0.00%)	1 / 87 (1.15%)
occurrences (all)	0	0	1
Vascular disorders			
Hypertension			
subjects affected / exposed	2 / 84 (2.38%)	8 / 85 (9.41%)	3 / 87 (3.45%)
occurrences (all)	2	8	3
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	1 / 84 (1.19%)	3 / 85 (3.53%)	2 / 87 (2.30%)
occurrences (all)	1	3	2
Respiratory, thoracic and mediastinal			

disorders			
Rhinitis allergic			
subjects affected / exposed	0 / 84 (0.00%)	0 / 85 (0.00%)	0 / 87 (0.00%)
occurrences (all)	0	0	0
Catarrh			
subjects affected / exposed	0 / 84 (0.00%)	1 / 85 (1.18%)	0 / 87 (0.00%)
occurrences (all)	0	1	0
Dyspnoea			
subjects affected / exposed	1 / 84 (1.19%)	0 / 85 (0.00%)	1 / 87 (1.15%)
occurrences (all)	1	0	1
Investigations			
Liver function test abnormal			
subjects affected / exposed	0 / 84 (0.00%)	0 / 85 (0.00%)	0 / 87 (0.00%)
occurrences (all)	0	0	0
Forced expiratory volume decreased			
subjects affected / exposed	0 / 84 (0.00%)	1 / 85 (1.18%)	1 / 87 (1.15%)
occurrences (all)	0	1	1
Alanine aminotransferase increased			
subjects affected / exposed	1 / 84 (1.19%)	5 / 85 (5.88%)	3 / 87 (3.45%)
occurrences (all)	1	7	3
Lymphocyte count decreased			
subjects affected / exposed	0 / 84 (0.00%)	0 / 85 (0.00%)	5 / 87 (5.75%)
occurrences (all)	0	0	5
Injury, poisoning and procedural complications			
Joint injury			
subjects affected / exposed	0 / 84 (0.00%)	0 / 85 (0.00%)	0 / 87 (0.00%)
occurrences (all)	0	0	0
Bone contusion			
subjects affected / exposed	0 / 84 (0.00%)	0 / 85 (0.00%)	0 / 87 (0.00%)
occurrences (all)	0	0	0
Ankle fracture			
subjects affected / exposed	0 / 84 (0.00%)	1 / 85 (1.18%)	0 / 87 (0.00%)
occurrences (all)	0	1	0
Cardiac disorders			
Sinus bradycardia			

subjects affected / exposed occurrences (all)	0 / 84 (0.00%) 0	0 / 85 (0.00%) 0	2 / 87 (2.30%) 3
Nervous system disorders			
Headache			
subjects affected / exposed	11 / 84 (13.10%)	12 / 85 (14.12%)	8 / 87 (9.20%)
occurrences (all)	12	13	9
Somnolence			
subjects affected / exposed	0 / 84 (0.00%)	0 / 85 (0.00%)	0 / 87 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	2 / 84 (2.38%)	4 / 85 (4.71%)	1 / 87 (1.15%)
occurrences (all)	2	7	1
Lymphopenia			
subjects affected / exposed	4 / 84 (4.76%)	10 / 85 (11.76%)	12 / 87 (13.79%)
occurrences (all)	4	12	18
Eye disorders			
Eye irritation			
subjects affected / exposed	0 / 84 (0.00%)	1 / 85 (1.18%)	0 / 87 (0.00%)
occurrences (all)	0	1	0
Dry eye			
subjects affected / exposed	3 / 84 (3.57%)	2 / 85 (2.35%)	9 / 87 (10.34%)
occurrences (all)	3	2	9
Cataract subcapsular			
subjects affected / exposed	1 / 84 (1.19%)	0 / 85 (0.00%)	0 / 87 (0.00%)
occurrences (all)	1	0	0
Vision blurred			
subjects affected / exposed	0 / 84 (0.00%)	0 / 85 (0.00%)	0 / 87 (0.00%)
occurrences (all)	0	0	0
Eye pain			
subjects affected / exposed	0 / 84 (0.00%)	0 / 85 (0.00%)	0 / 87 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Acid peptic disease			
subjects affected / exposed	1 / 84 (1.19%)	0 / 85 (0.00%)	1 / 87 (1.15%)
occurrences (all)	1	0	1
Abdominal pain upper			

subjects affected / exposed	0 / 84 (0.00%)	2 / 85 (2.35%)	0 / 87 (0.00%)
occurrences (all)	0	2	0
Abdominal pain			
subjects affected / exposed	1 / 84 (1.19%)	6 / 85 (7.06%)	0 / 87 (0.00%)
occurrences (all)	1	6	0
Abdominal distension			
subjects affected / exposed	0 / 84 (0.00%)	1 / 85 (1.18%)	1 / 87 (1.15%)
occurrences (all)	0	1	1
Diarrhoea			
subjects affected / exposed	4 / 84 (4.76%)	4 / 85 (4.71%)	3 / 87 (3.45%)
occurrences (all)	6	6	4
Dyspepsia			
subjects affected / exposed	1 / 84 (1.19%)	2 / 85 (2.35%)	1 / 87 (1.15%)
occurrences (all)	1	4	1
Gastritis			
subjects affected / exposed	1 / 84 (1.19%)	1 / 85 (1.18%)	0 / 87 (0.00%)
occurrences (all)	1	1	0
Nausea			
subjects affected / exposed	3 / 84 (3.57%)	1 / 85 (1.18%)	1 / 87 (1.15%)
occurrences (all)	3	3	1
Vomiting			
subjects affected / exposed	1 / 84 (1.19%)	1 / 85 (1.18%)	1 / 87 (1.15%)
occurrences (all)	1	1	1
Skin and subcutaneous tissue disorders			
Macule			
subjects affected / exposed	0 / 84 (0.00%)	0 / 85 (0.00%)	0 / 87 (0.00%)
occurrences (all)	0	0	0
Brachioradial pruritus			
subjects affected / exposed	0 / 84 (0.00%)	0 / 85 (0.00%)	0 / 87 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Myalgia			
subjects affected / exposed	1 / 84 (1.19%)	2 / 85 (2.35%)	1 / 87 (1.15%)
occurrences (all)	1	2	1
Muscle spasms			

subjects affected / exposed	0 / 84 (0.00%)	1 / 85 (1.18%)	1 / 87 (1.15%)
occurrences (all)	0	1	1
Arthralgia			
subjects affected / exposed	0 / 84 (0.00%)	3 / 85 (3.53%)	1 / 87 (1.15%)
occurrences (all)	0	4	1
Osteitis			
subjects affected / exposed	0 / 84 (0.00%)	0 / 85 (0.00%)	0 / 87 (0.00%)
occurrences (all)	0	0	0
Systemic lupus erythematosus			
subjects affected / exposed	0 / 84 (0.00%)	5 / 85 (5.88%)	1 / 87 (1.15%)
occurrences (all)	0	5	1
Infections and infestations			
COVID-19			
subjects affected / exposed	8 / 84 (9.52%)	8 / 85 (9.41%)	10 / 87 (11.49%)
occurrences (all)	8	9	10
Cellulitis			
subjects affected / exposed	0 / 84 (0.00%)	0 / 85 (0.00%)	1 / 87 (1.15%)
occurrences (all)	0	0	1
Eyelid infection			
subjects affected / exposed	0 / 84 (0.00%)	0 / 85 (0.00%)	0 / 87 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	5 / 84 (5.95%)	0 / 85 (0.00%)	6 / 87 (6.90%)
occurrences (all)	5	0	6
Ophthalmic herpes simplex			
subjects affected / exposed	0 / 84 (0.00%)	0 / 85 (0.00%)	0 / 87 (0.00%)
occurrences (all)	0	0	0
Oral herpes			
subjects affected / exposed	1 / 84 (1.19%)	0 / 85 (0.00%)	1 / 87 (1.15%)
occurrences (all)	1	0	1
Pharyngitis			
subjects affected / exposed	2 / 84 (2.38%)	2 / 85 (2.35%)	5 / 87 (5.75%)
occurrences (all)	2	5	5
Respiratory tract infection viral			
subjects affected / exposed	0 / 84 (0.00%)	1 / 85 (1.18%)	0 / 87 (0.00%)
occurrences (all)	0	1	0

Urinary tract infection subjects affected / exposed occurrences (all)	2 / 84 (2.38%) 2	2 / 85 (2.35%) 2	2 / 87 (2.30%) 2
Upper respiratory tract infection subjects affected / exposed occurrences (all)	7 / 84 (8.33%) 8	4 / 85 (4.71%) 5	5 / 87 (5.75%) 5
Metabolism and nutrition disorders Dyslipidaemia subjects affected / exposed occurrences (all)	0 / 84 (0.00%) 0	2 / 85 (2.35%) 2	3 / 87 (3.45%) 3
Hypercholesterolaemia subjects affected / exposed occurrences (all)	1 / 84 (1.19%) 1	2 / 85 (2.35%) 2	4 / 87 (4.60%) 6

Non-serious adverse events	Placebo	Placebo / Ex-4 mg	Not re-randomized / Ex-4 mg
Total subjects affected by non-serious adverse events subjects affected / exposed	39 / 86 (45.35%)	20 / 35 (57.14%)	13 / 14 (92.86%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps) Haemangioma of liver subjects affected / exposed occurrences (all)	0 / 86 (0.00%) 0	0 / 35 (0.00%) 0	1 / 14 (7.14%) 1
Vascular disorders Hypertension subjects affected / exposed occurrences (all)	2 / 86 (2.33%) 2	0 / 35 (0.00%) 0	0 / 14 (0.00%) 0
General disorders and administration site conditions Pyrexia subjects affected / exposed occurrences (all)	0 / 86 (0.00%) 0	1 / 35 (2.86%) 1	1 / 14 (7.14%) 1
Respiratory, thoracic and mediastinal disorders Rhinitis allergic subjects affected / exposed occurrences (all)	0 / 86 (0.00%) 0	0 / 35 (0.00%) 0	1 / 14 (7.14%) 1
Catarrh subjects affected / exposed occurrences (all)	0 / 86 (0.00%) 0	0 / 35 (0.00%) 0	1 / 14 (7.14%) 1

Dyspnoea subjects affected / exposed occurrences (all)	2 / 86 (2.33%) 2	1 / 35 (2.86%) 1	1 / 14 (7.14%) 1
Investigations			
Liver function test abnormal subjects affected / exposed occurrences (all)	0 / 86 (0.00%) 0	0 / 35 (0.00%) 0	1 / 14 (7.14%) 2
Forced expiratory volume decreased subjects affected / exposed occurrences (all)	2 / 86 (2.33%) 2	0 / 35 (0.00%) 0	1 / 14 (7.14%) 1
Alanine aminotransferase increased subjects affected / exposed occurrences (all)	0 / 86 (0.00%) 0	1 / 35 (2.86%) 1	0 / 14 (0.00%) 0
Lymphocyte count decreased subjects affected / exposed occurrences (all)	0 / 86 (0.00%) 0	1 / 35 (2.86%) 2	2 / 14 (14.29%) 2
Injury, poisoning and procedural complications			
Joint injury subjects affected / exposed occurrences (all)	0 / 86 (0.00%) 0	0 / 35 (0.00%) 0	1 / 14 (7.14%) 1
Bone contusion subjects affected / exposed occurrences (all)	0 / 86 (0.00%) 0	0 / 35 (0.00%) 0	1 / 14 (7.14%) 1
Ankle fracture subjects affected / exposed occurrences (all)	1 / 86 (1.16%) 1	0 / 35 (0.00%) 0	1 / 14 (7.14%) 1
Cardiac disorders			
Sinus bradycardia subjects affected / exposed occurrences (all)	1 / 86 (1.16%) 2	1 / 35 (2.86%) 1	1 / 14 (7.14%) 1
Nervous system disorders			
Headache subjects affected / exposed occurrences (all)	4 / 86 (4.65%) 5	2 / 35 (5.71%) 2	1 / 14 (7.14%) 1
Somnolence			

subjects affected / exposed occurrences (all)	0 / 86 (0.00%) 0	0 / 35 (0.00%) 0	1 / 14 (7.14%) 1
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	1 / 86 (1.16%)	2 / 35 (5.71%)	0 / 14 (0.00%)
occurrences (all)	1	4	0
Lymphopenia			
subjects affected / exposed	1 / 86 (1.16%)	4 / 35 (11.43%)	5 / 14 (35.71%)
occurrences (all)	1	4	7
Eye disorders			
Eye irritation			
subjects affected / exposed	0 / 86 (0.00%)	0 / 35 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Dry eye			
subjects affected / exposed	3 / 86 (3.49%)	2 / 35 (5.71%)	0 / 14 (0.00%)
occurrences (all)	3	2	0
Cataract subcapsular			
subjects affected / exposed	0 / 86 (0.00%)	0 / 35 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Vision blurred			
subjects affected / exposed	0 / 86 (0.00%)	0 / 35 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Eye pain			
subjects affected / exposed	1 / 86 (1.16%)	0 / 35 (0.00%)	1 / 14 (7.14%)
occurrences (all)	1	0	1
Gastrointestinal disorders			
Acid peptic disease			
subjects affected / exposed	0 / 86 (0.00%)	0 / 35 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Abdominal pain upper			
subjects affected / exposed	0 / 86 (0.00%)	0 / 35 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Abdominal pain			
subjects affected / exposed	2 / 86 (2.33%)	0 / 35 (0.00%)	1 / 14 (7.14%)
occurrences (all)	2	0	1
Abdominal distension			

subjects affected / exposed	0 / 86 (0.00%)	0 / 35 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Diarrhoea			
subjects affected / exposed	3 / 86 (3.49%)	0 / 35 (0.00%)	0 / 14 (0.00%)
occurrences (all)	4	0	0
Dyspepsia			
subjects affected / exposed	1 / 86 (1.16%)	0 / 35 (0.00%)	1 / 14 (7.14%)
occurrences (all)	1	0	1
Gastritis			
subjects affected / exposed	1 / 86 (1.16%)	0 / 35 (0.00%)	1 / 14 (7.14%)
occurrences (all)	1	0	1
Nausea			
subjects affected / exposed	2 / 86 (2.33%)	0 / 35 (0.00%)	1 / 14 (7.14%)
occurrences (all)	2	0	1
Vomiting			
subjects affected / exposed	1 / 86 (1.16%)	1 / 35 (2.86%)	1 / 14 (7.14%)
occurrences (all)	1	1	1
Skin and subcutaneous tissue disorders			
Macule			
subjects affected / exposed	0 / 86 (0.00%)	0 / 35 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Brachioradial pruritus			
subjects affected / exposed	0 / 86 (0.00%)	0 / 35 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Musculoskeletal and connective tissue disorders			
Myalgia			
subjects affected / exposed	0 / 86 (0.00%)	0 / 35 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Muscle spasms			
subjects affected / exposed	0 / 86 (0.00%)	0 / 35 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Arthralgia			
subjects affected / exposed	2 / 86 (2.33%)	0 / 35 (0.00%)	0 / 14 (0.00%)
occurrences (all)	2	0	0
Osteitis			

subjects affected / exposed	0 / 86 (0.00%)	0 / 35 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Systemic lupus erythematosus			
subjects affected / exposed	4 / 86 (4.65%)	2 / 35 (5.71%)	1 / 14 (7.14%)
occurrences (all)	8	2	1
Infections and infestations			
COVID-19			
subjects affected / exposed	11 / 86 (12.79%)	2 / 35 (5.71%)	2 / 14 (14.29%)
occurrences (all)	11	2	2
Cellulitis			
subjects affected / exposed	0 / 86 (0.00%)	2 / 35 (5.71%)	0 / 14 (0.00%)
occurrences (all)	0	2	0
Eyelid infection			
subjects affected / exposed	0 / 86 (0.00%)	0 / 35 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Nasopharyngitis			
subjects affected / exposed	5 / 86 (5.81%)	1 / 35 (2.86%)	1 / 14 (7.14%)
occurrences (all)	5	1	1
Ophthalmic herpes simplex			
subjects affected / exposed	0 / 86 (0.00%)	0 / 35 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	2
Oral herpes			
subjects affected / exposed	0 / 86 (0.00%)	0 / 35 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Pharyngitis			
subjects affected / exposed	2 / 86 (2.33%)	0 / 35 (0.00%)	0 / 14 (0.00%)
occurrences (all)	2	0	0
Respiratory tract infection viral			
subjects affected / exposed	1 / 86 (1.16%)	0 / 35 (0.00%)	0 / 14 (0.00%)
occurrences (all)	2	0	0
Urinary tract infection			
subjects affected / exposed	9 / 86 (10.47%)	0 / 35 (0.00%)	1 / 14 (7.14%)
occurrences (all)	9	0	1
Upper respiratory tract infection			
subjects affected / exposed	1 / 86 (1.16%)	2 / 35 (5.71%)	1 / 14 (7.14%)
occurrences (all)	1	2	1

Metabolism and nutrition disorders			
Dyslipidaemia			
subjects affected / exposed	0 / 86 (0.00%)	2 / 35 (5.71%)	0 / 14 (0.00%)
occurrences (all)	0	2	0
Hypercholesterolaemia			
subjects affected / exposed	1 / 86 (1.16%)	2 / 35 (5.71%)	0 / 14 (0.00%)
occurrences (all)	1	2	0

Non-serious adverse events	Cenerimod 2 mg / Ex-4 mg		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	23 / 35 (65.71%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Haemangioma of liver			
subjects affected / exposed	0 / 35 (0.00%)		
occurrences (all)	0		
Vascular disorders			
Hypertension			
subjects affected / exposed	8 / 35 (22.86%)		
occurrences (all)	10		
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 35 (0.00%)		
occurrences (all)	0		
Respiratory, thoracic and mediastinal disorders			
Rhinitis allergic			
subjects affected / exposed	0 / 35 (0.00%)		
occurrences (all)	0		
Catarrh			
subjects affected / exposed	0 / 35 (0.00%)		
occurrences (all)	0		
Dyspnoea			
subjects affected / exposed	0 / 35 (0.00%)		
occurrences (all)	0		
Investigations			
Liver function test abnormal			

subjects affected / exposed	0 / 35 (0.00%)		
occurrences (all)	0		
Forced expiratory volume decreased			
subjects affected / exposed	1 / 35 (2.86%)		
occurrences (all)	1		
Alanine aminotransferase increased			
subjects affected / exposed	0 / 35 (0.00%)		
occurrences (all)	0		
Lymphocyte count decreased			
subjects affected / exposed	0 / 35 (0.00%)		
occurrences (all)	0		
Injury, poisoning and procedural complications			
Joint injury			
subjects affected / exposed	0 / 35 (0.00%)		
occurrences (all)	0		
Bone contusion			
subjects affected / exposed	0 / 35 (0.00%)		
occurrences (all)	0		
Ankle fracture			
subjects affected / exposed	0 / 35 (0.00%)		
occurrences (all)	0		
Cardiac disorders			
Sinus bradycardia			
subjects affected / exposed	0 / 35 (0.00%)		
occurrences (all)	0		
Nervous system disorders			
Headache			
subjects affected / exposed	8 / 35 (22.86%)		
occurrences (all)	10		
Somnolence			
subjects affected / exposed	0 / 35 (0.00%)		
occurrences (all)	0		
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	1 / 35 (2.86%)		
occurrences (all)	1		

Lymphopenia subjects affected / exposed occurrences (all)	7 / 35 (20.00%) 12		
Eye disorders			
Eye irritation subjects affected / exposed occurrences (all)	0 / 35 (0.00%) 0		
Dry eye subjects affected / exposed occurrences (all)	0 / 35 (0.00%) 0		
Cataract subcapsular subjects affected / exposed occurrences (all)	1 / 35 (2.86%) 1		
Vision blurred subjects affected / exposed occurrences (all)	1 / 35 (2.86%) 1		
Eye pain subjects affected / exposed occurrences (all)	0 / 35 (0.00%) 0		
Gastrointestinal disorders			
Acid peptic disease subjects affected / exposed occurrences (all)	0 / 35 (0.00%) 0		
Abdominal pain upper subjects affected / exposed occurrences (all)	1 / 35 (2.86%) 1		
Abdominal pain subjects affected / exposed occurrences (all)	2 / 35 (5.71%) 2		
Abdominal distension subjects affected / exposed occurrences (all)	0 / 35 (0.00%) 0		
Diarrhoea subjects affected / exposed occurrences (all)	3 / 35 (8.57%) 4		
Dyspepsia			

<p>subjects affected / exposed</p> <p>0 / 35 (0.00%)</p> <p>occurrences (all)</p> <p>0</p>			
<p>Gastritis</p> <p>subjects affected / exposed</p> <p>0 / 35 (0.00%)</p> <p>occurrences (all)</p> <p>0</p>			
<p>Nausea</p> <p>subjects affected / exposed</p> <p>1 / 35 (2.86%)</p> <p>occurrences (all)</p> <p>2</p>			
<p>Vomiting</p> <p>subjects affected / exposed</p> <p>1 / 35 (2.86%)</p> <p>occurrences (all)</p> <p>1</p>			
<p>Skin and subcutaneous tissue disorders</p> <p>Macule</p> <p>subjects affected / exposed</p> <p>0 / 35 (0.00%)</p> <p>occurrences (all)</p> <p>0</p> <p>Brachioradial pruritus</p> <p>subjects affected / exposed</p> <p>0 / 35 (0.00%)</p> <p>occurrences (all)</p> <p>0</p>			
<p>Musculoskeletal and connective tissue disorders</p> <p>Myalgia</p> <p>subjects affected / exposed</p> <p>2 / 35 (5.71%)</p> <p>occurrences (all)</p> <p>2</p> <p>Muscle spasms</p> <p>subjects affected / exposed</p> <p>0 / 35 (0.00%)</p> <p>occurrences (all)</p> <p>0</p> <p>Arthralgia</p> <p>subjects affected / exposed</p> <p>2 / 35 (5.71%)</p> <p>occurrences (all)</p> <p>2</p> <p>Osteitis</p> <p>subjects affected / exposed</p> <p>0 / 35 (0.00%)</p> <p>occurrences (all)</p> <p>0</p> <p>Systemic lupus erythematosus</p> <p>subjects affected / exposed</p> <p>0 / 35 (0.00%)</p> <p>occurrences (all)</p> <p>0</p>			
<p>Infections and infestations</p>			

COVID-19			
subjects affected / exposed	1 / 35 (2.86%)		
occurrences (all)	1		
Cellulitis			
subjects affected / exposed	0 / 35 (0.00%)		
occurrences (all)	0		
Eyelid infection			
subjects affected / exposed	0 / 35 (0.00%)		
occurrences (all)	0		
Nasopharyngitis			
subjects affected / exposed	3 / 35 (8.57%)		
occurrences (all)	3		
Ophthalmic herpes simplex			
subjects affected / exposed	0 / 35 (0.00%)		
occurrences (all)	0		
Oral herpes			
subjects affected / exposed	2 / 35 (5.71%)		
occurrences (all)	5		
Pharyngitis			
subjects affected / exposed	0 / 35 (0.00%)		
occurrences (all)	0		
Respiratory tract infection viral			
subjects affected / exposed	2 / 35 (5.71%)		
occurrences (all)	3		
Urinary tract infection			
subjects affected / exposed	4 / 35 (11.43%)		
occurrences (all)	4		
Upper respiratory tract infection			
subjects affected / exposed	4 / 35 (11.43%)		
occurrences (all)	4		
Metabolism and nutrition disorders			
Dyslipidaemia			
subjects affected / exposed	1 / 35 (2.86%)		
occurrences (all)	1		
Hypercholesterolaemia			

subjects affected / exposed	2 / 35 (5.71%)		
occurrences (all)	2		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
05 September 2019	Protocol amendment dated 31 July 2019. Addition of Functional Assessment of Chronic Illness Therapy (FACIT) - Fatigue questionnaire. Inclusion of anchor patient global assessment questions for FACIT - questionnaire and other questionnaires to inform definition of responders and clinical meaningfulness of difference between groups.
27 March 2020	Protocol amendment dated 3 March 2020. Revision of specific stopping criteria and discharge criteria on Day 1. Introduction of the re-screening procedure for subjects who failed screening due to a transient non-eligibility reason.
11 January 2021	Protocol amendment dated 2 December 2020. Adjustment in sample size due to the slower than anticipated enrollment and unpredictable future impact of the COVID-19 pandemic. Study treatment was extended to 12 months for all randomized subjects. All subjects who completed Treatment Period 1 entered Treatment Period 2 for an additional 6 months.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported