Clinical trial results:
A Randomized, Controlled, Double-blind, Continuation Study Comparing the Long-term Safety and Efficacy of voclosporin (23.7 mg Twice Daily) with Placebo in Subjects with Lupus Nephritis

Summary

EudraCT number	2016-004046-28
Trial protocol	ES BG HR
Global end of trial date	07 October 2021

Results information

Result version number	v1 (current)
This version publication date	25 October 2022
First version publication date	25 October 2022

Trial information

Trial identification

Sponsor protocol code	AUR-VCS-2016-02

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03597464
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Aurinia Pharmaceuticals Inc.
Sponsor organisation address	1203-4464 Markham Street, Victoria, Canada,
Public contact	Clinical Trials Information, Aurinia Pharmaceuticals Inc., clinicaltrials@auriniapharma.com
Scientific contact	Clinical Trials Information, Aurinia Pharmaceuticals Inc., clinicaltrials@auriniapharma.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	03 December 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	07 October 2021
Global end of trial reached?	Yes
Global end of trial date	07 October 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The aim of this Phase 3 continuation study is to assess the long-term safety and tolerability of voclosporin compared with placebo, when added to the standard of care treatment in lupus nephritis (LN), for an additional 24 months, following a treatment period of 52 weeks in the AURORA 1 (AUR-VCS-2016-01). All subjects will continue to receive background therapy of mycophenolate mofetil (MMF) and/or corticosteroids starting at the same dose as at the end of the AURORA 1 study. Subjects with LN, who have completed 52 weeks of treatment with study drug in the AURORA 1 study, will be eligible to enter AURORA 2. The long-term safety and tolerability of the drug combination will be assessed from its safety profile while demonstrating the continued ability to achieve and maintain long-term renal response.

Protection of trial subjects:

Dose of voclosporin could be reduced in subjects with controlled urine protein creatine ratio (UPCR) if considered appropriate at the discretion of the investigator and in consultation with the Medical Monitor

When clinically indicated, dose of oral corticosteroid could be adjusted or discontinued in consultation with the Medical Monitor.

Background therapy:

mycophenolate mofetil (MMF) + oral corticosteroids

Evidence for comparator: -

Actual start date of recruitment	29 September 2019
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	Japan: 6
Country: Number of subjects enrolled	Malaysia: 3
Country: Number of subjects enrolled	Philippines: 13
Country: Number of subjects enrolled	Thailand: 19
Country: Number of subjects enrolled	Taiwan: 7
Country: Number of subjects enrolled	Viet Nam: 8
Country: Number of subjects enrolled	Belarus: 9
Country: Number of subjects enrolled	Russian Federation: 31
Country: Number of subjects enrolled	Serbia: 9
Country: Number of subjects enrolled	Turkey: 2
Country: Number of subjects enrolled	Ukraine: 11
Country: Number of subjects enrolled	South Africa: 6
Country: Number of subjects enrolled	Argentina: 1

Country: Number of subjects enrolled	Netherlands: 3
Country: Number of subjects enrolled	Spain: 3
Country: Number of subjects enrolled	Croatia: 1
Country: Number of subjects enrolled	Brazil: 4
Country: Number of subjects enrolled	Chile: 3
Country: Number of subjects enrolled	Colombia: 14
Country: Number of subjects enrolled	Dominican Republic: 9
Country: Number of subjects enrolled	Guatemala: 9
Country: Number of subjects enrolled	Mexico: 5
Country: Number of subjects enrolled	Peru: 16
Country: Number of subjects enrolled	United States: 24
Worldwide total number of subjects	216
EEA total number of subjects	7

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)	215
From 65 to 84 years	1
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Subjects were recruited in 100 centers in 24 countries in North America, Latin America, Europe, South Africa, and Asia. The first subject was enrolled on 29 September 2019 and the last subject, last visit date was 07 October 2021.

Pre-assignment

Screening details:

Eligible subjects included male or female subjects who:
1. Had completed 52 weeks of treatment with study drug in the AURORA 1 study
2. Provided prior written informed consent
3. In the opinion of the Investigator, required continued immunosuppressive therapy
4. Were willing to continue taking oral MMF for the study duration

Period 1

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

Blinding implementation details:

Subjects continued to receive the blinded treatments that were assigned at the start of AURORA 1. Background therapies (MMF + corticosteroids) were administered at the same doses as at the end of AURORA 1.

Arms

Are arms mutually exclusive?	Yes
Arm title	Voclosporin

Arm description: -

Arm type	Experimental
Investigational medicinal product name	voclosporin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, soft
Routes of administration	Oral use

Dosage and administration details:

three 7.9 mg capsules (23.7 mg total), administered twice daily

Arm title	Placebo

Arm description: -

Arm type	Placebo
Investigational medicinal product name	placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, soft
Routes of administration	Oral use

Dosage and administration details:

placebo, oral, three capsules administered twice daily

Number of subjects in period 1	Voclosporin	Placebo
Started	116	100
Completed	101	85
Not completed	15	15
Consent withdrawn by subject	4	5
Physician decision	2	2
Adverse event, non-fatal	-	2
Death	-	3
Pregnancy	3	1
Non-compliance	1	1
Lost to follow-up	3	1
Lack of efficacy	2	-

Baseline characteristics

Reporting groups	
Reporting group title	Voclosporin
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	

Reporting group values	Voclosporin	Placebo	Total
Number of subjects	116	100	216
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	32.3	35.4	
standard deviation	± 10.31	± 11.64	-
Gender categorical Units: Subjects			
Female	105	88	193
Male	11	12	23
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	39	33	72
Not Hispanic or Latino	77	67	144
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	30	30	60
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	18	7	25
White	44	40	84
Not Reported	24	23	47
Region of Enrollment			
Southeast Asia ("Asia Pacific") includes Japan, Malaysia, Philippines, Thailand, Taiwan & Vietnam Europe ("Europe") includes Belarus, Croatia, Netherlands, Russia, Serbia, Spain, Turkey, Ukraine as well as South Africa South America ("Latin America") includes Argentina, Brazil, Chile, Colombia, Dominican Republic, Guatemala, Mexico & Peru			
Units: Subjects			
United States	15	9	24
Southeast Asia	29	27	56
Europe	38	37	75
South America	34	27	61
Lupus Nephritis History - Years since diagnosis of systemic lupus erythematosus (SLE) Units: Years			

arithmetic mean	6.6	7.3	
standard deviation	± 6.66	± 6.85	-
Lupus Nephritis History - Years since diagnosis of lupus nephritis (LN) Units: Years			
arithmetic mean	4.8	5.0	
standard deviation	± 5.27	± 5.23	-
Lupus Nephritis History - Years since first instance of significant proteinuria (> 500 mg/day) Units: Years			
arithmetic mean	5.0	4.7	
standard deviation	± 5.15	± 4.49	-
Baseline Urine Protein Creatinine Ratio (UPCR)			
Average pre-randomisation values			
Units: mg/mg			
arithmetic mean	3.941	3.868	
standard deviation	± 2.5766	± 2.4764	-
Baseline Estimated Glomerular Filtration Rate (eGFR)			
Baseline estimated Glomerular Filtration Rate Chronic Kidney Disease Epidemiology Collaboration (CKD-Epi formula) (lowest pre-randomisation value)			
Units: mL/min/1.73 m2			
arithmetic mean	94.1	92.0	
standard deviation	± 31.36	± 28.04	-

End points

End points reporting groups

Reporting group title	Voclosporin
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	

Primary: Adverse events, routine biochemical and hematological assessments

End point title	Adverse events, routine biochemical and hematological assessments[1]

End point description:

This study evaluated the safety of continued treatment with voclosporin for up to three years. Voclosporin was well tolerated in the study with no new or unexpected safety signals observed. The overall profile of adverse events seen in Years 2 and 3 of treatment was similar to that seen in the first year of treatment (in AURORA 1); however, the frequency of adverse events reduced each year.

End point type	Primary

End point timeframe:

36 Months

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Estimand for AEs is the proportion of subjects reporting AEs in the Safety Population when comparing voclosporin and placebo. Estimands for biochemical and hematological assessments are the mean absolute values and mean changes from AURORA 1 baseline in the Safety
Population when comparing voclosporin and placebo.

End point values	Voclosporin	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	116	100		
Units: Number of subjects				
Any treatment-emergent adverse event (TEAE)	100	80		
Treatment-related TEAE	28	21		
Serious TEAE	21	23		
TEAE leading to study drug discontinuation	11	17		
TEAE leading to death	0	3		
Treatment-related TEAE leading to death	0	0		
Disease-related TEAE	50	34		
Disease-related serious TEAE	7	11		

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of subjects in renal response

End point title	Proportion of subjects in renal response

End point description:

Proportion of subjects in renal response defined as:
o Urine protein creatinine ratio (UPCR) of ≤0.5 mg/mg, and
o Estimated glomerular filtration rate (eGFR) ≥60 mL/min/1.73 m2 or no confirmed decrease from baseline in eGFR of >20%, and
o Received no rescue medication for LN, and
o Did not receive more than 10 mg prednisone for ≥3 consecutive days or for ≥7 days in total during the 8 weeks prior to the renal response assessment.
Subjects who withdrew from the study prior to the response assessment were defined as non-responders.

End point type	Secondary

End point timeframe:

Months 12 (AURORA 2 Baseline) , 18, 24, 30 and 36

End point values	Voclosporin	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	116	100		
Units: Number of participants				
Renal Response - 12 Months	61	34		
Renal Response - 18 Months	74	46		
Renal Response - 24 Months	65	43		
Renal Response - 30 Months	69	42		
Renal Response - 36 Months	59	39		

Statistical analyses

Statistical analysis title	Renal Response - 12 Months (AURORA 2 Baseline)

Statistical analysis description:

The model is based on a logistic regression with terms for treatment, baseline UPCR, biopsy class, MMF use at baseline and region.
Subjects who withdrew from the study prior to the visit assessments and thus provide insufficient visit data were defined as non-responders.

Comparison groups	Voclosporin v Placebo
Number of subjects included in analysis	216
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.004
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.3
upper limit	4.05

	Renal Response - 18 Months

Statistical analysis title	

Statistical analysis description:

The model is based on a logistic regression with terms for treatment, baseline UPCR, biopsy class, MMF use at baseline and region.
Subjects who withdrew from the study prior to the visit assessments and thus provide insufficient visit data were defined as non-responders.

Comparison groups	Voclosporin v Placebo
Number of subjects included in analysis	216
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.006
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.19
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.25
upper limit	3.83

Statistical analysis title	Renal Response - 24 Months

Statistical analysis description:

The model is based on a logistic regression with terms for treatment, baseline UPCR, biopsy class, MMF use at baseline and region.
Subjects who withdrew from the study prior to the visit assessments and thus provide insufficient visit data were defined as non-responders.

Comparison groups	Voclosporin v Placebo
Number of subjects included in analysis	216
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.035
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.81
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.04
upper limit	3.16

Statistical analysis title	Renal Response - 30 Months

Statistical analysis description:

The model is based on a logistic regression with terms for treatment, baseline UPCR, biopsy class, MMF use at baseline and region.
Subjects who withdrew from the study prior to the visit assessments and thus provide insufficient visit data were defined as non-responders.

Comparison groups	Voclosporin v Placebo

Number of subjects included in analysis	216
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.005
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.24
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.28
upper limit	3.92

Statistical analysis title	Renal Response - 36 Months

Statistical analysis description:

The model is based on a logistic regression with terms for treatment, baseline UPCR, biopsy class, MMF use at baseline and region.
Subjects who withdrew from the study prior to the visit assessments and thus provide insufficient visit data were defined as non-responders.

Comparison groups	Voclosporin v Placebo
Number of subjects included in analysis	216
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.051
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.74
Confidence interval	
level	95 %
sides	2-sided
lower limit	1
upper limit	3.03

Secondary: Proportion of subjects in partial renal response

End point title	Proportion of subjects in partial renal response

End point description:

Partial renal response defined as 50% reduction from AURORA 1 baseline in UPCR.

The model is based on a logistic regression with terms for treatment, baseline UPCR, biopsy class, MMF use at baseline and region.

Subjects who withdrew from the study prior to the visit assessments and thus provide insufficient visit data were defined as non-responders.

End point type	Secondary

End point timeframe:

Months 12 (AURORA 2 Baseline), 18, 24, 30 and 36

End point values	Voclosporin	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	116	100		
Units: Number of Subjects				
Partial Renal Response - Month 12	104	70		
Partial Renal Response - Month 18	96	68		
Partial Renal Response - Month 24	90	58		
Partial Renal Response - Month 30	85	61		
Partial Renal Response - Month 36	86	69		

Statistical analyses

Statistical analysis title	Partial Renal Response - 12 Months

Statistical analysis description:

The model is based on a logistic regression with terms for treatment, baseline UPCR, biopsy class, MMF use at baseline and region.
Subjects who withdrew from the study prior to the visit assessments and thus provide insufficient visit data were defined as non-responders.

Comparison groups	Voclosporin v Placebo
Number of subjects included in analysis	216
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	3.99
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.88
upper limit	8.46

Statistical analysis title	Partial Renal Response - 18 Months

Statistical analysis description:

The model is based on a logistic regression with terms for treatment, baseline UPCR, biopsy class, MMF use at baseline and region.
Subjects who withdrew from the study prior to the visit assessments and thus provide insufficient visit data were defined as non-responders.

Comparison groups	Voclosporin v Placebo

Number of subjects included in analysis	216
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.008
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.28
upper limit	4.88

Statistical analysis title	Partial Renal Response - 24 Months

Statistical analysis description:

The model is based on a logistic regression with terms for treatment, baseline UPCR, biopsy class, MMF use at baseline and region.
Subjects who withdrew from the study prior to the visit assessments and thus provide insufficient visit data were defined as non-responders.

Comparison groups	Voclosporin v Placebo
Number of subjects included in analysis	216
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.68
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.46
upper limit	4.91

Statistical analysis title	Partial Renal Response - 30 Months

Statistical analysis description:

The model is based on a logistic regression with terms for treatment, baseline UPCR, biopsy class, MMF use at baseline and region.
Subjects who withdrew from the study prior to the visit assessments and thus provide insufficient visit data were defined as non-responders.

Comparison groups	Voclosporin v Placebo
Number of subjects included in analysis	216
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.04
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.86

Confidence interval	
level	95 %
sides	2-sided
lower limit	1.03
upper limit	3.34

Statistical analysis title	Partial Renal Response - 36 Months

Statistical analysis description:

The model is based on a logistic regression with terms for treatment, baseline UPCR, biopsy class, MMF use at baseline and region.
Subjects who withdrew from the study prior to the visit assessments and thus provide insufficient visit data were defined as non-responders.

Comparison groups	Voclosporin v Placebo
Number of subjects included in analysis	216
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.29
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.39
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.75
upper limit	2.58

Secondary: Renal flare as adjudicated by the Clinical Endpoints Committee (CEC)

End point title	Renal flare as adjudicated by the Clinical Endpoints Committee (CEC)

End point description:

A patient could experience a flare from the point they achieved a response (or recovery). Renal flares were judged according to the following criteria:
- A reproducible increase to UPCR >1 mg/mg from a post-response baseline of <0.2 mg/mg or
- an increase to UPCR >2 mg/mg from a post-response baseline between 0.2 to 1.0 mg/mg or
- a doubling of UPCR for baseline values of UPCR >1 mg/mg

End point type	Secondary

End point timeframe:

up to 36 months

End point values	Voclosporin	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	116	100		
Units: Number of Subjects (%)				
number (not applicable)				
Subjects without Adequate Response or with Flares	39	46		

Subjects with Adequate Response & without Flares	77	54		

Statistical analyses

Statistical analysis title	Number of Subjects with Adequate Renal Response
Comparison groups	Voclosporin v Placebo
Number of subjects included in analysis	216
Analysis specification	Pre-specified
Analysis type	other[2]
P-value	= 0.045
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.56
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.32
upper limit	0.99

Notes:

[2] - The model is based on a logistic regression with terms for treatment, baseline UPCR, biopsy class, MMF use at baseline and Region. An odds ration < unity indicates benefit of voclosporin

Secondary: Change from AURORA 1 baseline in urine protein creatinine ratio (UPCR)

End point title	Change from AURORA 1 baseline in urine protein creatinine ratio (UPCR)

End point description:

Participants analyzed included all subjects who were randomized treatment during AURORA 1 AND who consented to continue their treatment in AURORA 2. Baseline values were collected at the start of AURORA 1 but only for those subjects that continued in AURORA 2.

Reductions in UPCR are indicative of better renal outcomes.

The number of subjects analyzed may not be aligned with overall number analyzed due to early withdrawals from study and missed study visits.

End point type	Secondary

End point timeframe:

Months 12 (AURORA 2 baseline), 18, 24, 30 and 36

End point values	Voclosporin	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	116[3]	100[4]		
Units: mg/mg				
least squares mean (standard error)				
Month 12 (AURORA 2 Baseline)	-3.17 (± 0.164)	-2.52 (± 0.175)		
Month 18	-3.05 (± 0.216)	-2.42 (± 0.232)		

Month 24	-3.18 (± 0.188)	-2.41 (± 0.202)		
Month 30	-3.12 (± 0.219)	-2.21 (± 0.235)		
Month 36	-3.00 (± 0.222)	-2.52 (± 0.236)		

Notes:

[3] - # participants:
116 (Month 12)
113 (Month 18)
105 (Month 24)
100 (Month 30)
99 (Month 36)

[4] - # participants:
100 (Month 12)
96 (Month 18)
81 (Month 24)
87 (Month 30)
87 (Month 36)

Statistical analyses

Statistical analysis title	UPCR change from baseline at Month 12
Comparison groups	Voclosporin v Placebo
Number of subjects included in analysis	216
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.001
Method	Mixed models analysis
Parameter estimate	Least Squares Mean difference
Point estimate	-0.65
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.05
upper limit	-0.26

Statistical analysis title	UPCR change from baseline at Month 18
Comparison groups	Voclosporin v Placebo
Number of subjects included in analysis	216
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.029
Method	Mixed models analysis
Parameter estimate	Least Squares Mean difference
Point estimate	-0.63
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.2
upper limit	-0.07

Statistical analysis title	UPCR change from baseline at Month 24
Comparison groups	Voclosporin v Placebo
Number of subjects included in analysis	216
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.002
Method	Mixed models analysis
Parameter estimate	Least Squares Mean difference
Point estimate	-0.77
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.24
upper limit	-0.29

Statistical analysis title	UPCR change from baseline at Month 30
Comparison groups	Voclosporin v Placebo
Number of subjects included in analysis	216
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.002
Method	Mixed models analysis
Parameter estimate	Least Squares Mean difference
Point estimate	-0.91
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.49
upper limit	-0.33

Statistical analysis title	UPCR change from baseline at Month 36
Comparison groups	Voclosporin v Placebo
Number of subjects included in analysis	216
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.106
Method	Mixed models analysis
Parameter estimate	Least Squares Mean difference
Point estimate	-0.48

Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.06
upper limit	-0.1

Secondary: Change from AURORA 1 baseline in urine protein

End point title	Change from AURORA 1 baseline in urine protein

End point description:

Participants analyzed included all subjects who were randomized treatment during AURORA 1 AND who consented to continue their treatment in AURORA 2. Baseline values were collected at the start of AURORA 1 but only for those subjects that continued in AURORA 2.

Reductions in Urine Protein levels are indicative of better renal outcomes.

The number of subjects analyzed may not be aligned with overall number analyzed due to early withdrawals from study and missed study visits.

End point type	Secondary

End point timeframe:

Months 12 (AURORA 2 baseline), 18, 24, 30 and 36

End point values	Voclosporin	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	116[5]	100[6]		
Units: mg/dL				
least squares mean (standard error)				
Month 12	-302.4 (± 16.91)	-234.6 (± 18.05)		
Month 18	-297.8 (± 23.41)	-210.1 (± 25.15)		
Month 24	-295.8 (± 17.10)	-248.8 (± 18.51)		
Month 30	-304.7 (± 19.23)	-231.6 (± 20.67)		
Month 36	-280.7 (± 22.66)	-261.7 (± 24.01)		

Notes:

[5] - # participants:
116 (Month 12)
112 (Month 18)
104 (Month 24)
99 (Month 30)
99 (Month 36)

[6] - # participants:
100 (Month 12)
95 (Month 18)
81 (Month 24)
87 (Month 30)
86 (Month 36)

Statistical analyses

Statistical analysis title	Urine protein change from baseline at Month 12
Comparison groups	Voclosporin v Placebo
Number of subjects included in analysis	216
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.002
Method	Mixed models analysis
Parameter estimate	Least Squares Mean difference
Point estimate	-67.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-110.4
upper limit	-25.1

Statistical analysis title	Urine protein change from baseline at Month 18
Comparison groups	Voclosporin v Placebo
Number of subjects included in analysis	216
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.007
Method	Mixed models analysis
Parameter estimate	Least Squares Mean difference
Point estimate	-87.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-151.2
upper limit	-24.2

Statistical analysis title	Urine protein change from baseline at Month 24
Comparison groups	Voclosporin v Placebo
Number of subjects included in analysis	216
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.035
Method	Mixed models analysis
Parameter estimate	Least Squares Mean difference
Point estimate	-47
Confidence interval	
level	95 %
sides	2-sided
lower limit	-90.8
upper limit	-3.3

Statistical analysis title	Urine protein change from baseline at Month 30
Comparison groups	Voclosporin v Placebo
Number of subjects included in analysis	216
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.005
Method	Mixed models analysis
Parameter estimate	Least Squares Mean difference
Point estimate	-73.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-123.5
upper limit	-22.6

Statistical analysis title	Urine protein change from baseline at Month 36
Comparison groups	Voclosporin v Placebo
Number of subjects included in analysis	216
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.537
Method	Mixed models analysis
Parameter estimate	Least Squares Mean difference
Point estimate	-19
Confidence interval	
level	95 %
sides	2-sided
lower limit	-79.7
upper limit	41.7

Secondary: Change from AURORA 1 baseline in serum creatinine (SCr)

End point title	Change from AURORA 1 baseline in serum creatinine (SCr)

End point description:

Participants analyzed included all subjects who were randomized treatment during AURORA 1 AND who consented to continue their treatment in AURORA 2. Baseline values were collected at the start of AURORA 1 but only for those subjects that continued in AURORA 2.

Decreases in SCr levels can be indicative of better renal outcomes.

The number of subjects analyzed may not be aligned with overall number analyzed due to early withdrawals from study and missed study visits.

End point type	Secondary

End point timeframe:

Months 12 (AURORA 2 baseline), 18, 24, 30 and 36

End point values	Voclosporin	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	116[7]	100[8]		
Units: mg/dL				
least squares mean (standard error)				
Month 12	0.051 (± 0.0207)	-0.034 (± 0.0221)		
Month 18	0.078 (± 0.0300)	0.027 (± 0.0323)		
Month 24	0.117 (± 0.0429)	0.060 (± 0.0466)		
Month 30	0.094 (± 0.0494)	0.129 (± 0.0534)		
Month 36	0.119 (± 0.0597)	0.197 (± 0.0644)		

Notes:

[7] - # participants:
116 (Month 12)
114 (Month 18)
103 (Month 24)
99 (Month 30)
100 (Month 36)
[8] - # participants:
100 (Month 12)
96 (Month 18)
81 (Month 24)
85 (Month 30)
87 (Month 36)

Statistical analyses

Statistical analysis title	Serum creatinine change from baseline at Month 12
Comparison groups	Voclosporin v Placebo
Number of subjects included in analysis	216
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	Least Squares Mean difference
Point estimate	0.084
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.035
upper limit	0.134

Statistical analysis title	Serum creatinine change from baseline at Month 18
Comparison groups	Voclosporin v Placebo

Number of subjects included in analysis	216
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.209
Method	Mixed models analysis
Parameter estimate	Least Squares Mean difference
Point estimate	0.051
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.029
upper limit	0.131

Statistical analysis title	Serum creatinine change from baseline at Month 24
Comparison groups	Voclosporin v Placebo
Number of subjects included in analysis	216
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.353
Method	Mixed models analysis
Parameter estimate	Least Squares Mean difference
Point estimate	0.057
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.064
upper limit	0.178

Statistical analysis title	Serum creatinine change from baseline at Month 30
Comparison groups	Voclosporin v Placebo
Number of subjects included in analysis	216
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.616
Method	Mixed models analysis
Parameter estimate	Least Squares Mean difference
Point estimate	-0.036
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.176
upper limit	0.105

Statistical analysis title	Serum creatinine change from baseline at Month 36

Comparison groups	Voclosporin v Placebo
Number of subjects included in analysis	216
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.372
Method	Mixed models analysis
Parameter estimate	Least Squares Mean difference
Point estimate	-0.077
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.248
upper limit	0.094

Secondary: Change from AURORA 1 baseline in estimated glomerular filtration rate (eGFR)

End point title	Change from AURORA 1 baseline in estimated glomerular filtration rate (eGFR)

End point description:

Participants analyzed included all subjects who were randomized treatment during AURORA 1 AND who consented to continue their treatment in AURORA 2. Baseline values were collected at the start of AURORA 1 but only for those subjects that continued in AURORA 2.

This endpoint incorporated Corrected eGFR values with a ceiling set to 90 mL/min/1.73 m2.

Increases in eGFR levels are indicative of better renal outcomes.

The number of subjects analyzed may not be aligned with overall number analyzed due to early withdrawals from study and missed study visits.

The number of subjects analyzed may not be aligned with overall number analyzed due to early withdrawals from study and missed study visits.

End point type	Secondary

End point timeframe:

Months 12 (AURORA 2 baseline), 18, 24, 30 and 36

End point values	Voclosporin	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	116[9]	100[10]		
Units: mL/min/1.73 m2				
least squares mean (standard error)				
Month 12	1.8 (± 1.08)	4.4 (± 1.15)		
Month 18	-0.2 (± 1.31)	1.6 (± 1.40)		
Month 24	-1.3 (± 1.48)	0.9 (± 1.60)		
Month 30	0.2 (± 1.56)	-0.8 (± 1.67)		
Month 36	-0.2 (± 1.69)	-2.0 (± 1.81)		

Notes:

[9] - # participants:
116 (Month 12)
114 (Month 18)
103 (Month 24)

99 (Month 30)
100 (Month 36)
[10] - # participants:
100 (Month 12)
96 (Month 18)
81 (Month 24)
85 (Month 30)
87 (Month 36)

Statistical analyses

Statistical analysis title	eGFR change from baseline at Month 12
Comparison groups	Voclosporin v Placebo
Number of subjects included in analysis	216
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.041
Method	Mixed models analysis
Parameter estimate	Least Squares Mean difference
Point estimate	-2.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.3
upper limit	-0.1

Statistical analysis title	eGFR change from baseline at Month 18
Comparison groups	Voclosporin v Placebo
Number of subjects included in analysis	216
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.292
Method	Mixed models analysis
Parameter estimate	Least Squares Mean difference
Point estimate	-1.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.1
upper limit	1.6

Statistical analysis title	eGFR change from baseline at Month 24
Comparison groups	Voclosporin v Placebo

Number of subjects included in analysis	216
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.282
Method	Mixed models analysis
Parameter estimate	Least Squares Mean difference
Point estimate	-2.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.1
upper limit	1.8

Statistical analysis title	eGFR change from baseline at Month 30
Comparison groups	Voclosporin v Placebo
Number of subjects included in analysis	216
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.659
Method	Mixed models analysis
Parameter estimate	Least Squares Mean difference
Point estimate	0.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.2
upper limit	5.1

Statistical analysis title	eGFR change from baseline at Month 36
Comparison groups	Voclosporin v Placebo
Number of subjects included in analysis	216
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.438
Method	Mixed models analysis
Parameter estimate	Least Squares Mean difference
Point estimate	1.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.8
upper limit	6.4

Secondary: Change from AURORA 1 baseline in Safety of Estrogens in Lupus

Erythematosus National Assessment - Systemic Lupus Erythematosus Disease Activity Index (SELENA-SLEDAI) score

End point title	Change from AURORA 1 baseline in Safety of Estrogens in Lupus Erythematosus National Assessment - Systemic Lupus Erythematosus Disease Activity Index (SELENA-SLEDAI) score

End point description:

Participants analyzed included all subjects who were randomized treatment during AURORA 1 AND who consented to continue their treatment in AURORA 2. Baseline values were collected at the start of AURORA 1 but only for those subjects that continued in AURORA 2.

Assessment of Systemic Lupus Erythematosus (SLE) Disease Activity within the last 10 days. It scores 24 disease descriptors across 9 organ systems which are summed to a minimum of <2 (considered indicative of no activity) and maximum of 105 points. Scores are weighted and a score of 6 is considered clinically significant. Higher scores indicate worse disease activity.

The number of subjects analyzed may not be aligned with overall number analyzed due to early withdrawals from study and missed study visits.

End point type	Secondary

End point timeframe:

Months 18, 24 and 36

End point values	Voclosporin	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	116[11]	100[12]		
Units: SELENA-SLEDAI Score				
least squares mean (confidence interval 95%)				
Month 18	-6.4 (-7.4 to -5.4)	-5.6 (-6.6 to -4.5)		
Month 24	-6.8 (-7.7 to -5.9)	-6.1 (-7.0 to -5.1)		
Month 36	-6.8 (-7.7 to -5.9)	-6.1 (-7.1 to -5.2)		

Notes:

[11] - 112 participants (Month 18)
100 participants (Month 24)
97 participants (Month 36)

[12] - 96 participants (Month 18)
84 participants (Month 24)
85 participants (Month 36)

Statistical analyses

Statistical analysis title	SELENA-SLEDAI change from baseline at Month 18
Comparison groups	Voclosporin v Placebo
Number of subjects included in analysis	216
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.238
Method	Mixed models analysis
Parameter estimate	Least Squares Mean difference
Point estimate	-0.8

Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.1
upper limit	0.5

Statistical analysis title	SELENA-SLEDAI change from baseline at Month 24
Comparison groups	Voclosporin v Placebo
Number of subjects included in analysis	216
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.215
Method	Mixed models analysis
Parameter estimate	Least Squares Mean difference
Point estimate	-0.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.8
upper limit	0.4

Statistical analysis title	SELENA-SLEDAI change from baseline at Month 36
Comparison groups	Voclosporin v Placebo
Number of subjects included in analysis	216
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.246
Method	Mixed models analysis
Parameter estimate	Least Squares Mean difference
Point estimate	-0.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.8
upper limit	0.5

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Treatment-emergent adverse events (TEAEs) are events starting in AURORA 2 up to 30 days after study treatment end.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	20.0

Reporting groups

Reporting group title	Voclosporin
Reporting group description: -	
Reporting group title	Placebo

Reporting group description: -

Serious adverse events	Voclosporin	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	21 / 116 (18.10%)	23 / 100 (23.00%)	
number of deaths (all causes)	0	3	
number of deaths resulting from adverse events	0	3	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Uterine leiomyoma			
subjects affected / exposed	0 / 116 (0.00%)	1 / 100 (1.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 116 (0.00%)	1 / 100 (1.00%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Venous thrombosis limb			
subjects affected / exposed	0 / 116 (0.00%)	1 / 100 (1.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			
Abortion induced			

subjects affected / exposed	1 / 116 (0.86%)	0 / 100 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	1 / 116 (0.86%)	0 / 100 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Endometriosis			
subjects affected / exposed	1 / 116 (0.86%)	0 / 100 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism			
subjects affected / exposed	0 / 116 (0.00%)	1 / 100 (1.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Investigations			
Glomerular filtration rate decreased			
subjects affected / exposed	1 / 116 (0.86%)	0 / 100 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Fibula fracture			
subjects affected / exposed	1 / 116 (0.86%)	0 / 100 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural haematoma			
subjects affected / exposed	1 / 116 (0.86%)	0 / 100 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural haemorrhage			

subjects affected / exposed	1 / 116 (0.86%)	0 / 100 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Radius fracture			
subjects affected / exposed	0 / 116 (0.00%)	1 / 100 (1.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Pericarditis lupus			
subjects affected / exposed	1 / 116 (0.86%)	0 / 100 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Syncope			
subjects affected / exposed	0 / 116 (0.00%)	1 / 100 (1.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Thrombocytopenia			
subjects affected / exposed	0 / 116 (0.00%)	1 / 100 (1.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Cataract			
subjects affected / exposed	1 / 116 (0.86%)	1 / 100 (1.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malignant glaucoma			
subjects affected / exposed	0 / 116 (0.00%)	1 / 100 (1.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Gastritis			

subjects affected / exposed	0 / 116 (0.00%)	1 / 100 (1.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Hepatitis toxic			
subjects affected / exposed	1 / 116 (0.86%)	0 / 100 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis			
subjects affected / exposed	0 / 116 (0.00%)	1 / 100 (1.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Lupus nephritis			
subjects affected / exposed	2 / 116 (1.72%)	3 / 100 (3.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephropathy toxic			
subjects affected / exposed	0 / 116 (0.00%)	1 / 100 (1.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephrotic syndrome			
subjects affected / exposed	0 / 116 (0.00%)	1 / 100 (1.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Systemic lupus erythematosus			
subjects affected / exposed	1 / 116 (0.86%)	3 / 100 (3.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteonecrosis			
subjects affected / exposed	0 / 116 (0.00%)	2 / 100 (2.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

Arthralgia			
subjects affected / exposed	0 / 116 (0.00%)	1 / 100 (1.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Flank pain			
subjects affected / exposed	0 / 116 (0.00%)	1 / 100 (1.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteoarthritis			
subjects affected / exposed	0 / 116 (0.00%)	1 / 100 (1.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Corona virus infection			
subjects affected / exposed	2 / 116 (1.72%)	5 / 100 (5.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 2	
Urinary tract infection			
subjects affected / exposed	2 / 116 (1.72%)	0 / 100 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia viral			
subjects affected / exposed	0 / 116 (0.00%)	2 / 100 (2.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Disseminated tuberculosis			
subjects affected / exposed	0 / 116 (0.00%)	1 / 100 (1.00%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	1 / 116 (0.86%)	1 / 100 (1.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			

subjects affected / exposed	1 / 116 (0.86%)	1 / 100 (1.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Appendicitis			
subjects affected / exposed	1 / 116 (0.86%)	0 / 100 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper respiratory tract infection			
subjects affected / exposed	1 / 116 (0.86%)	0 / 100 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 2 %

Non-serious adverse events	Voclosporin	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	84 / 116 (72.41%)	60 / 100 (60.00%)	
Vascular disorders			
Hypertension			
subjects affected / exposed	10 / 116 (8.62%)	6 / 100 (6.00%)	
occurrences (all)	10	6	
General disorders and administration site conditions			
Oedema peripheral			
subjects affected / exposed	4 / 116 (3.45%)	8 / 100 (8.00%)	
occurrences (all)	4	9	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	3 / 116 (2.59%)	4 / 100 (4.00%)	
occurrences (all)	3	5	
Investigations			
Glomerular filtration rate decreased			
subjects affected / exposed	11 / 116 (9.48%)	5 / 100 (5.00%)	
occurrences (all)	14	5	
Neutrophil count decreased			

subjects affected / exposed	2 / 116 (1.72%)	3 / 100 (3.00%)	
occurrences (all)	2	3	
Injury, poisoning and procedural complications			
Ligament sprain			
subjects affected / exposed	4 / 116 (3.45%)	1 / 100 (1.00%)	
occurrences (all)	5	2	
Nervous system disorders			
Headache			
subjects affected / exposed	8 / 116 (6.90%)	5 / 100 (5.00%)	
occurrences (all)	12	6	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	7 / 116 (6.03%)	0 / 100 (0.00%)	
occurrences (all)	7	0	
Neutropenia			
subjects affected / exposed	6 / 116 (5.17%)	5 / 100 (5.00%)	
occurrences (all)	8	5	
Eye disorders			
Dry eye			
subjects affected / exposed	4 / 116 (3.45%)	1 / 100 (1.00%)	
occurrences (all)	4	1	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	10 / 116 (8.62%)	5 / 100 (5.00%)	
occurrences (all)	15	5	
Nausea			
subjects affected / exposed	3 / 116 (2.59%)	5 / 100 (5.00%)	
occurrences (all)	3	6	
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	5 / 116 (4.31%)	2 / 100 (2.00%)	
occurrences (all)	5	2	
Rash			
subjects affected / exposed	3 / 116 (2.59%)	2 / 100 (2.00%)	
occurrences (all)	3	2	
Renal and urinary disorders			

Lupus nephritis			
subjects affected / exposed	8 / 116 (6.90%)	1 / 100 (1.00%)	
occurrences (all)	9	1	
Renal impairment			
subjects affected / exposed	4 / 116 (3.45%)	2 / 100 (2.00%)	
occurrences (all)	4	2	
Proteinuria			
subjects affected / exposed	4 / 116 (3.45%)	1 / 100 (1.00%)	
occurrences (all)	6	2	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	7 / 116 (6.03%)	3 / 100 (3.00%)	
occurrences (all)	7	4	
Systemic lupus erythematosus			
subjects affected / exposed	5 / 116 (4.31%)	7 / 100 (7.00%)	
occurrences (all)	5	9	
Arthritis			
subjects affected / exposed	4 / 116 (3.45%)	2 / 100 (2.00%)	
occurrences (all)	5	2	
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	14 / 116 (12.07%)	8 / 100 (8.00%)	
occurrences (all)	22	10	
Upper respiratory tract infection			
subjects affected / exposed	10 / 116 (8.62%)	3 / 100 (3.00%)	
occurrences (all)	11	6	
Viral upper respiratory tract infection			
subjects affected / exposed	10 / 116 (8.62%)	4 / 100 (4.00%)	
occurrences (all)	10	6	
Bronchitis			
subjects affected / exposed	5 / 116 (4.31%)	4 / 100 (4.00%)	
occurrences (all)	5	4	
Corona virus infection			
subjects affected / exposed	5 / 116 (4.31%)	8 / 100 (8.00%)	
occurrences (all)	6	9	
Gastroenteritis			

subjects affected / exposed	5 / 116 (4.31%)	2 / 100 (2.00%)	
occurrences (all)	5	2	
Herpes zoster			
subjects affected / exposed	4 / 116 (3.45%)	7 / 100 (7.00%)	
occurrences (all)	4	7	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
10 October 2018	Editorial changes for clarification and changes to correct errors.
21 December 2018	Editorial changes for clarification and changes to correct errors.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported