# Clinical trial results:
# A Randomized, Controlled Double-blind Study Comparing the Efficacy and Safety of Orelvo (voclosporin) (23.7 mg Twice Daily) with Placebo in Achieving Renal Response in Subjects with Active Lupus Nephritis

## Summary

| | |
|---|---|
| EudraCT number | 2016-004045-81 |
| Trial protocol | BG ES NL PL HR |
| Global end of trial date | 10 October 2019 |

### Results information

| | |
|---|---|
| Result version number | v1 (current) |
| This version publication date | 12 May 2021 |
| First version publication date | 12 May 2021 |

## Trial information

### Trial identification

| | |
|---|---|
| Sponsor protocol code | AUR-VCS-2016-01 |

### Additional study identifiers

| | |
|---|---|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT03021499 |
| WHO universal trial number (UTN) | - |

Notes:

### Sponsors

| | |
|---|---|
| Sponsor organisation name | Aurinia Pharmaceuticals Inc. |
| Sponsor organisation address | 1203-4464 Markham St, Victoria, Canada, |
| Public contact | Clinical Trials Information, Aurinia Pharmaceuticals Inc., 1 (250) 744-2487, clinicaltrials@auriniapharma.com |
| Scientific contact | Clinical Trials Information, Aurinia Pharmaceuticals Inc., 1 (250) 744-2487, 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 | 10 October 2019 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 10 October 2019 |
| Global end of trial reached? | Yes |
| Global end of trial date | 10 October 2019 |
| Was the trial ended prematurely? | No |

Notes:

## General information about the trial

Main objective of the trial:

To assess the efficacy of Orelvo (voclosporin) compared with placebo in achieving renal response after 52 weeks of therapy in subjects with active lupus nephritis (LN)

Protection of trial subjects:

A Data and Safety Monitoring Board (DSMB) was constituted to monitor the safety of study participants and to evaluate the safety and efficacy of voclosporin in the treatment of active LN.
The DSMB comprised three members, including a nephrologist and a rheumatologist, who were independent of Aurinia and recognized for their clinical expertise in LN.
Safety criteria included AEs, serious adverse events (SAEs) and abnormal clinical laboratory tests. Efficacy was evaluated using the primary endpoint of renal response and other relevant markers of disease activity as recommended by the committee. Blinded and partially unblinded (where appropriate) individual subject data were reviewed on an ongoing basis for safety and efficacy, and final results were reviewed for safety and efficacy findings. The DSMB also evaluated protocol adherence and subject withdrawal. Based on the observed benefits or adverse effects, the DSMB made recommendations to Aurinia concerning continuation, termination, or modifications of the study.

Background therapy: -

Evidence for comparator: -

| | |
|---|---|
| Actual start date of recruitment | 17 May 2017 |
| 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: 13 |
| Country: Number of subjects enrolled | Korea, Republic of: 6 |
| Country: Number of subjects enrolled | Malaysia: 12 |
| Country: Number of subjects enrolled | Philippines: 23 |
| Country: Number of subjects enrolled | Thailand: 22 |
| Country: Number of subjects enrolled | Taiwan: 13 |
| Country: Number of subjects enrolled | Vietnam: 15 |
| Country: Number of subjects enrolled | Bulgaria: 1 |
| Country: Number of subjects enrolled | Belarus: 14 |
| Country: Number of subjects enrolled | Spain: 4 |
| Country: Number of subjects enrolled | Croatia: 1 |
| Country: Number of subjects enrolled | Netherlands: 4 |
| Country: Number of subjects enrolled | Poland: 2 |
| Country: Number of subjects enrolled | Russian Federation: 37 |

| | |
|---|---|
| Country: Number of subjects enrolled | Serbia: 10 |
| Country: Number of subjects enrolled | Turkey: 7 |
| Country: Number of subjects enrolled | Ukraine: 17 |
| Country: Number of subjects enrolled | South Africa: 7 |
| Country: Number of subjects enrolled | Argentina: 2 |
| Country: Number of subjects enrolled | Brazil: 8 |
| Country: Number of subjects enrolled | Chile: 3 |
| Country: Number of subjects enrolled | Colombia: 21 |
| Country: Number of subjects enrolled | Dominican Republic: 13 |
| Country: Number of subjects enrolled | Guatemala: 13 |
| Country: Number of subjects enrolled | Mexico: 18 |
| Country: Number of subjects enrolled | Peru: 19 |
| Country: Number of subjects enrolled | United States: 52 |
| Worldwide total number of subjects | 357 |
| EEA total number of subjects | 12 |

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) | 355 |
| From 65 to 84 years | 2 |
| 85 years and over | 0 |

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

Screening will include provision of informed consent, physical examination including weight and height, medical history (including SLE and LN history), vital signs measurements, 12-lead ECG, and review of prior and concomitant medications and entry criteria.

### 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, Carer |

### Arms

| | |
|---|---|
| Are arms mutually exclusive? | Yes |
| **Arm title** | Voclosporin |

Arm description:

Voclosporin 23.7 mg BID

| | |
|---|---|
| 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:

Voclosporin was orally administered at a dose of 23.7 mg BID given as three 7.9 mg softgel capsules per dose for 52 weeks

| | |
|---|---|
| **Arm title** | Placebo |

Arm description:

Matching placebo softgel capsules

| | |
|---|---|
| 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:

Matching placebo softgel capsules were orally administered at a dose of 3 capsules BID for 52 weeks

| **Number of subjects in period 1** | Voclosporin | Placebo |
|---|---|---|
| Started | 179 | 178 |
| Completed | 163 | 147 |
| Not completed | 16 | 31 |
| Adverse event, serious fatal | 1 | 5 |
| Physician decision | 2 | 3 |
| Lack of Efficacy | - | 1 |
| Prohibited medication required | 1 | - |
| Protocol Non-compliance | 1 | 1 |
| Consent withdrawn by subject | 7 | 14 |
| Adverse event, non-fatal | 1 | - |
| Subject withdrew prior to first dose | 1 | - |
| Lost to follow-up | 1 | 3 |
| Unblinding of Study Treatment | - | 1 |
| Pregnancy | 1 | - |
| Subject Decided to Stop Medication | - | 2 |
| Subject Moved to a new Country | - | 1 |

## Baseline characteristics

| Reporting groups | |
|---|---|
| Reporting group title | Voclosporin |
| Reporting group description: Voclosporin 23.7 mg BID | |
| Reporting group title | Placebo |
| Reporting group description: Matching placebo softgel capsules | |

| Reporting group values | Voclosporin | Placebo | Total |
|---|---|---|---|
| Number of subjects | 179 | 178 | 357 |
| Age categorical<br>Units: Subjects | | | |
| Adults (18-64 years) | 179 | 176 | 355 |
| From 65-84 years | 0 | 2 | 2 |
| Age continuous<br>Units: years | | | |
| arithmetic mean | 32.8 | 33.6 | |
| standard deviation | ± 10.93 | ± 11.00 | - |
| Gender categorical<br>Units: Subjects | | | |
| Female | 161 | 152 | 313 |
| Male | 18 | 26 | 44 |
| Race<br>Units: Subjects | | | |
| White | 68 | 61 | 129 |
| Black or African American | 21 | 13 | 34 |
| American Indian or Alaska Native | 0 | 4 | 4 |
| Asian | 53 | 56 | 109 |
| Multiple Race | 0 | 1 | 1 |
| Other | 37 | 43 | 80 |
| Ethnicity<br>Units: Subjects | | | |
| Hispanic or Latino | 57 | 59 | 116 |
| Not Hispanic or Latino | 122 | 118 | 240 |
| Unknown | 0 | 1 | 1 |
| Years since diagnosis of systemic lupus erythematosus | | | |
| Number of years since diagnosis of systemic lupus erythematosus | | | |
| Units: years | | | |
| arithmetic mean | 6.6 | 6.9 | |
| standard deviation | ± 6.41 | ± 6.07 | - |
| Years since diagnosis of lupus nephritis | | | |
| Number of years since diagnosis of lupus nephritis | | | |
| Units: years | | | |
| arithmetic mean | 4.6 | 4.7 | |
| standard deviation | ± 5.07 | ± 4.89 | - |
| Years since first significant proteinuria | | | |

| Number of years since first significant proteinuria | | | |
|---|---|---|---|
| Units: years | | | |
| arithmetic mean | 4.8 | 4.6 | |
| standard deviation | ± 5.2 | ± 4.51 | - |
| Baseline Urine Protein Creatinine Ratio | | | |
| Baseline Urine Protein Creatinine Ratio (Average of pre-randomization values) | | | |
| Units: mg/mg | | | |
| arithmetic mean | 4.14 | 3.87 | |
| standard deviation | ± 2.711 | ± 2.363 | - |
| Baseline estimated glomerular filtration rate | | | |
| Baseline estimated glomerular filtration rate CKD Epi formula (lowest pre-randomization value) | | | |
| Units: mL/min/1.73m2 | | | |
| arithmetic mean | 92.1 | 90.4 | |
| standard deviation | ± 30.60 | ± 28.97 | - |

## End points

### End points reporting groups

| | |
|---|---|
| Reporting group title | Voclosporin |
| Reporting group description: Voclosporin 23.7 mg BID | |
| Reporting group title | Placebo |
| Reporting group description: Matching placebo softgel capsules | |

### Primary: Number of Participants with Adjudicated Renal Response at Week 52

| | |
|---|---|
| End point title | Number of Participants with Adjudicated Renal Response at Week 52 |

End point description:

The primary efficacy endpoint was the number of subjects showing renal response at Week 52. Renal response was adjudicated based on blinded data by an independent Clinical Endpoints Committee based on meeting the following criteria:
- UPCR of ≤0.5 mg/mg, and
- eGFR ≥60 mL/min/1.73 m2 or no confirmed decrease from baseline in eGFR of >20%, and
- Received no rescue medication for LN and
- Did not receive more than 10 mg prednisone for ≥3 consecutive days or for ≥7 days in total during Weeks 44 through 52, prior to assessment

Note: To be disqualified from renal response, the subject had to fail both eGFR measures (i.e., confirmed eGFR <60 mL/min/1.73 m2 AND confirmed >20% drop from BL) and have an associated treatment-related or disease-related AE that impacted eGFR Withdrawals prior to Week 52 with insufficient Week 52 data to determine response were defined non responders. Subjects who discontinued study drug but continued to attend study visits had their data assessed for respon

| | |
|---|---|
| End point type | Primary |
| End point timeframe: 52 Weeks | |

| End point values | Voclosporin | Placebo | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 179 | 178 | | |
| Units: Participants | 73 | 40 | | |

### Statistical analyses

| Statistical analysis title | Statistical Analysis 1 |
|---|---|

Statistical analysis description:

The primary endpoint was the proportion of subjects showing renal response at Week 52 as adjudicated by the Clinical Endpoints Committee.

| | |
|---|---|
| Comparison groups | Voclosporin v Placebo |

| | |
|---|---|
| Number of subjects included in analysis | 357 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 2.65 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.64 |
| upper limit | 4.27 |

## Secondary: Number of Participants with Reduction in Urine Protein Creatinine Ratio to 0.5 mg/mg or less

| | |
|---|---|
| End point title | Number of Participants with Reduction in Urine Protein Creatinine Ratio to 0.5 mg/mg or less |

End point description:

| | |
|---|---|
| End point type | Secondary |

End point timeframe:

52 Weeks

| End point values | Voclosporin | Placebo | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 179 | 178 | | |
| Units: participants | 116 | 78 | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Participants with Renal Response at Week 24

| | |
|---|---|
| End point title | Number of Participants with Renal Response at Week 24 |

End point description:

Number of subjects showing renal response at Week 24. Renal response was adjudicated based on blinded data by an Independent Clinical Endpoints Committee based on:
- UPCR of ≤0.5 mg/mg, and
- eGFR ≥60 mL/min/1.73 m2 or no confirmed decrease from baseline in eGFR of >20%, and
- Received no rescue medication for LN, and did not receive more than 10 mg prednisone for ≥3 consecutive days or for ≥7 days in total during Weeks 16 through 24, just prior to the renal response assessment.
Note: To be disqualified from renal response, the subject had to fail both eGFR measures (i.e., confirmed eGFR <60 mL/min/1.73 m2 AND confirmed >20% drop from BL) & have an associated treatment-related or disease-related AE that impacted eGFR. Subjects who withdrew prior to the Week 24 assessment and provided insufficient Week 24 data to
determine response were defined as non-responders. Subjects who discontinued study drug but

continued to attend study visits had their data assessed for response.

| End point type | Secondary |
|---|---|

End point timeframe:

Week 24

| **End point values** | Voclosporin | Placebo | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 179 | 178 | | |
| Units: Participants | 58 | 35 | | |

**Statistical analyses**

| **Statistical analysis title** | Statistical Analysis 1 |
|---|---|
| Comparison groups | Placebo v Voclosporin |
| Number of subjects included in analysis | 357 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.002 |
| Method | Regression, Cox |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 2.23 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.34 |
| upper limit | 3.72 |

## Secondary: Number of Participants with Partial Renal Response at Weeks 24 & 52

| End point title | Number of Participants with Partial Renal Response at Weeks 24 & 52 |
|---|---|

End point description:

Number of subjects with partial Renal Response (defined as a 50% reduction in UPCR from baseline) at week 24 and at week 52. Baseline UPCR is the average of 2 pre-randomisation values.

| End point type | Secondary |
|---|---|

End point timeframe:

Week 24 and Week 52

| End point values | Voclosporin | Placebo | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 179 | 178 | | |
| Units: Participants | | | | |
| Partial Response at Week 24 | 126 | 89 | | |
| Partial Response at Week 52 | 125 | 92 | | |

**Statistical analyses**

| Statistical analysis title | Statistical Analysis 1 |
|---|---|
| Statistical analysis description: Week 24 | |
| Comparison groups | Voclosporin v Placebo |
| Number of subjects included in analysis | 357 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 2.43 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.56 |
| upper limit | 3.79 |

| Statistical analysis title | Statistical Analysis 2 |
|---|---|
| Statistical analysis description: Week 52 | |
| Comparison groups | Voclosporin v Placebo |
| Number of subjects included in analysis | 357 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 2.26 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.45 |
| upper limit | 3.51 |

**Secondary: Number of Participants achieving, and remaining in, renal response**

| (Urine Protein Creatinine ratio ≤0.5 mg/mg) | |
|---|---|
| End point title | Number of Participants achieving, and remaining in, renal response (Urine Protein Creatinine ratio ≤0.5 mg/mg) |
| End point description: | |
| Duration in days until second occurrence of UPCR >0.5 mg/mg in subjects who achieve a reduction in UPCR to below 0.5 mg/mg | |
| End point type | Secondary |
| End point timeframe: | |
| Week 52 | |

| End point values | Voclosporin | Placebo | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 179 | 178 | | |
| Units: Participants | | | | |
| Subjects Achieving UPCR ≤0.5 mg/mg | 116 | 78 | | |
| Subjects with Second Occurrence of UPCR >0.5 mg/mg | 53 | 37 | | |
| Subjects without Second Occurrence UPCR >0.5 mg/mg | 63 | 41 | | |

### Statistical analyses

| Statistical analysis title | Statistical Analysis 1 |
|---|---|
| Comparison groups | Voclosporin v Placebo |
| Number of subjects included in analysis | 357 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.646 |
| Method | Logrank |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.81 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.53 |
| upper limit | 1.25 |

| Secondary: Number of Participants achieving 50% reduction in Urine Protein Creatinine Ratio | |
|---|---|
| End point title | Number of Participants achieving 50% reduction in Urine Protein Creatinine Ratio |
| End point description: | |
| End point type | Secondary |

End point timeframe:

Week 52

| End point values | Voclosporin | Placebo | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 179 | 178 | | |
| Units: Participants | | | | |
| Participants with 50% UPCR Reduction | 173 | 135 | | |
| Participants without 50% UPCR Reduction | 6 | 43 | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Time to 50% Reduction in Urine Protein Creatinine Ratio (Number of Days)

| End point title | Time to 50% Reduction in Urine Protein Creatinine Ratio (Number of Days) |
|---|---|

End point description:

Time in days to reduction in Urine Protein Creatinine ratio to decrease by 50% compared to baseline. Baseline is the average of two pre-randomisation values.

| End point type | Secondary |
|---|---|

End point timeframe:

Week 52

| End point values | Voclosporin | Placebo | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 179 | 178 | | |
| Units: days | | | | |
| median (confidence interval 95%) | 29 (29 to 32) | 63 (57 to 87) | | |

## Statistical analyses

| Statistical analysis title | Statistical Analysis 1 |
|---|---|

Statistical analysis description:

Time taken to reach 50% reduction in urine protein creatinine ratio

| Comparison groups | Voclosporin v Placebo |
|---|---|

| | |
|---|---|
| Number of subjects included in analysis | 357 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | Regression, Logistic |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 2.05 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.62 |
| upper limit | 2.6 |

## Secondary: Change From Baseline in estimated Glomerular Filtration Rate

| | |
|---|---|
| End point title | Change From Baseline in estimated Glomerular Filtration Rate |
| End point description: | |
| Change from baseline by visit in estimated Glomerular Filtration rate (eGFR). eGFR is corrected to a maximum value of 90 ml/min/1.73 m2 | |
| End point type | Secondary |
| End point timeframe: | |
| Baseline and Weeks 2, 4, 8, 12, 16, 20, 24, 30, 36, 42, 48 and 52 | |

| End point values | Voclosporin | Placebo | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 179 | 178 | | |
| Units: mL/min/1.73m2 | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline | 78.3 (± 15.83) | 77.4 (± 16.98) | | |
| Week 2 Change from Baseline | -1.5 (± 9.44) | 3.3 (± 10.12) | | |
| Week 4 Change from Baseline | -0.4 (± 10.39) | 3.2 (± 9.86) | | |
| Week 8 Change from Baseline | -0.9 (± 13.1) | 3.8 (± 11.27) | | |
| Week 12 Change from Baseline | -0.3 (± 11.74) | 3.3 (± 12.85) | | |
| Week 16 Change from Baseline | -0.1 (± 12.27) | 2.8 (± 13.25) | | |
| Week 20 Change from Baseline | -0.7 (± 12.09) | 3.2 (± 13.04) | | |
| Week 24 Change from Baseline | -0.3 (± 13.8) | 2.8 (± 13.84) | | |
| Week 30 Change from Baseline | -0.8 (± 14.2) | 1.8 (± 14.4) | | |
| Week 36 Change from Baseline | -1.9 (± 14.89) | 1.5 (± 14.84) | | |
| Week 42 Change from Baseline | -2.8 (± 16.7) | 1.5 (± 15.53) | | |
| Week 48 Change from Baseline | -3.6 (± 17.2) | 1.1 (± 15.71) | | |
| Week 52 Change from Baseline | -1.5 (± 16.16) | 1.5 (± 15) | | |

### Statistical analyses

| **Statistical analysis title** | Statistical Analysis 1 |
|---|---|
| Statistical analysis description: | |
| Change from Baseline in Corrected eGFR (mL/min/1.73m2) at Week 2 | |
| Comparison groups | Voclosporin v Placebo |
| Number of subjects included in analysis | 357 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | Mixed models analysis |
| Parameter estimate | Least Squares Mean Difference |
| Point estimate | -4.6 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -7.3 |
| upper limit | -1.9 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 1.39 |

| **Statistical analysis title** | Statistical Analysis 2 |
|---|---|
| Statistical analysis description: | |
| Change from Baseline in Corrected eGFR (mL/min/1.73m2) at Week 4 | |
| Comparison groups | Voclosporin v Placebo |
| Number of subjects included in analysis | 357 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.014 |
| Method | Mixed models analysis |
| Parameter estimate | Least Squares Mean Difference |
| Point estimate | -3.4 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -6.1 |
| upper limit | -0.7 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 1.39 |

| **Statistical analysis title** | Statistical Analysis 3 |
|---|---|
| Statistical analysis description: | |
| Change from Baseline in Corrected eGFR (mL/min/1.73m2) at Week 8 | |
| Comparison groups | Voclosporin v Placebo |

| | |
|---|---|
| Number of subjects included in analysis | 357 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | Mixed models analysis |
| Parameter estimate | Least Squares Mean Difference |
| Point estimate | -4.6 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -7.3 |
| upper limit | -1.9 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 1.39 |

| **Statistical analysis title** | Statistical Analysis 4 |
|---|---|
| Statistical analysis description: | |
| Change from Baseline in Corrected eGFR (mL/min/1.73m2) at Week 12 | |
| Comparison groups | Voclosporin v Placebo |
| Number of subjects included in analysis | 357 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.017 |
| Method | Mixed models analysis |
| Parameter estimate | Least Squares Mean Difference |
| Point estimate | -3.3 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -6 |
| upper limit | -0.6 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 1.39 |

| **Statistical analysis title** | Statistical Analysis 5 |
|---|---|
| Statistical analysis description: | |
| Change from Baseline in Corrected eGFR (mL/min/1.73m2) at Week 16 | |
| Comparison groups | Voclosporin v Placebo |
| Number of subjects included in analysis | 357 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.085 |
| Method | Mixed models analysis |
| Parameter estimate | Least Squares Mean Difference |
| Point estimate | -2.4 |

| | |
|---|---|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -5.1 |
| upper limit | 0.3 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 1.4 |

| **Statistical analysis title** | Statistical Analysis 6 |
|---|---|
| Statistical analysis description: | |
| Change from Baseline in Corrected eGFR (mL/min/1.73m2) at Week 20 | |
| Comparison groups | Voclosporin v Placebo |
| Number of subjects included in analysis | 357 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.035 |
| Method | Mixed models analysis |
| Parameter estimate | Least Squares Mean Difference |
| Point estimate | -3 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -5.7 |
| upper limit | -0.2 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 1.4 |

| **Statistical analysis title** | Statistical Analysis 7 |
|---|---|
| Statistical analysis description: | |
| Change from Baseline in Corrected eGFR (mL/min/1.73m2) at Week 24 | |
| Comparison groups | Voclosporin v Placebo |
| Number of subjects included in analysis | 357 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.121 |
| Method | Mixed models analysis |
| Parameter estimate | Least Squares Mean Difference |
| Point estimate | -2.2 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -5 |
| upper limit | 0.6 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 1.41 |

| **Statistical analysis title** | Statistical Analysis 8 |
|---|---|
| Statistical analysis description:<br>Change from Baseline in Corrected eGFR (mL/min/1.73m2) at Week 30 | |
| Comparison groups | Voclosporin v Placebo |
| Number of subjects included in analysis | 357 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.12 |
| Method | Mixed models analysis |
| Parameter estimate | Least Squares Mean Difference |
| Point estimate | -2.2 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -5 |
| upper limit | 0.6 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 1.42 |

| **Statistical analysis title** | Statistical Analysis 9 |
|---|---|
| Statistical analysis description:<br>Change from Baseline in Corrected eGFR (mL/min/1.73m2) at Week 36 | |
| Comparison groups | Voclosporin v Placebo |
| Number of subjects included in analysis | 357 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.102 |
| Method | Mixed models analysis |
| Parameter estimate | Least Squares Mean Difference |
| Point estimate | -2.3 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -5.1 |
| upper limit | 0.5 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 1.43 |

| **Statistical analysis title** | Statistical Analysis 10 |
|---|---|
| Statistical analysis description:<br>Change from Baseline in Corrected eGFR (mL/min/1.73m2) at Week 42 | |
| Comparison groups | Voclosporin v Placebo |

| | |
|---|---|
| Number of subjects included in analysis | 357 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.022 |
| Method | Mixed models analysis |
| Parameter estimate | Least Squares Mean Difference |
| Point estimate | -3.3 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -6.1 |
| upper limit | -0.5 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 1.44 |

| **Statistical analysis title** | Statistical Analysis 11 |
|---|---|
| Statistical analysis description: | |
| Change from Baseline in Corrected eGFR (mL/min/1.73m2) at Week 48 | |
| Comparison groups | Voclosporin v Placebo |
| Number of subjects included in analysis | 357 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.004 |
| Method | Mixed models analysis |
| Parameter estimate | Least Squares Mean Difference |
| Point estimate | -4.1 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -7 |
| upper limit | -1.3 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 1.45 |

| **Statistical analysis title** | Statistical Analysis 12 |
|---|---|
| Statistical analysis description: | |
| Change from Baseline in Corrected eGFR (mL/min/1.73m2) at Week 52 | |
| Comparison groups | Voclosporin v Placebo |
| Number of subjects included in analysis | 357 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.055 |
| Method | Mixed models analysis |
| Parameter estimate | Least Squares Mean Difference |
| Point estimate | -2.8 |

| | |
|---|---|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -5.7 |
| upper limit | 0.1 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 1.46 |

## Secondary: Change in Baseline in Urinary Protein Creatinine Ratio

| | |
|---|---|
| End point title | Change in Baseline in Urinary Protein Creatinine Ratio |

End point description:

Change from baseline by visit in Urine Protein Creatinine ratio. Baseline is the average of two pre-randomisation values.

| | |
|---|---|
| End point type | Secondary |

End point timeframe:

Baseline and Weeks 2, 4, 8, 12, 16, 20, 24, 30, 36, 42, 48 and 52

| End point values | Voclosporin | Placebo | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 179 | 178 | | |
| Units: mg/mg | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline | 4.14 (± 2.711) | 3.87 (± 2.363) | | |
| Week 2 Change from Baseline | -1.46 (± 1.991) | -0.7 (± 2.312) | | |
| Week 4 Change from Baseline | -1.98 (± 2.29) | -1.07 (± 2.155) | | |
| Week 8 Change from Baseline | -2.23 (± 2.213) | -1.43 (± 2.448) | | |
| Week 12 Change from Baseline | -2.56 (± 2.293) | -1.48 (± 2.688) | | |
| Week 16 Change from Baseline | -2.75 (± 2.462) | -1.58 (± 2.81) | | |
| Week 20 Change from Baseline | -2.74 (± 2.968) | -1.54 (± 2.82) | | |
| Week 24 Change from Baseline | -2.74 (± 2.567) | -1.59 (± 2.899) | | |
| Week 30 Change from Baseline | -2.66 (± 3.336) | -1.7 (± 3.112) | | |
| Week 36 Change from Baseline | -2.74 (± 2.871) | -1.63 (± 3.188) | | |
| Week 42 Change from Baseline | -2.91 (± 2.522) | -1.78 (± 3.39) | | |
| Week 48 Change from Baseline | -2.71 (± 2.807) | -1.8 (± 3.004) | | |
| Week 52 Change from Baseline | -2.65 (± 2.872) | -1.88 (± 3.05) | | |

## Statistical analyses

| **Statistical analysis title** | Statistical Analysis 1 |
|---|---|
| Statistical analysis description:<br>Change from Baseline in UPCR (mg/mg) at Week 2 | |
| Comparison groups | Voclosporin v Placebo |
| Number of subjects included in analysis | 357 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.011 |
| Method | Mixed models analysis |
| Parameter estimate | Least Squares Mean Difference |
| Point estimate | -0.56 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1 |
| upper limit | -0.13 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.22 |

| **Statistical analysis title** | Statistical Analysis 2 |
|---|---|
| Statistical analysis description:<br>Change from Baseline in UPCR (mg/mg) at Week 4 | |
| Comparison groups | Voclosporin v Placebo |
| Number of subjects included in analysis | 357 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | Mixed models analysis |
| Parameter estimate | Least Squares Mean Difference |
| Point estimate | -0.76 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.13 |
| upper limit | -0.4 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.187 |

| **Statistical analysis title** | Statistical Analysis 3 |
|---|---|
| Statistical analysis description:<br>Change from Baseline in UPCR (mg/mg) at Week 8 | |
| Comparison groups | Voclosporin v Placebo |

| | |
|---|---|
| Number of subjects included in analysis | 357 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | Mixed models analysis |
| Parameter estimate | Least Squares Mean Difference |
| Point estimate | -0.7 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.05 |
| upper limit | -0.34 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.181 |

| **Statistical analysis title** | Statistical Analysis 4 |
|---|---|
| Statistical analysis description: | |
| Change from Baseline in UPCR (mg/mg) at Week 12 | |
| Comparison groups | Voclosporin v Placebo |
| Number of subjects included in analysis | 357 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | Mixed models analysis |
| Parameter estimate | Least Squares Mean Difference |
| Point estimate | -0.94 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.33 |
| upper limit | -0.55 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.196 |

| **Statistical analysis title** | Statistical Analysis 5 |
|---|---|
| Statistical analysis description: | |
| Change from Baseline in UPCR (mg/mg) at Week 16 | |
| Comparison groups | Voclosporin v Placebo |
| Number of subjects included in analysis | 357 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | Mixed models analysis |
| Parameter estimate | Least Squares Mean Difference |
| Point estimate | -1.18 |

| | |
|---|---|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.6 |
| upper limit | -0.76 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.214 |

| **Statistical analysis title** | Statistical Analysis 6 |
|---|---|
| Statistical analysis description: | |
| Change from Baseline in UPCR (mg/mg) at Week 20 | |
| Comparison groups | Voclosporin v Placebo |
| Number of subjects included in analysis | 357 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | Mixed models analysis |
| Parameter estimate | Least Squares Mean Difference |
| Point estimate | -1.16 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.63 |
| upper limit | -0.68 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.241 |

| **Statistical analysis title** | Statistical Analysis 7 |
|---|---|
| Statistical analysis description: | |
| Change from Baseline in UPCR (mg/mg) at Week 24 | |
| Comparison groups | Voclosporin v Placebo |
| Number of subjects included in analysis | 357 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | Mixed models analysis |
| Parameter estimate | Least Squares Mean Difference |
| Point estimate | -1.15 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.59 |
| upper limit | -0.72 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.222 |

| **Statistical analysis title** | Statistical Analysis 8 |
|---|---|
| Statistical analysis description:<br>Change from Baseline in UPCR (mg/mg) at Week 30 | |
| Comparison groups | Voclosporin v Placebo |
| Number of subjects included in analysis | 357 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | Mixed models analysis |
| Parameter estimate | Least Squares Mean Difference |
| Point estimate | -1.02 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.58 |
| upper limit | -0.46 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.284 |

| **Statistical analysis title** | Statistical Analysis 9 |
|---|---|
| Statistical analysis description:<br>Change from Baseline in UPCR (mg/mg) at Week 36 | |
| Comparison groups | Voclosporin v Placebo |
| Number of subjects included in analysis | 357 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | Mixed models analysis |
| Parameter estimate | Least Squares Mean Difference |
| Point estimate | -1.21 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.73 |
| upper limit | -0.69 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.264 |

| **Statistical analysis title** | Statistical Analysis 10 |
|---|---|
| Statistical analysis description:<br>Change from Baseline in UPCR (mg/mg) at Week 42 | |
| Comparison groups | Voclosporin v Placebo |

| | |
|---|---|
| Number of subjects included in analysis | 357 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | Mixed models analysis |
| Parameter estimate | Least Squares Mean Difference |
| Point estimate | -1.37 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.87 |
| upper limit | -0.86 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.256 |

| **Statistical analysis title** | Statistical Analysis 11 |
|---|---|
| Statistical analysis description: | |
| Change from Baseline in UPCR (mg/mg) at Week 48 | |
| Comparison groups | Voclosporin v Placebo |
| Number of subjects included in analysis | 357 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | Mixed models analysis |
| Parameter estimate | Least Squares Mean Difference |
| Point estimate | -1.06 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.56 |
| upper limit | -0.55 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.256 |

| **Statistical analysis title** | Statistical Analysis 12 |
|---|---|
| Statistical analysis description: | |
| Change from Baseline in UPCR (mg/mg) at Week 52 | |
| Comparison groups | Voclosporin v Placebo |
| Number of subjects included in analysis | 357 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | Mixed models analysis |
| Parameter estimate | Least Squares Mean Difference |
| Point estimate | -0.99 |

| | |
|---|---|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.52 |
| upper limit | -0.46 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.27 |

## Secondary: Number of Participants with Renal Response with Low Dose Steroids

| | |
|---|---|
| End point title | Number of Participants with Renal Response with Low Dose Steroids |
| End point description: | |
| Programmed Renal Response while on low dose steroids (<2.5 mg/day) for the preceding 8 weeks at weeks 24 and 52 | |
| End point type | Secondary |
| End point timeframe: | |
| Week 24 and Week 52 | |

| End point values | Voclosporin | Placebo | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 179 | 178 | | |
| Units: Participants | | | | |
| Renal Response at Week 24 | 32 | 16 | | |
| Renal Response at Week 52 | 64 | 36 | | |

### Statistical analyses

| Statistical analysis title | Statistical Analysis 1 |
|---|---|
| Statistical analysis description: | |
| Renal Response at Week 24 | |
| Comparison groups | Voclosporin v Placebo |
| Number of subjects included in analysis | 357 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.008 |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 2.44 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.26 |
| upper limit | 4.71 |

| **Statistical analysis title** | Statistical Analysis 2 |
|---|---|
| Statistical analysis description:<br>Renal Response at Week 52 | |
| Comparison groups | Voclosporin v Placebo |
| Number of subjects included in analysis | 357 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | Regression, Logistic |
| Parameter estimate | Risk ratio (RR) |
| Point estimate | 2.44 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.48 |
| upper limit | 4 |

## Secondary: Change from Baseline in Safety of Estrogens in Systemic Lupus Erythematosus National Assessment Systemic Lupus Erythematosus Disease Activity Index (SELENA - SLEDAI)

| End point title | Change from Baseline in Safety of Estrogens in Systemic Lupus Erythematosus National Assessment Systemic Lupus Erythematosus Disease Activity Index (SELENA - SLEDAI) |
|---|---|

End point description:

SELENA-SLEDAI were analyzed using a mixed effect model repeated measures (MMRM) analysis with treatment arm, visit, treatment by visit interaction, biopsy class, MMF use at baseline, region, and baseline UPCR included as covariates in the model. Results are expressed as differences between treatment arms along with the associated 95% CI. The least squares means (LS means) and their corresponding 95% confidence intervals of the change from baseline values are also presented for each visit and for the overall change.

| End point type | Secondary |
|---|---|

End point timeframe:

Week 24 and Week 52

| **End point values** | Voclosporin | Placebo | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 179 | 178 | | |
| Units: Scores on a Scale | | | | |
| least squares mean (confidence interval 95%) | | | | |
| Week 24 Change from Baseline | -4.5 (-5.4 to -3.7) | -4.1 (-5.0 to -3.2) | | |
| Week 52 Change from Baseline | -6 (-6.7 to -5.2) | -5.5 (-6.3 to -4.7) | | |

**Statistical analyses**

| **Statistical analysis title** | Statistical Analysis 1 |
|---|---|
| Statistical analysis description:<br>Change from Baseline at Week 24 | |
| Comparison groups | Voclosporin v Placebo |
| Number of subjects included in analysis | 357 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.373 |
| Method | Mixed models analysis |
| Parameter estimate | Least Squares Mean Difference |
| Point estimate | -0.5 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.6 |
| upper limit | 0.6 |

| **Statistical analysis title** | Statistical Analysis 2 |
|---|---|
| Statistical analysis description:<br>Change from Baseline at Week 52 | |
| Comparison groups | Voclosporin v Placebo |
| Number of subjects included in analysis | 357 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.277 |
| Method | Mixed models analysis |
| Parameter estimate | Least Squares Mean Difference |
| Point estimate | -0.5 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.4 |
| upper limit | 0.4 |

**Secondary: Change from Baseline in Patient Report Outcomes**

| End point title | Change from Baseline in Patient Report Outcomes |
|---|---|

End point description:

Health-related quality of life (HRQoL) information was collected using the Short Form Health Survey (SF-

36) HRQoL assessment and the LupusPRO (v1.7) assessment.
- SF-36 is a 36-item patient-reported questionnaire of patient health
- LupusPro assessment is a patient-reported questionnaire regarding the effect of lupus or its treatment on the patient's health, quality of life, and the medical care received related to lupus.

| End point type | Secondary |
|---|---|
| End point timeframe: | |
| Week 24 and Week 52 | |

| **End point values** | Voclosporin | Placebo | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 179 | 178 | | |
| Units: Scores on a scale | | | | |
| least squares mean (confidence interval 95%) | | | | |
| SF-36 Change from Baseline at Week 24 | 6.64 (4.34 to 8.93) | 7.11 (4.80 to 9.42) | | |
| SF-36 Change from Baseline at Week 52 | 10.44 (8.04 to 12.83) | 10.81 (8.37 to 13.25) | | |
| LupusPRO HRQOL Change from Baseline at Week 24 | 7.76 (5.40 to 10.13) | 6.06 (3.68 to 8.45) | | |
| LupusPRO HRQOL Change from Baseline at Week 52 | 9.24 (6.78 to 11.70) | 9.84 (7.33 to 12.35) | | |
| LupusPRO non-HRQOL Change from Baseline at Week 24 | 1.06 (-1.32 to 3.44) | 2.94 (0.54 to 5.35) | | |
| LupusPRO non-HRQOL Change from Baseline at Week 52 | 4.08 (1.60 to 6.56) | 3.74 (1.22 to 6.26) | | |

## Statistical analyses

| **Statistical analysis title** | Statistical Analysis 1 |
|---|---|
| Statistical analysis description: | |
| SF-36 Change from Baseline Week 24 | |
| Comparison groups | Placebo v Voclosporin |
| Number of subjects included in analysis | 357 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.733 |
| Method | Mixed models analysis |
| Parameter estimate | Least Squares Mean Difference |
| Point estimate | -0.47 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -3.21 |
| upper limit | 2.26 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 1.389 |

| **Statistical analysis title** | Statistical Analysis 2 |
|---|---|
| Statistical analysis description:<br>SF-36 Change from Baseline at Week 52 | |
| Comparison groups | Voclosporin v Placebo |
| Number of subjects included in analysis | 357 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.801 |
| Method | Mixed models analysis |
| Parameter estimate | Least Squares Mean Difference |
| Point estimate | -0.37 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -3.29 |
| upper limit | 2.54 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 1.481 |

| **Statistical analysis title** | Statistical Analysis 3 |
|---|---|
| Statistical analysis description:<br>LupusPRO HRQOL Change from Baseline at Week 24 | |
| Comparison groups | Voclosporin v Placebo |
| Number of subjects included in analysis | 357 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.239 |
| Method | Mixed models analysis |
| Parameter estimate | Least Squares Mean Difference |
| Point estimate | 1.7 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.14 |
| upper limit | 4.54 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 1.442 |

| **Statistical analysis title** | Statistical Analysis 4 |
|---|---|
| Statistical analysis description:<br>LupusPRO HRQOL Change from Baseline at Week 52 | |
| Comparison groups | Voclosporin v Placebo |

| | |
|---|---|
| Number of subjects included in analysis | 357 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.695 |
| Method | Mixed models analysis |
| Parameter estimate | Least Squares Mean Difference |
| Point estimate | -0.6 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -3.62 |
| upper limit | 2.42 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 1.535 |

| **Statistical analysis title** | Statistical Analysis 5 |
|---|---|
| Statistical analysis description: | |
| LupusPRO non-HRQOL Change from Baseline at Week 24 | |
| Comparison groups | Voclosporin v Placebo |
| Number of subjects included in analysis | 357 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.19 |
| Method | Mixed models analysis |
| Parameter estimate | Least Squares Mean Difference |
| Point estimate | -1.89 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -4.72 |
| upper limit | 0.94 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 1.439 |

| **Statistical analysis title** | Statistical Analysis 6 |
|---|---|
| Statistical analysis description: | |
| LupusPRO non-HRQOL Change from Baseline at Week 52 | |
| Comparison groups | Voclosporin v Placebo |
| Number of subjects included in analysis | 357 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.826 |
| Method | Mixed models analysis |
| Parameter estimate | Least Squares Mean Difference |
| Point estimate | 0.826 |

| | |
|---|---|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -2.67 |
| upper limit | 3.35 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 1.531 |

## Adverse events

| Adverse events information | |
|---|---|
| Timeframe for reporting adverse events: AEs occurring after first dose and up to 30 days post-last dose of voclosporin/placebo | |
| Assessment type | Systematic |

| Dictionary used | |
|---|---|
| Dictionary name | MedDRA |
| Dictionary version | 20 |

| Reporting groups | |
|---|---|
| Reporting group title | Voclosporin |
| Reporting group description: Voclosporin 23.7 mg BID | |
| Reporting group title | Placebo Oral Capsule |
| Reporting group description: Matching placebo | |

| Serious adverse events | Voclosporin | Placebo Oral Capsule | |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 37 / 178 (20.79%) | 38 / 178 (21.35%) | |
| number of deaths (all causes) | 1 | 5 | |
| number of deaths resulting from adverse events | 0 | 3 | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Cervix carcinoma stage 0 | | | |
| subjects affected / exposed | 1 / 178 (0.56%) | 0 / 178 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Schwannoma | | | |
| subjects affected / exposed | 0 / 178 (0.00%) | 1 / 178 (0.56%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vascular disorders | | | |
| Hypertension | | | |
| subjects affected / exposed | 3 / 178 (1.69%) | 1 / 178 (0.56%) | |
| occurrences causally related to treatment / all | 2 / 3 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypertensive crisis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 178 (0.56%) | 2 / 178 (1.12%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Surgical and medical procedures | | | |
| Abortion induced | | | |
| subjects affected / exposed | 1 / 178 (0.56%) | 0 / 178 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pregnancy, puerperium and perinatal conditions | | | |
| Abortion spontaneous | | | |
| subjects affected / exposed | 0 / 178 (0.00%) | 1 / 178 (0.56%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| General disorders and administration site conditions | | | |
| Generalised oedema | | | |
| subjects affected / exposed | 1 / 178 (0.56%) | 1 / 178 (0.56%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Reproductive system and breast disorders | | | |
| Uterine haemorrhage | | | |
| subjects affected / exposed | 0 / 178 (0.00%) | 1 / 178 (0.56%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Pleural effusion | | | |
| subjects affected / exposed | 1 / 178 (0.56%) | 1 / 178 (0.56%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lupus pleurisy | | | |
| subjects affected / exposed | 0 / 178 (0.00%) | 1 / 178 (0.56%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pulmonary embolism | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 178 (0.00%) | 1 / 178 (0.56%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Investigations | | | |
| Glomerular filtration rate decreased | | | |
| subjects affected / exposed | 1 / 178 (0.56%) | 1 / 178 (0.56%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Blood lactate dehydrogenase increased | | | |
| subjects affected / exposed | 1 / 178 (0.56%) | 0 / 178 (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 | | | |
| Intentional overdose | | | |
| subjects affected / exposed | 1 / 178 (0.56%) | 0 / 178 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Congenital, familial and genetic disorders | | | |
| Developmental hip dysplasia | | | |
| subjects affected / exposed | 1 / 178 (0.56%) | 0 / 178 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac disorders | | | |
| Acute coronary syndrome | | | |
| subjects affected / exposed | 1 / 178 (0.56%) | 0 / 178 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac failure | | | |
| subjects affected / exposed | 1 / 178 (0.56%) | 0 / 178 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac failure acute | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 178 (0.56%) | 0 / 178 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac failure congestive | | | |
| subjects affected / exposed | 1 / 178 (0.56%) | 0 / 178 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Acute myocardial infarction | | | |
| subjects affected / exposed | 0 / 178 (0.00%) | 1 / 178 (0.56%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nervous system disorders | | | |
| Cerebral infarction | | | |
| subjects affected / exposed | 1 / 178 (0.56%) | 0 / 178 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Headache | | | |
| subjects affected / exposed | 1 / 178 (0.56%) | 0 / 178 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lupus encephalitis | | | |
| subjects affected / exposed | 1 / 178 (0.56%) | 0 / 178 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Migraine | | | |
| subjects affected / exposed | 1 / 178 (0.56%) | 0 / 178 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Neuropsychiatric lupus | | | |
| subjects affected / exposed | 1 / 178 (0.56%) | 0 / 178 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Haemorrhagic stroke | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 178 (0.00%) | 1 / 178 (0.56%) | |
| 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 | | | |
| Anaemia | | | |
| subjects affected / exposed | 3 / 178 (1.69%) | 0 / 178 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 4 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Neutropenia | | | |
| subjects affected / exposed | 1 / 178 (0.56%) | 0 / 178 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal disorders | | | |
| Gastritis | | | |
| subjects affected / exposed | 1 / 178 (0.56%) | 0 / 178 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Diarrhoea | | | |
| subjects affected / exposed | 0 / 178 (0.00%) | 1 / 178 (0.56%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrooesophageal reflux disease | | | |
| subjects affected / exposed | 0 / 178 (0.00%) | 1 / 178 (0.56%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Upper gastrointestinal haemorrhage | | | |
| subjects affected / exposed | 0 / 178 (0.00%) | 1 / 178 (0.56%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatobiliary disorders | | | |
| Cholecystitis chronic | | | |
| subjects affected / exposed | 0 / 178 (0.00%) | 1 / 178 (0.56%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|---|---|---|
| Renal and urinary disorders | | | |
| Acute kidney injury | | | |
| subjects affected / exposed | 4 / 178 (2.25%) | 2 / 178 (1.12%) | |
| occurrences causally related to treatment / all | 1 / 5 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal impairment | | | |
| subjects affected / exposed | 2 / 178 (1.12%) | 1 / 178 (0.56%) | |
| occurrences causally related to treatment / all | 1 / 2 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lupus nephritis | | | |
| subjects affected / exposed | 1 / 178 (0.56%) | 4 / 178 (2.25%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Renal failure | | | |
| subjects affected / exposed | 1 / 178 (0.56%) | 1 / 178 (0.56%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Musculoskeletal and connective tissue disorders | | | |
| Systemic lupus erythematosus | | | |
| subjects affected / exposed | 3 / 178 (1.69%) | 3 / 178 (1.69%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Musculoskeletal pain | | | |
| subjects affected / exposed | 0 / 178 (0.00%) | 1 / 178 (0.56%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infections and infestations | | | |
| Pneumonia | | | |
| subjects affected / exposed | 7 / 178 (3.93%) | 8 / 178 (4.49%) | |
| occurrences causally related to treatment / all | 1 / 8 | 2 / 9 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 2 | |
| Gastroenteritis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 3 / 178 (1.69%) | 0 / 178 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Urinary tract infection | | | |
| subjects affected / exposed | 2 / 178 (1.12%) | 1 / 178 (0.56%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pyelonephritis acute | | | |
| subjects affected / exposed | 1 / 178 (0.56%) | 1 / 178 (0.56%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 1 / 178 (0.56%) | 1 / 178 (0.56%) | |
| occurrences causally related to treatment / all | 1 / 1 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Acute sinusitis | | | |
| subjects affected / exposed | 1 / 178 (0.56%) | 0 / 178 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bacterial diarrhoea | | | |
| subjects affected / exposed | 1 / 178 (0.56%) | 0 / 178 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cystitis | | | |
| subjects affected / exposed | 1 / 178 (0.56%) | 0 / 178 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Herpes zoster | | | |
| subjects affected / exposed | 1 / 178 (0.56%) | 0 / 178 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lung abscess | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 178 (0.56%) | 0 / 178 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonia cytomegaloviral | | | |
| subjects affected / exposed | 1 / 178 (0.56%) | 0 / 178 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pulmonary tuberculosis | | | |
| subjects affected / exposed | 1 / 178 (0.56%) | 0 / 178 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bronchitis | | | |
| subjects affected / exposed | 0 / 178 (0.00%) | 3 / 178 (1.69%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Diarrhoea infectious | | | |
| subjects affected / exposed | 0 / 178 (0.00%) | 1 / 178 (0.56%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Escherichia sepsis | | | |
| subjects affected / exposed | 0 / 178 (0.00%) | 1 / 178 (0.56%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Herpes zoster disseminated | | | |
| subjects affected / exposed | 0 / 178 (0.00%) | 1 / 178 (0.56%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Intervertebral discitis | | | |
| subjects affected / exposed | 0 / 178 (0.00%) | 1 / 178 (0.56%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Paraspinal abscess | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 178 (0.00%) | 1 / 178 (0.56%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pyelonephritis | | | |
| subjects affected / exposed | 0 / 178 (0.00%) | 1 / 178 (0.56%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Salmonellosis | | | |
| subjects affected / exposed | 0 / 178 (0.00%) | 1 / 178 (0.56%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Salpingitis | | | |
| subjects affected / exposed | 0 / 178 (0.00%) | 1 / 178 (0.56%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Sepsis | | | |
| subjects affected / exposed | 0 / 178 (0.00%) | 1 / 178 (0.56%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Septic shock | | | |
| subjects affected / exposed | 0 / 178 (0.00%) | 1 / 178 (0.56%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Metabolism and nutrition disorders | | | |
| Hypokalaemia | | | |
| subjects affected / exposed | 0 / 178 (0.00%) | 1 / 178 (0.56%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Metabolic acidosis | | | |
| subjects affected / exposed | 0 / 178 (0.00%) | 1 / 178 (0.56%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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

| **Non-serious adverse events** | Voclosporin | Placebo Oral Capsule | |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 161 / 178 (90.45%) | 156 / 178 (87.64%) | |
| Investigations | | | |
| Glomerular filtration rate decreased | | | |
| subjects affected / exposed | 43 / 178 (24.16%) | 15 / 178 (8.43%) | |
| occurrences (all) | 61 | 19 | |
| Vascular disorders | | | |
| Hypertension | | | |
| subjects affected / exposed | 35 / 178 (19.66%) | 14 / 178 (7.87%) | |
| occurrences (all) | 38 | 15 | |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 29 / 178 (16.29%) | 11 / 178 (6.18%) | |
| occurrences (all) | 34 | 16 | |
| General disorders and administration site conditions | | | |
| Oedema peripheral | | | |
| subjects affected / exposed | 11 / 178 (6.18%) | 11 / 178 (6.18%) | |
| occurrences (all) | 11 | 11 | |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 18 / 178 (10.11%) | 10 / 178 (5.62%) | |
| occurrences (all) | 19 | 11 | |
| Leukopenia | | | |
| subjects affected / exposed | 7 / 178 (3.93%) | 10 / 178 (5.62%) | |
| occurrences (all) | 8 | 12 | |
| Gastrointestinal disorders | | | |
| Diarrhoea | | | |
| subjects affected / exposed | 34 / 178 (19.10%) | 21 / 178 (11.80%) | |
| occurrences (all) | 43 | 23 | |
| Abdominal pain upper | | | |
| subjects affected / exposed | 13 / 178 (7.30%) | 1 / 178 (0.56%) | |
| occurrences (all) | 13 | 2 | |
| Abdominal pain | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 10 / 178 (5.62%) | 2 / 178 (1.12%) | |
| occurrences (all) | 11 | 3 | |
| Nausea | | | |
| subjects affected / exposed | 10 / 178 (5.62%) | 17 / 178 (9.55%) | |
| occurrences (all) | 10 | 18 | |
| Dyspepsia | | | |
| subjects affected / exposed | 10 / 178 (5.62%) | 3 / 178 (1.69%) | |
| occurrences (all) | 10 | 3 | |
| Vomiting | | | |
| subjects affected / exposed | 5 / 178 (2.81%) | 12 / 178 (6.74%) | |
| occurrences (all) | 6 | 17 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Cough | | | |
| subjects affected / exposed | 13 / 178 (7.30%) | 3 / 178 (1.69%) | |
| occurrences (all) | 13 | 3 | |
| Skin and subcutaneous tissue disorders | | | |
| Alopecia | | | |
| subjects affected / exposed | 10 / 178 (5.62%) | 5 / 178 (2.81%) | |
| occurrences (all) | 10 | 5 | |
| Renal and urinary disorders | | | |
| Renal impairment | | | |
| subjects affected / exposed | 11 / 178 (6.18%) | 5 / 178 (2.81%) | |
| occurrences (all) | 14 | 6 | |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 8 / 178 (4.49%) | 17 / 178 (9.55%) | |
| occurrences (all) | 9 | 20 | |
| Infections and infestations | | | |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 31 / 178 (17.42%) | 26 / 178 (14.61%) | |
| occurrences (all) | 44 | 33 | |
| Viral upper respiratory tract infection | | | |
| subjects affected / exposed | 20 / 178 (11.24%) | 18 / 178 (10.11%) | |
| occurrences (all) | 24 | 20 | |
| Urinary tract infection | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 17 / 178 (9.55%) | 13 / 178 (7.30%) | |
| occurrences (all) | 25 | 14 | |
| Herpes zoster | | | |
| subjects affected / exposed | 13 / 178 (7.30%) | 9 / 178 (5.06%) | |
| occurrences (all) | 13 | 9 | |
| Influenza | | | |
| subjects affected / exposed | 12 / 178 (6.74%) | 10 / 178 (5.62%) | |
| occurrences (all) | 15 | 12 | |
| Gastroenteritis | | | |
| subjects affected / exposed | 7 / 178 (3.93%) | 10 / 178 (5.62%) | |
| occurrences (all) | 8 | 10 | |
| Pharyngitis | | | |
| subjects affected / exposed | 3 / 178 (1.69%) | 9 / 178 (5.06%) | |
| occurrences (all) | 3 | 11 | |
| Metabolism and nutrition disorders | | | |
| Hypokalaemia | | | |
| subjects affected / exposed | 3 / 178 (1.69%) | 9 / 178 (5.06%) | |
| occurrences (all) | 3 | 9 | |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|---|---|
| 04 May 2017 | 1. Time point for primary efficacy endpoint changed from Week 24 to Week 52<br>2. Change in the primary and secondary efficacy endpoints for renal response<br>3. Addition of secondary efficacy endpoint for decrease in eGFR<br>4. Change in the time window of the biopsy used for screening and to include Class V lupus nephritis<br>5. Change in handling increases in blood pressure or hypertension and pulse<br>6. Change in stratification of randomization<br>7. Addition of the evaluation of biomarkers<br>8. Clarification of regarding definition of treatment emergent adverse events<br>9. Editorial changes for clarification made throughout |

Notes:

### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported