# Clinical trial results:
# A Pivotal Phase 3 Trial to Evaluate the Safety and Efficacy of Clazakizumab for the Treatment of Chronic Active Antibody-Mediated Rejection in Kidney Transplant Recipients

## Summary

| | |
|---|---|
| EudraCT number | 2018-003682-34 |
| Trial protocol | CZ HU BE DE NL AT ES |
| Global end of trial date | 08 April 2024 |

### Results information

| | |
|---|---|
| Result version number | v2 (current) |
| This version publication date | 04 September 2025 |
| First version publication date | 19 April 2025 |
| Version creation reason | • Correction of full data set<br>The data in some of the endpoints have been corrected/updated, and some endpoint descriptions/time frames have been updated to provide additional clarity. |

## Trial information

### Trial identification

| | |
|---|---|
| Sponsor protocol code | CSL300_3001 (previously VKTX01) |

### Additional study identifiers

| | |
|---|---|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT03744910 |
| WHO universal trial number (UTN) | - |
| Other trial identifiers | Vitaeris: VKTX01 |

Notes:

### Sponsors

| | |
|---|---|
| Sponsor organisation name | CSL Behring LLC |
| Sponsor organisation address | 1020 First Avenue, King of Prussia, PA, United States, 19406 |
| Public contact | Trial Registration Coordinator, CSL Behring LLC, +1 610-878-4697, clinicaltrials@cslbehring.com |
| Scientific contact | Trial Registration Coordinator, CSL Behring LLC, +1 610-878-4697, clinicaltrials@cslbehring.com |

Notes:

### Paediatric regulatory details

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

Notes:

## Results analysis stage

| | |
|---|---|
| Analysis stage | Final |
| Date of interim/final analysis | 24 June 2024 |
| Is this the analysis of the primary completion data? | No |

| | |
|---|---|
| Global end of trial reached? | Yes |
| Global end of trial date | 08 April 2024 |
| Was the trial ended prematurely? | Yes |

Notes:

## General information about the trial

Main objective of the trial:

1. To evaluate the efficacy of clazakizumab in preventing all-cause allograft loss (including death) or irreversible loss of allograft function due to CABMR.
2. To evaluate the efficacy of clazakizumab in slowing/preventing the progressive loss of kidney function (as measured by eGFR using the Modification of Diet in Renal Disease 4 (MDRD4) equation [Interim analysis #2]).
3. To evaluate the safety of clazakizumab.

Protection of trial subjects:

The study was conducted according to the principles of the World Medical Association's Declaration of Helsinki and the International Council for Harmonisation (ICH) guidelines for Good Clinical Practice (GCP), CSL Behring has ensured that the study complies with all local, federal or country-specific regulatory requirements. A written informed consent in compliance with Part 50 of Title 21 of the Code of Federal Regulations (CFR), with the Declaration of Helsinki, ICH guidelines, federal and / or local regulations, and advance approval by the Institutional Review Board / Independent Ethics Committee (IRB / IEC) was obtained from each participant prior to entering the study or performing any unusual or non-routine procedure that involves risk to the participant, including washout of any medications.
Any amendments to the protocol or informed consent form (ICF) were reviewed and approved by the IRB / IEC before the changes were implemented in the study.

| | |
|---|---|
| Background therapy: - | |
| Evidence for comparator: - | |
| Actual start date of recruitment | 14 October 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 | Netherlands: 12 |
| Country: Number of subjects enrolled | Spain: 23 |
| Country: Number of subjects enrolled | Sweden: 1 |
| Country: Number of subjects enrolled | Austria: 1 |
| Country: Number of subjects enrolled | Czechia: 4 |
| Country: Number of subjects enrolled | France: 21 |
| Country: Number of subjects enrolled | Germany: 9 |
| Country: Number of subjects enrolled | Hungary: 15 |
| Country: Number of subjects enrolled | Australia: 9 |
| Country: Number of subjects enrolled | Canada: 11 |

| | |
|---|---|
| Country: Number of subjects enrolled | Korea, Democratic People's Republic of: 22 |
| Country: Number of subjects enrolled | Switzerland: 5 |
| Country: Number of subjects enrolled | United States: 61 |
| Worldwide total number of subjects | 194 |
| EEA total number of subjects | 86 |

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) | 180 |
| From 65 to 84 years | 14 |
| 85 years and over | 0 |

## Subject disposition

### Recruitment

Recruitment details:

The study was conducted at 139 study sites in 13 countries: Canada, United States, Austria, Czechia, France, Germany, Hungary, Netherlands, Spain, Sweden, Switzerland, Democratic People's Republic of Korea, and Australia.

### Pre-assignment

Screening details:

A total of 382 participants were screened, of which 188 were screen failures. Of the screened participants, 194 were randomized in a 1:1 ratio to receive study interventions (Clazakizumab or Placebo). Participants who reached the primary endpoint of allograft loss or death are combined and reported as Completed in the participant flow.

### Period 1

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

### Arms

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

Arm description:

Participants received clazakizumab via subcutaneous (SC) injection once every 4 weeks (Q4W) until the participant: permanently discontinued the investigational product (IP), withdrew from the study, experienced allograft loss, died, or reached the common treatment end date (CTED), whichever occurred first during this study.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Clazakizumab |
| Investigational medicinal product code | CSL300 |
| Other name | Genetically engineered humanized anti-IL-6 mAb |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

12.5 milligram per millilliter (mg/mL) SC injection Q4W.

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

Arm description:

Participants received Placebo by SC injection Q4W until the participant: permanently discontinued IP, withdrew from the study, experienced allograft loss, died, or reached the CTED, whichever occurred first during this study.

| | |
|---|---|
| Arm type | Placebo |
| Investigational medicinal product name | Placebo |
| Investigational medicinal product code | Placebo |
| Other name | |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

0.9% w/v NaCl, SC injection Q4W.

| **Number of subjects in period 1** | Clazakizumab | Placebo |
|---|---|---|
| Started | 94 | 100 |
| Completed | 16 | 15 |
| Not completed | 78 | 85 |
| Physician decision | 5 | 4 |
| Withdrew Consent | 1 | 8 |
| Other-unspecified | 4 | 1 |
| Sponsor Decision | 68 | 71 |
| Lost to follow-up | - | 1 |

## Baseline characteristics

| Reporting groups | |
|---|---|
| Reporting group title | Clazakizumab |
| Reporting group description: | |
| Participants received clazakizumab via subcutaneous (SC) injection once every 4 weeks (Q4W) until the participant: permanently discontinued the investigational product (IP), withdrew from the study, experienced allograft loss, died, or reached the common treatment end date (CTED), whichever occurred first during this study. | |
| Reporting group title | Placebo |
| Reporting group description: | |
| Participants received Placebo by SC injection Q4W until the participant: permanently discontinued IP, withdrew from the study, experienced allograft loss, died, or reached the CTED, whichever occurred first during this study. | |

| Reporting group values | Clazakizumab | Placebo | Total |
|---|---|---|---|
| Number of subjects | 94 | 100 | 194 |
| Age categorical<br>Units: Subjects | | | |
| Age continuous<br>Units: years | | | |
| arithmetic mean | 46.3 | 47.0 | |
| standard deviation | ± 11.87 | ± 12.24 | - |
| Gender categorical<br>Units: Subjects | | | |
| Female | 29 | 26 | 55 |
| Male | 65 | 74 | 139 |
| Ethnicity<br>Units: Subjects | | | |
| Hispanic or Latino | 18 | 16 | 34 |
| Not Hispanic or Latino | 69 | 78 | 147 |
| Not reported | 5 | 4 | 9 |
| Unknown | 2 | 2 | 4 |
| Race (NIH/OMB)<br>Units: Subjects | | | |
| White | 62 | 69 | 131 |
| Black or African American | 10 | 7 | 17 |
| Korean | 9 | 13 | 22 |
| Other | 6 | 8 | 14 |
| Asian Indian | 3 | 1 | 4 |
| Other Asian | 2 | 1 | 3 |
| American or Alaskan Native | 1 | 0 | 1 |
| Filipino | 1 | 0 | 1 |
| Missing | 0 | 1 | 1 |

## End points

### End points reporting groups

| | |
|---|---|
| Reporting group title | Clazakizumab |
| Reporting group description: | |
| Participants received clazakizumab via subcutaneous (SC) injection once every 4 weeks (Q4W) until the participant: permanently discontinued the investigational product (IP), withdrew from the study, experienced allograft loss, died, or reached the common treatment end date (CTED), whichever occurred first during this study. | |
| Reporting group title | Placebo |
| Reporting group description: | |
| Participants received Placebo by SC injection Q4W until the participant: permanently discontinued IP, withdrew from the study, experienced allograft loss, died, or reached the CTED, whichever occurred first during this study. | |

### Primary: Change From Baseline to Week 52 in Estimated Glomerular Filtration Rate (eGFR)

| | |
|---|---|
| End point title | Change From Baseline to Week 52 in Estimated Glomerular Filtration Rate (eGFR) |
| End point description: | |
| This primary outcome measure was the one from the first interim analysis. Analysis was performed on the intent-to-treat (ITT) analysis set. The ITT analysis set consisted of all participants who received at least 1 dose of study drug and who had a baseline assessment and at least 1 post baseline assessment of eGFR. | |
| End point type | Primary |
| End point timeframe: | |
| From Baseline to Week 52 | |

| End point values | Clazakizumab | Placebo | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 92 | 99 | | |
| Units: milliliter per minute per 1.73 meter^2 | | | | |
| least squares mean (confidence interval 95%) | -8.0 (-10.2 to -5.8) | -5.2 (-7.4 to -3.1) | | |

### Statistical analyses

| | |
|---|---|
| **Statistical analysis title** | Clazakizumab versus (v) Placebo |
| Comparison groups | Clazakizumab v Placebo |

| | |
|---|---|
| Number of subjects included in analysis | 191 |
| Analysis specification | Pre-specified |
| Analysis type | other[1] |
| Parameter estimate | Treatment difference |
| Point estimate | -2.75 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -5.84 |
| upper limit | 0.35 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 1.563 |

Notes:

[1] - Pre-specified for interim analysis.

## Primary: Number of Participants With Composite All-cause Allograft Loss or Irreversible Loss of Allograft Function

| | |
|---|---|
| End point title | Number of Participants With Composite All-cause Allograft Loss or Irreversible Loss of Allograft Function[2] |

End point description:

Composite all-cause allograft loss or irreversible loss of allograft function, defined as time to first occurrence of any of the following components:
• eGFR < 15 milliliters per minute per 1.73 square meters (mL/min/1.73 m^2)*
• return to dialysis*
• allograft nephrectomy
• retransplantation
• death from any cause, or
• a sustained (greater than or equal to [>=] 60 days) 40% decline in eGFR from Baseline.
*Total cumulative duration of sustained eGFR < 15 mL/min/1.73 m^2 AND / OR dialysis >= 60 days.
If the eGFR < 15 mL/min/1.73 m^2 was the only component reached, the value must be sustained over at least 60 days and must be confirmed by a repeat measurement after >= 60 days from the first measurement. The number of participants with composite all-cause allograft loss or irreversible loss of allograft function are reported here. Time-to-event data were not calculated due to the study's termination. Analysis was performed on the ITT analysis set.

| | |
|---|---|
| End point type | Primary |

End point timeframe:

From Baseline to 4 years

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Statistical analysis assessment was not performed as planned because of early study termination due to futility (at Interim Analysis).

| End point values | Clazakizumab | Placebo | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 92 | 99 | | |
| Units: participants | 26 | 22 | | |

### Statistical analyses

No statistical analyses for this end point

## Primary: Percentage of Participants With Composite All-cause Allograft Loss or

## Irreversible Loss of Allograft Function

| End point title | Percentage of Participants With Composite All-cause Allograft Loss or Irreversible Loss of Allograft Function[3] |
|---|---|

End point description:

Composite all-cause allograft loss or irreversible loss of allograft function, defined as time to first occurrence of any of the following components:
• eGFR < 15 mL/min/1.73 m^2*
• return to dialysis*
• allograft nephrectomy
• retransplantation
• death from any cause, or
• a sustained (>= 60 days) 40% decline in eGFR from Baseline.
*Total cumulative duration of sustained eGFR < 15 mL/min/1.73 m^2 AND / OR dialysis >= 60 days.
If the eGFR < 15 mL/min/1.73 m^2 was the only component reached, the value must be sustained over at least 60 days and must be confirmed by a repeat measurement after >= 60 days from the first measurement. The percentage of participants with composite allograft loss or irreversible loss of allograft function are reported here. Time-to-event data were not calculated due to the study's termination. Analysis was performed on the ITT analysis set.

| End point type | Primary |
|---|---|

End point timeframe:

From Baseline to 4 years

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Statistical analysis assessment was not performed as planned because of early study termination due to futility (at Interim Analysis).

| **End point values** | Clazakizumab | Placebo | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 92 | 99 | | |
| Units: percentage of participants | | | | |
| number (not applicable) | 28.3 | 22.2 | | |

## Statistical analyses

No statistical analyses for this end point

## Primary: Number of Participants With Treatment-emergent Adverse Events (TEAEs), Serious TEAEs, and Adverse Events of Special Interest (AESIs)

| End point title | Number of Participants With Treatment-emergent Adverse Events (TEAEs), Serious TEAEs, and Adverse Events of Special Interest (AESIs)[4] |
|---|---|

End point description:

Analysis was performed on the safety analysis set (SAS). The SAS consisted of all randomized participants who had received at least 1 dose of study drug.

| End point type | Primary |
|---|---|

End point timeframe:

Up to 4 years

Notes:

[4] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Statistical analysis assessment was not performed as planned because of early study termination due to futility (at Interim Analysis).

| End point values | Clazakizumab | Placebo | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 93 | 100 | | |
| Units: participants | | | | |
| TEAEs | 89 | 88 | | |
| Serious TEAEs | 39 | 39 | | |
| AESIs | 56 | 52 | | |

## Statistical analyses

No statistical analyses for this end point

## Primary: Percentage of Participants With TEAEs, Serious TEAEs, and AESIs

| End point title | Percentage of Participants With TEAEs, Serious TEAEs, and AESIs[5] |
|---|---|

End point description:

Analysis was performed on the SAS. The SAS consisted of all randomized participants who had received at least 1 dose of study drug.

| End point type | Primary |
|---|---|

End point timeframe:

Up to 4 years

Notes:

[5] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Statistical analysis assessment was not performed as planned because of early study termination due to futility (at Interim Analysis).

| End point values | Clazakizumab | Placebo | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 93 | 100 | | |
| Units: percentage of participants | | | | |
| number (not applicable) | | | | |
| TEAEs | 95.7 | 88.0 | | |
| Serious TEAEs | 41.9 | 39.0 | | |
| AESIs | 60.2 | 52.0 | | |

## Statistical analyses

No statistical analyses for this end point

## Primary: Number of Participants Who Tested Positive for Polyoma BK Virus (BKV), Cytomegalovirus (CMV) and Epstein-Barr Virus (EBV)

| End point title | Number of Participants Who Tested Positive for Polyoma BK Virus (BKV), Cytomegalovirus (CMV) and Epstein-Barr Virus (EBV)[6] |
|---|---|

End point description:

Number of participants who tested positive for BKV, CMV or EBV according to the maximum measured viral amount (International Units/mL [IU/mL]) after baseline are reported here. Analysis was performed on the SAS. The SAS consisted of all randomized participants who had received at least 1 dose of study

drug. Here, ‘number analyzed’, 'n' = participants with available data for each specified category. Lower limit of quantification = LLOQ.

| End point type | Primary |
|---|---|

End point timeframe:

From baseline up to 4 years

Notes:

[6] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Statistical analysis assessment was not performed as planned because of early study termination due to futility (at Interim Analysis).

| **End point values** | Clazakizumab | Placebo | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 93 | 100 | | |
| Units: participants | | | | |
| BKV >LLOQ to <320 IU/mL (n=93,99) | 3 | 2 | | |
| BKV >=320 IU/mL to <3200 IU/mL (n=93,99) | 1 | 0 | | |
| BKV >=3200 IU/mL (n=93,99) | 1 | 0 | | |
| CMV >LLOQ to <1000 IU/mL (n=93,99) | 5 | 1 | | |
| CMV >=1000 IU/mL to <5000 IU/mL (n=93,99) | 2 | 2 | | |
| CMV >=5000 IU/mL (n=93,99) | 0 | 0 | | |
| EBV >LLOQ to <10200 IU/mL (n=92,99) | 8 | 7 | | |
| EBV >=10200 IU/mL to <20400 IU/mL (n=92,99) | 0 | 0 | | |
| EBV >=20400 IU/mL (n=92,99) | 0 | 0 | | |

## Statistical analyses

No statistical analyses for this end point

## Primary: Number of Participants With Abnormal Laboratory Test Results

| End point title | Number of Participants With Abnormal Laboratory Test |
|---|---|

End point description:

Laboratory tests included liver function test (LFTs), complete blood count (CBC), plasma lipids, high-sensitivity C-reactive protein (hsCRP). Only participants with abnormal laboratory test results are reported here. Here, ULN = upper limit of normal, LLN = lower limit of normal, ALT = Alanine aminotransferase and AST = Aspartate aminotransferase. Analysis was performed on the SAS. The SAS consisted of all randomized participants who had received at least 1 dose of study drug. Here, ‘overall number of participants analyzed’, 'N' = participants with evaluable data for this outcome measure.

| End point type | Primary |
|---|---|

End point timeframe:

Up to 4 years

Notes:

[7] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Statistical analysis assessment was not performed as planned because of early study termination due to futility (at Interim Analysis).

| End point values | Clazakizumab | Placebo | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 93 | 99 | | |
| Units: participants | | | | |
| ALT : >ULN to 3 x ULN | 15 | 6 | | |
| ALT : > 3 to 5 × ULN | 0 | 1 | | |
| AST : >ULN to 3 x ULN | 11 | 4 | | |
| AST : > 3 to 5 × ULN | 1 | 0 | | |
| AST : > 5 × ULN | 0 | 2 | | |
| Bilirubin: > ULN to 2 × ULN | 20 | 6 | | |
| Bilirubin: > 2 × ULN | 5 | 0 | | |
| Neutrophils: < 2.5 to 1.5 10^9/L | 33 | 21 | | |
| Neutrophils: < 1.5 to 1.0 10^9/L | 15 | 5 | | |
| Neutrophils: < 1.0 10^9/L | 7 | 0 | | |
| Platelets: < LLN to 75.0 10^9/L | 39 | 10 | | |
| Platelets: < 75.0 to 50.0 10^9/L | 1 | 0 | | |

## Statistical analyses

No statistical analyses for this end point

## Primary: Percentage of Participants With Abnormal Laboratory Test Results

| End point title | Percentage of Participants With Abnormal Laboratory Test Results[8] |
|---|---|

End point description:

Laboratory tests included LFTs, CBC, plasma lipids, hsCRP. Only percentage of participants with abnormal laboratory test results are reported here. Here, ULN = upper limit of normal, LLN = lower limit of normal, ALT = Alanine aminotransferase and AST = Aspartate aminotransferase. Analysis was performed on the SAS. The SAS consisted of all randomized participants who had received at least 1 dose of study drug. Here, 'overall number of participants analyzed' = participants with evaluable data for this outcome measure.

| End point type | Primary |
|---|---|

End point timeframe:

Up to 4 years

Notes:

[8] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Statistical analysis assessment was not performed as planned because of early study termination due to futility (at Interim Analysis).

| End point values | Clazakizumab | Placebo | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 93 | 99 | | |
| Units: percentage of participants | | | | |
| number (not applicable) | | | | |
| ALT : >ULN to 3 x ULN | 16.1 | 6.1 | | |
| ALT : > 3 to 5 × ULN | 0 | 1.0 | | |
| AST : >ULN to 3 x ULN | 11.8 | 4.0 | | |
| AST : > 3 to 5 × ULN | 1.1 | 0 | | |
| AST : > 5 × ULN | 0 | 2.0 | | |
| Bilirubin: > ULN to 2 × ULN | 21.5 | 6.1 | | |

| | | | | |
|---|---|---|---|---|
| Bilirubin: > 2 × ULN | 5.4 | 0 | | |
| Neutrophils: < 2.5 to 1.5 10^9/L | 35.5 | 21.2 | | |
| Neutrophils: < 1.5 to 1.0 10^9/L | 16.1 | 5.1 | | |
| Neutrophils: < 1.0 10^9/L | 7.5 | 0 | | |
| Platelets: < LLN to 75.0 10^9/L | 41.9 | 10.1 | | |
| Platelets: < 75.0 to 50.0 10^9/L | 1.1 | 0 | | |

### Statistical analyses

No statistical analyses for this end point

## Primary: Number of Participants With Abnormal Vital Signs, Electrocardiograms (ECGs), and Physical Examination

| End point title | Number of Participants With Abnormal Vital Signs, Electrocardiograms (ECGs), and Physical Examination[9] |
|---|---|

End point description:

Analysis was performed on the SAS. The SAS consisted of all randomized participants who had received at least 1 dose of study drug.

| End point type | Primary |
|---|---|

End point timeframe:

Up to 4 years

Notes:

[9] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Statistical analysis assessment was not performed as planned because of early study termination due to futility (at Interim Analysis).

| End point values | Clazakizumab | Placebo | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 93 | 100 | | |
| Units: participants | 0 | 0 | | |

### Statistical analyses

No statistical analyses for this end point

## Primary: Number of Participants With Positive Anti-drug Antibodies

| End point title | Number of Participants With Positive Anti-drug Antibodies[10] |
|---|---|

End point description:

Analysis was performed on the SAS. The SAS consisted of all randomized participants who had received at least 1 dose of study drug. Here, ‘overall number of participants’ = participants with available data for this outcome measure and 'number analyzed', 'n' = participants with available data for each specified timepoint.

| End point type | Primary |
|---|---|

End point timeframe:

Baseline, Weeks 12, 24, and 48

Notes:

[10] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Statistical analysis assessment was not performed as planned because of early study termination due to futility (at Interim Analysis).

| **End point values** | Clazakizumab | Placebo | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 88 | 97 | | |
| Units: participants | | | | |
| Baseline (n=88,97) | 5 | 10 | | |
| Week 12 (n=74,82) | 3 | 8 | | |
| Week 24 (n=68,72) | 2 | 7 | | |
| Week 48 (n=52,52) | 0 | 4 | | |

## Statistical analyses

No statistical analyses for this end point

## Primary: Percentage of Participants With Positive Anti-drug Antibodies

| End point title | Percentage of Participants With Positive Anti-drug Antibodies[11] |
|---|---|

End point description:

Analysis was performed on the SAS. The SAS consisted of all randomized participants who had received at least 1 dose of study drug. Here, 'overall number of participants' = participants with available data for this outcome measure and 'number analyzed', 'n' = participants with available data for each specified timepoint.

| End point type | Primary |
|---|---|

End point timeframe:

Baseline, Weeks 12, 24, and 48

Notes:

[11] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Statistical analysis assessment was not performed as planned because of early study termination due to futility (at Interim Analysis).

| **End point values** | Clazakizumab | Placebo | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 88 | 97 | | |
| Units: percentage of participants | | | | |
| number (not applicable) | | | | |
| Baseline (n=88,97) | 5.7 | 10.3 | | |
| Week 12 (n=74,82) | 4.1 | 9.8 | | |
| Week 24 (n=68,72) | 2.9 | 9.7 | | |
| Week 48 (n=52,52) | 0 | 7.7 | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Participants With Composite All-cause Allograft Loss

| End point title | Number of Participants With Composite All-cause Allograft Loss |
|---|---|

End point description:

Composite all-cause allograft loss, defined as, time to first occurrence of any of the following components:
• eGFR < 15 mL/min/1.73 m^2*
• return to dialysis*
• allograft nephrectomy
• retransplantation, or
• death from any cause.
(*Total cumulative duration of sustained eGFR < 15 mL/min/1.73 m^2 AND / OR dialysis >= 60 days.)
If the eGFR < 15 mL/min/1.73 m^2 was the only component reached, the value must be sustained over at least 60 days and must be confirmed by a repeat measurement after >= 60 days from the first measurement. The number of participants with composite all-cause allograft loss are reported here.
Analysis was performed on the ITT analysis set. The ITT analysis set consisted of all participants who received at least 1 dose of study drug and who had a baseline assessment and at least 1 post baseline assessment of eGFR.

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

End point timeframe:

From Baseline to 4 years

| **End point values** | Clazakizumab | Placebo | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 92 | 99 | | |
| Units: participants | 17 | 14 | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of Participants With Composite All-cause Allograft Loss

| End point title | Percentage of Participants With Composite All-cause Allograft Loss |
|---|---|

End point description:

Composite all-cause allograft loss, defined as, time to first occurrence of any of the following components:
- eGFR < 15 mL/min/1.73 m^2*
- return to dialysis*
- allograft nephrectomy
- retransplantation, or
- death from any cause

(*Total cumulative duration of sustained eGFR < 15 mL/min/1.73 m^2 AND / OR dialysis >= 60 days.)
If the eGFR < 15 mL/min/1.73 m^2 was the only component reached, the value must be sustained over at least 60 days and must be confirmed by a repeat measurement after >= 60 days from the first measurement. The percentage of participants with composite all-cause allograft loss are reported here.
Analysis was performed on the ITT analysis set. The ITT analysis set consisted of all participants who received at least 1 dose of study drug and who had a baseline assessment and at least 1 post baseline assessment of eGFR.

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

End point timeframe:

From Baseline to 4 years

| End point values | Clazakizumab | Placebo | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 92 | 99 | | |
| Units: percentage of participants | | | | |
| number (not applicable) | 18.5 | 14.1 | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Participants With Irreversible Loss of Allograft Function

| End point title | Number of Participants With Irreversible Loss of Allograft Function |
|---|---|

End point description:

Irreversible loss of allograft function as defined by a 40% decline in eGFR from Baseline sustained for at least 60 days. Analysis was performed on the ITT analysis set. The ITT analysis set consisted of all participants who received at least 1 dose of the investigational product, had a Baseline assessment, and had at least 1 post-baseline assessment of eGFR.

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

End point timeframe:

From Baseline to 4 years

| End point values | Clazakizumab | Placebo | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 92 | 99 | | |
| Units: participants | 22 | 18 | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of Participants With Irreversible Loss of Allograft Function

| End point title | Percentage of Participants With Irreversible Loss of Allograft Function |
|---|---|

End point description:

Irreversible loss of allograft function as defined by a 40% decline in eGFR from Baseline sustained for at least 60 days. Analysis was performed on the ITT analysis set. The ITT analysis set consisted of all participants who received at least 1 dose of the investigational product, had a Baseline assessment, and had at least 1 post-baseline assessment of eGFR.

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

End point timeframe:
From Baseline to 4 years

| End point values | Clazakizumab | Placebo | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 92 | 99 | | |
| Units: percentage of participants | | | | |
| number (not applicable) | 23.9 | 18.2 | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Participants With Death-censored Allograft Loss

| End point title | Number of Participants With Death-censored Allograft Loss |
|---|---|

End point description:

Time to death-censored allograft loss, was defined as occurrence of any of the following components:
• eGFR < 15 mL/min/1.73 m^2*
• return to dialysis*
• allograft nephrectomy, or
• retransplantation.
(*Total cumulative duration of sustained eGFR < 15 mL/min/1.73 m^2 AND / OR dialysis >= 60 days.)
If the eGFR < 15 mL/min/1.73 m^2 was the only component reached, the value must be sustained over at least 60 days and must be confirmed by a repeat measurement after >= 60 days from the first measurement. The number of participants with death-censored allograft loss are reported here. Analysis was performed on the ITT analysis set. The ITT analysis set consisted of all participants who received at least 1 dose of study drug and who had a baseline assessment and at least 1 post baseline assessment of eGFR.

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

End point timeframe:
From Baseline to 4 years

| End point values | Clazakizumab | Placebo | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 92 | 99 | | |
| Units: participants | 16 | 13 | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of Participants With Death-censored Allograft Loss

| End point title | Percentage of Participants With Death-censored Allograft Loss |
|---|---|

End point description:

Time to death-censored allograft loss, was defined as occurrence of any of the following components:
• eGFR < 15 mL/min/1.73 m^2*
• return to dialysis*
• allograft nephrectomy, or
• retransplantation.
(*Total cumulative duration of sustained eGFR < 15 mL/min/1.73 m^2 AND / OR dialysis >= 60 days.)
If the eGFR < 15 mL/min/1.73 m^2 was the only component reached, the value must be sustained over at least 60 days and must be confirmed by a repeat measurement after >= 60 days from the first measurement. The percentage of participants who experienced death-censored allograft loss are reported here. Analysis was performed on the ITT analysis set. The ITT analysis set consisted of all participants who received at least 1 dose of study drug and who had a baseline assessment and at least 1 post-baseline assessment of eGFR.

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

End point timeframe:

From Baseline to 4 years

| **End point values** | Clazakizumab | Placebo | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 92 | 99 | | |
| Units: percentage of participants | | | | |
| number (not applicable) | 17.4 | 13.1 | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Change From Baseline in Urine Albumin Creatinine Ratio (UACR)

| End point title | Change From Baseline in Urine Albumin Creatinine Ratio (UACR) |
|---|---|

End point description:

Analysis was performed on the SAS. The SAS consisted of all randomized participants who had received at least 1 dose of study drug. Here, 'overall number of participants analyzed' = participants with available data for this outcome measure.

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

End point timeframe:

From Baseline to Week 52

| **End point values** | Clazakizumab | Placebo | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 83 | 88 | | |
| Units: gram per mole | | | | |
| arithmetic mean (standard deviation) | 50.734 (± 125.5628) | 31.178 (± 112.8894) | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Percent Change From Baseline in Mean Fluorescent Intensity for Donor-Specific Antibodies (DSA)

| End point title | Percent Change From Baseline in Mean Fluorescent Intensity for Donor-Specific Antibodies (DSA) |
|---|---|

End point description:

Analysis was performed on the SAS. The SAS consisted of all randomized participants who had received at least 1 dose of study drug. The Overall Number of Participants Analyzed reported here reflects all participants who were analyzed, which includes all (N = 93 Clazakizumab and 100 Placebo) participants assessed at baseline to determine DSA class I or II. Here, 'Number Analyzed' = the number of participants in Class I or II classified at baseline who had available MFI data at Week 52.

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

End point timeframe:

From Baseline to Week 52

| End point values | Clazakizumab | Placebo | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 93 | 100 | | |
| Units: percent change | | | | |
| median (inter-quartile range (Q1-Q3)) | | | | |
| DSA Class I (n=21,16) | -23.20 (-53.34 to -4.54) | -39.71 (-69.67 to -20.22) | | |
| DSA Class II (n=39,45) | -27.15 (-46.32 to -5.05) | -13.68 (-26.69 to -1.75) | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change From Baseline in Banff Lesion Grading Score (2015 Criteria) of Pre-treatment to Post-treatment (Week 52) Kidney Biopsies

| End point title | Change From Baseline in Banff Lesion Grading Score (2015 Criteria) of Pre-treatment to Post-treatment (Week 52) Kidney Biopsies |
|---|---|

End point description:

Banff lesion grading scores assess the presence and the degree of histopathological changes in the different compartments of kidney biopsies. Here, the improved category is defined as a decline in the Banff lesion grading score. Participants with improved scores, not improved scores, and missing biopsies for C4d staining, interstitial fibrosis, tubular atrophy, glomerular basement membrane double contours, glomerulitis and peritubular capillaritis are reported for this outcome measure. Analysis was performed on the ITT analysis set. The ITT analysis set consisted of all randomized participants who received at

least 1 dose of the investigational product, had a Baseline assessment, and had at least 1 post-baseline assessment of eGFR. Here, Glomerular Basement Membrane Double Contours = GBMDC.

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

End point timeframe:

From Baseline to Week 52

| **End point values** | Clazakizumab | Placebo | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 92 | 99 | | |
| Units: participants | | | | |
| C4d Staining - Improved score | 10 | 10 | | |
| C4d Staining - Not improved score | 17 | 21 | | |
| C4d Staining - Missing biopsies | 65 | 68 | | |
| Interstitial Fibrosis - Improved score | 3 | 8 | | |
| Interstitial Fibrosis - Not improved score | 24 | 23 | | |
| Interstitial Fibrosis - Missing biopsies | 65 | 68 | | |
| Tubular Atrophy - Improved score | 1 | 5 | | |
| Tubular Atrophy - Not improved score | 26 | 26 | | |
| Tubular Atrophy - Missing biopsies | 65 | 68 | | |
| GBMDC - Improved score | 6 | 10 | | |
| GBMDC - Not improved score | 21 | 21 | | |
| GBMDC - Missing biopsies | 65 | 68 | | |
| Glomerulitis - Improved score | 14 | 17 | | |
| Glomerulitis - Not improved score | 13 | 14 | | |
| Glomerulitis - Missing biopsies | 65 | 68 | | |
| Peritubular Capillaritis - Improved score | 14 | 15 | | |
| Peritubular Capillaritis - Not improved score | 13 | 16 | | |
| Peritubular Capillaritis - Missing biopsies | 65 | 68 | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Incidence of Acute Rejection Episodes of T Cell-mediated Rejection (TCMR) and Antibody-mediated Rejection (ABMR)

| End point title | Incidence of Acute Rejection Episodes of T Cell-mediated Rejection (TCMR) and Antibody-mediated Rejection (ABMR) |
|---|---|

End point description:

Number of participants who had at least one acute rejection episode (TCMR or ABMR) are reported for this outcome measure. Analysis was performed on the ITT analysis set. The ITT analysis set consisted of all randomized participants who received at least 1 dose of study drug and who had a baseline assessment and at least 1 post baseline assessment of eGFR.

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

End point timeframe:

Baseline up to End of treatment (up to approximately 4 years)

| End point values | Clazakizumab | Placebo | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 92 | 99 | | |
| Units: participants | 2 | 3 | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Overall Participant Survival

| End point title | Overall Participant Survival |
|---|---|

End point description:

Number of participants who were alive up to Week 52 are reported for this outcome measure. Analysis was performed on the ITT analysis set. The ITT analysis set consisted of all randomized participants who received at least 1 dose of the investigational product, had a Baseline assessment, and had at least 1 post-baseline assessment of eGFR.

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

End point timeframe:

Up to Week 52

| End point values | Clazakizumab | Placebo | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 92 | 99 | | |
| Units: participants | 90 | 98 | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Maximum Concentration at Steady State (Cmax ss) of CSL300

| End point title | Maximum Concentration at Steady State (Cmax ss) of |
|---|---|

End point description:

A subset of participants (out of the enrolled participants in the main study) had the option to participate in a pharmacokinetic (PK)/ Pharmacodynamic (PD) sub-study. Analysis was performed on the PK/ PD analysis set. The PK/PD substudy analysis set consisted of all participants in the SAS who consented to be a part of the PK / PD substudy and had at least 1 quantifiable PK concentration of investigational product after administration. Here, "overall number of participants analyzed' = participants with available data for this outcome measure.

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

End point timeframe:

Up to Week 24

Notes:

[12] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: As planned, PK Data is reported for the applicable arm "Clazakizumab" only.

| **End point values** | Clazakizumab | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 3 | | | |
| Units: nanograms per milliliter | | | | |
| geometric mean (geometric coefficient of variation) | 3556.8 (± 10.5) | | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Trough Concentrations at Steady State (Ctrough ss) of CSL300

| End point title | Trough Concentrations at Steady State (Ctrough ss) of |
|---|---|

End point description:

A subset of participants (out of the enrolled participants in the main study) had the option to participate in a PK/PD sub-study. Analysis was performed on the PK/PD analysis set. The PK/PD substudy analysis set consisted of all participants in the SAS who consented to be a part of the PK / PD substudy and had at least 1 quantifiable PK concentration of investigational product after administration. Here, "overall number of participants analyzed' = participants with available data for this outcome measure.

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

End point timeframe:

Up to Week 24

Notes:

[13] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: As planned, PK Data is reported for the applicable arm "Clazakizumab" only.

| **End point values** | Clazakizumab | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 3 | | | |
| Units: nanograms per milliliter | | | | |
| geometric mean (geometric coefficient of variation) | 2366.8 (± 9.2) | | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Area Under the Concentration-time Curve (AUC0-tau) at Steady State of CSL300

| End point title | Area Under the Concentration-time Curve (AUC0-tau) at Steady State of CSL300[14] |
|---|---|

End point description:

A subset of participants (out of the enrolled participants in the main study) had the option to participate in a PK/PD sub-study. Analysis was performed on the PK/PD analysis set. The PK/PD substudy analysis set consisted of all participants in the SAS who consented to be a part of the PK / PD substudy and had at least 1 quantifiable PK concentration of investigational product after administration. Here, "overall number of participants analyzed' = participants with available data for this outcome measure.

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

End point timeframe:

Up to Week 24

Notes:

[14] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: As planned, PK Data is reported for the applicable arm "Clazakizumab" only.

| **End point values** | Clazakizumab | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 3 | | | |
| Units: days*nanograms per milliliter | | | | |
| geometric mean (geometric coefficient of variation) | 78080.34636 (± 7.19614) | | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Time of Maximum Concentration at Steady State (Tmax ss) of CSL300

| End point title | Time of Maximum Concentration at Steady State (Tmax ss) of CSL300[15] |
|---|---|

End point description:

A subset of participants (out of the enrolled participants in the main study) had the option to participate in a PK/PD sub-study. Analysis was performed on the PK/PD analysis set. The PK/PD substudy analysis set consisted of all participants in the SAS who consented to be a part of the PK / PD substudy and had at least 1 quantifiable PK concentration of investigational product after administration. Here, "overall number of participants analyzed' = participants with available data for this outcome measure.

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

End point timeframe:

Up to Week 24

Notes:

[15] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: As planned, PK Data is reported for the applicable arm "Clazakizumab" only.

| **End point values** | Clazakizumab | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 3 | | | |
| Units: day | | | | |
| median (full range (min-max)) | 6.92292 (4.9986 to 11.9299) | | | |

## Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Up to 4 years

Adverse event reporting additional description:

The SAS consisted of all randomized participants who received at least 1 dose of study drug. The participants in the SAS were analyzed according to the actual treatment received.

| | |
|---|---|
| Assessment type | Systematic |

### Dictionary used

| | |
|---|---|
| Dictionary name | MedDRA |
| Dictionary version | 24.0 |

### Reporting groups

| | |
|---|---|
| Reporting group title | Clazakizumab |

Reporting group description:

Participants received clazakizumab via SC injection Q4W until the participant: permanently discontinued the IP, withdrew from the study, experienced allograft loss, died, or reached the CTED, whichever occurred first during this study.

| | |
|---|---|
| Reporting group title | Placebo |

Reporting group description:

Participants received Placebo via SC injection Q4W until the participant: permanently discontinued IP, withdrew from the study, experienced allograft loss, died, or reached the CTED, whichever occurred first during this study.

| Serious adverse events | Clazakizumab | Placebo | |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 39 / 93 (41.94%) | 39 / 100 (39.00%) | |
| number of deaths (all causes) | 3 | 1 | |
| number of deaths resulting from adverse events | 2 | 1 | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Post transplant lymphoproliferative disorder | | | |
| subjects affected / exposed | 0 / 93 (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 | |
| Vascular disorders | | | |
| Hypertensive crisis | | | |
| subjects affected / exposed | 1 / 93 (1.08%) | 0 / 100 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Angiopathy | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 93 (1.08%) | 0 / 100 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Aortic stenosis | | | |
| subjects affected / exposed | 1 / 93 (1.08%) | 0 / 100 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypertensive urgency | | | |
| subjects affected / exposed | 0 / 93 (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 | |
| Lymphocele | | | |
| subjects affected / exposed | 1 / 93 (1.08%) | 0 / 100 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Peripheral ischaemia | | | |
| subjects affected / exposed | 1 / 93 (1.08%) | 0 / 100 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Venous thrombosis limb | | | |
| subjects affected / exposed | 1 / 93 (1.08%) | 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 | 2 / 93 (2.15%) | 0 / 100 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pyrexia | | | |
| subjects affected / exposed | 1 / 93 (1.08%) | 1 / 100 (1.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Asthenia | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 93 (1.08%) | 0 / 100 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Immune system disorders | | | |
| Transplant rejection | | | |
| subjects affected / exposed | 1 / 93 (1.08%) | 2 / 100 (2.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Chronic allograft nephropathy | | | |
| subjects affected / exposed | 0 / 93 (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 | |
| Kidney transplant rejection | | | |
| subjects affected / exposed | 0 / 93 (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 pancreas transplant rejection | | | |
| subjects affected / exposed | 1 / 93 (1.08%) | 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 | | | |
| Benign prostatic hyperplasia | | | |
| subjects affected / exposed | 1 / 93 (1.08%) | 0 / 100 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Prostatomegaly | | | |
| subjects affected / exposed | 0 / 93 (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 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Pulmonary embolism | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 2 / 93 (2.15%) | 0 / 100 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Acute pulmonary oedema | | | |
| subjects affected / exposed | 1 / 93 (1.08%) | 0 / 100 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Acute respiratory failure | | | |
| subjects affected / exposed | 0 / 93 (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 | |
| Asthma | | | |
| subjects affected / exposed | 1 / 93 (1.08%) | 0 / 100 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Dyspnoea | | | |
| subjects affected / exposed | 1 / 93 (1.08%) | 0 / 100 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Organising pneumonia | | | |
| subjects affected / exposed | 1 / 93 (1.08%) | 0 / 100 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory failure | | | |
| subjects affected / exposed | 0 / 93 (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 | |
| Psychiatric disorders | | | |
| Depression | | | |
| subjects affected / exposed | 0 / 93 (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 | |
| Investigations | | | |

| | | | |
|---|---|---|---|
| Blood creatinine increased | | | |
| subjects affected / exposed | 0 / 93 (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 triglycerides increased | | | |
| subjects affected / exposed | 0 / 93 (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 | |
| Troponin increased | | | |
| subjects affected / exposed | 1 / 93 (1.08%) | 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 | | | |
| Complications of transplanted pancreas | | | |
| subjects affected / exposed | 1 / 93 (1.08%) | 0 / 100 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Craniocerebral injury | | | |
| subjects affected / exposed | 0 / 93 (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 | |
| Fall | | | |
| subjects affected / exposed | 1 / 93 (1.08%) | 0 / 100 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal stoma complication | | | |
| subjects affected / exposed | 0 / 93 (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 | |
| Post procedural haematoma | | | |
| subjects affected / exposed | 1 / 93 (1.08%) | 0 / 100 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|---|---|---|
| Procedural hypertension | | | |
| subjects affected / exposed | 0 / 93 (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 | |
| Road traffic accident | | | |
| subjects affected / exposed | 1 / 93 (1.08%) | 0 / 100 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Subdural haematoma | | | |
| subjects affected / exposed | 1 / 93 (1.08%) | 0 / 100 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Transplant failure | | | |
| subjects affected / exposed | 1 / 93 (1.08%) | 0 / 100 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vascular pseudoaneurysm ruptured | | | |
| subjects affected / exposed | 1 / 93 (1.08%) | 0 / 100 (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 myocardial infarction | | | |
| subjects affected / exposed | 2 / 93 (2.15%) | 0 / 100 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac arrest | | | |
| subjects affected / exposed | 1 / 93 (1.08%) | 0 / 100 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Cardiac failure congestive | | | |
| subjects affected / exposed | 1 / 93 (1.08%) | 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 | | | |

| | | | |
|---|---|---|---|
| Cerebrovascular accident | | | |
| subjects affected / exposed | 0 / 93 (0.00%) | 1 / 100 (1.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Dizziness | | | |
| subjects affected / exposed | 0 / 93 (0.00%) | 1 / 100 (1.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ischaemic stroke | | | |
| subjects affected / exposed | 1 / 93 (1.08%) | 0 / 100 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cerebral infarction | | | |
| subjects affected / exposed | 1 / 93 (1.08%) | 0 / 100 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Epilepsy | | | |
| subjects affected / exposed | 1 / 93 (1.08%) | 0 / 100 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 3 / 93 (3.23%) | 2 / 100 (2.00%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lymphatic obstruction | | | |
| subjects affected / exposed | 1 / 93 (1.08%) | 0 / 100 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Neutropenia | | | |
| subjects affected / exposed | 1 / 93 (1.08%) | 0 / 100 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pancytopenia | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 93 (1.08%) | 0 / 100 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal disorders | | | |
| Diarrhoea | | | |
| subjects affected / exposed | 4 / 93 (4.30%) | 3 / 100 (3.00%) | |
| occurrences causally related to treatment / all | 0 / 5 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Abdominal pain | | | |
| subjects affected / exposed | 1 / 93 (1.08%) | 1 / 100 (1.00%) | |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal haemorrhage | | | |
| subjects affected / exposed | 1 / 93 (1.08%) | 1 / 100 (1.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Abdominal pain upper | | | |
| subjects affected / exposed | 1 / 93 (1.08%) | 0 / 100 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Abdominal wall haematoma | | | |
| subjects affected / exposed | 1 / 93 (1.08%) | 0 / 100 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Colitis | | | |
| subjects affected / exposed | 1 / 93 (1.08%) | 0 / 100 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Enteritis | | | |
| subjects affected / exposed | 0 / 93 (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 | |
| Haematochezia | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 93 (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 | |
| Retroperitoneal haematoma | | | |
| subjects affected / exposed | 1 / 93 (1.08%) | 0 / 100 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Terminal ileitis | | | |
| subjects affected / exposed | 1 / 93 (1.08%) | 0 / 100 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatobiliary disorders | | | |
| Cholelithiasis | | | |
| subjects affected / exposed | 0 / 93 (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 | | | |
| Acute kidney injury | | | |
| subjects affected / exposed | 13 / 93 (13.98%) | 6 / 100 (6.00%) | |
| occurrences causally related to treatment / all | 1 / 15 | 0 / 7 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal impairment | | | |
| subjects affected / exposed | 2 / 93 (2.15%) | 1 / 100 (1.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| End stage renal disease | | | |
| subjects affected / exposed | 1 / 93 (1.08%) | 1 / 100 (1.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Azotaemia | | | |
| subjects affected / exposed | 0 / 93 (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 | |
| Chronic kidney disease | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 93 (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 | |
| Glomerulonephritis | | | |
| subjects affected / exposed | 0 / 93 (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 | |
| Tubulointerstitial nephritis | | | |
| subjects affected / exposed | 0 / 93 (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** | | | |
| Osteonecrosis | | | |
| subjects affected / exposed | 0 / 93 (0.00%) | 1 / 100 (1.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Arthritis | | | |
| subjects affected / exposed | 1 / 93 (1.08%) | 0 / 100 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Back pain | | | |
| subjects affected / exposed | 1 / 93 (1.08%) | 0 / 100 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Muscular weakness | | | |
| subjects affected / exposed | 0 / 93 (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 chest pain | | | |
| subjects affected / exposed | 0 / 93 (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 | |
| Rhabdomyolysis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 93 (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 | | | |
| COVID-19 | | | |
| subjects affected / exposed | 13 / 93 (13.98%) | 10 / 100 (10.00%) | |
| occurrences causally related to treatment / all | 0 / 15 | 1 / 12 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Pneumonia | | | |
| subjects affected / exposed | 3 / 93 (3.23%) | 1 / 100 (1.00%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| COVID-19 pneumonia | | | |
| subjects affected / exposed | 2 / 93 (2.15%) | 1 / 100 (1.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastroenteritis | | | |
| subjects affected / exposed | 1 / 93 (1.08%) | 2 / 100 (2.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Clostridium difficile infection | | | |
| subjects affected / exposed | 2 / 93 (2.15%) | 0 / 100 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 4 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Urinary tract infection | | | |
| subjects affected / exposed | 2 / 93 (2.15%) | 0 / 100 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cytomegalovirus infection | | | |
| subjects affected / exposed | 1 / 93 (1.08%) | 1 / 100 (1.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Influenza | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 93 (1.08%) | 1 / 100 (1.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Arteriovenous graft site infection | | | |
| subjects affected / exposed | 1 / 93 (1.08%) | 0 / 100 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Arthritis bacterial | | | |
| subjects affected / exposed | 0 / 93 (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 | |
| Atypical pneumonia | | | |
| subjects affected / exposed | 0 / 93 (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 | |
| Bacteraemia | | | |
| subjects affected / exposed | 1 / 93 (1.08%) | 0 / 100 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bacteriuria | | | |
| subjects affected / exposed | 1 / 93 (1.08%) | 0 / 100 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Clostridium difficile colitis | | | |
| subjects affected / exposed | 0 / 93 (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 | |
| Coronavirus infection | | | |
| subjects affected / exposed | 0 / 93 (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 | |
| Cytomegalovirus colitis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 93 (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 | |
| Diverticulitis | | | |
| subjects affected / exposed | 1 / 93 (1.08%) | 0 / 100 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Escherichia sepsis | | | |
| subjects affected / exposed | 1 / 93 (1.08%) | 0 / 100 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastroenteritis norovirus | | | |
| subjects affected / exposed | 1 / 93 (1.08%) | 0 / 100 (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 | 0 / 93 (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 | |
| Ophthalmic herpes zoster | | | |
| subjects affected / exposed | 1 / 93 (1.08%) | 0 / 100 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Parainfluenzae virus infection | | | |
| subjects affected / exposed | 1 / 93 (1.08%) | 0 / 100 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonia viral | | | |
| subjects affected / exposed | 0 / 93 (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 | |
| Pseudomonas infection | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 93 (1.08%) | 0 / 100 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pyelonephritis | | | |
| subjects affected / exposed | 1 / 93 (1.08%) | 0 / 100 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Syphilis | | | |
| subjects affected / exposed | 1 / 93 (1.08%) | 0 / 100 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Systemic candida | | | |
| subjects affected / exposed | 1 / 93 (1.08%) | 0 / 100 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Urosepsis | | | |
| subjects affected / exposed | 1 / 93 (1.08%) | 0 / 100 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Viral diarrhoea | | | |
| subjects affected / exposed | 1 / 93 (1.08%) | 0 / 100 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Viral infection | | | |
| subjects affected / exposed | 1 / 93 (1.08%) | 0 / 100 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Metabolism and nutrition disorders | | | |
| Diabetic ketoacidosis | | | |
| subjects affected / exposed | 1 / 93 (1.08%) | 0 / 100 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Fluid overload | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 93 (1.08%) | 0 / 100 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hyperkalaemia | | | |
| subjects affected / exposed | 0 / 93 (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 | |
| Metabolic acidosis | | | |
| subjects affected / exposed | 1 / 93 (1.08%) | 0 / 100 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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

| **Non-serious adverse events** | Clazakizumab | Placebo | |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 81 / 93 (87.10%) | 80 / 100 (80.00%) | |
| Vascular disorders | | | |
| Hypertension | | | |
| subjects affected / exposed | 12 / 93 (12.90%) | 13 / 100 (13.00%) | |
| occurrences (all) | 12 | 15 | |
| General disorders and administration site conditions | | | |
| Oedema peripheral | | | |
| subjects affected / exposed | 24 / 93 (25.81%) | 11 / 100 (11.00%) | |
| occurrences (all) | 31 | 12 | |
| Fatigue | | | |
| subjects affected / exposed | 8 / 93 (8.60%) | 8 / 100 (8.00%) | |
| occurrences (all) | 9 | 10 | |
| Asthenia | | | |
| subjects affected / exposed | 1 / 93 (1.08%) | 5 / 100 (5.00%) | |
| occurrences (all) | 1 | 5 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Cough | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 5 / 93 (5.38%) | 8 / 100 (8.00%) | |
| occurrences (all) | 8 | 12 | |
| Oropharyngeal pain | | | |
| subjects affected / exposed | 8 / 93 (8.60%) | 1 / 100 (1.00%) | |
| occurrences (all) | 8 | 1 | |
| Dyspnoea | | | |
| subjects affected / exposed | 5 / 93 (5.38%) | 2 / 100 (2.00%) | |
| occurrences (all) | 5 | 2 | |
| Psychiatric disorders | | | |
| Insomnia | | | |
| subjects affected / exposed | 6 / 93 (6.45%) | 3 / 100 (3.00%) | |
| occurrences (all) | 7 | 3 | |
| Investigations | | | |
| Blood creatinine increased | | | |
| subjects affected / exposed | 9 / 93 (9.68%) | 13 / 100 (13.00%) | |
| occurrences (all) | 12 | 15 | |
| Immunosuppressant drug level decreased | | | |
| subjects affected / exposed | 4 / 93 (4.30%) | 6 / 100 (6.00%) | |
| occurrences (all) | 9 | 10 | |
| Immunosuppressant drug level increased | | | |
| subjects affected / exposed | 4 / 93 (4.30%) | 6 / 100 (6.00%) | |
| occurrences (all) | 6 | 10 | |
| Weight decreased | | | |
| subjects affected / exposed | 3 / 93 (3.23%) | 6 / 100 (6.00%) | |
| occurrences (all) | 3 | 6 | |
| Blood bilirubin increased | | | |
| subjects affected / exposed | 5 / 93 (5.38%) | 0 / 100 (0.00%) | |
| occurrences (all) | 5 | 0 | |
| Neutrophil count decreased | | | |
| subjects affected / exposed | 5 / 93 (5.38%) | 0 / 100 (0.00%) | |
| occurrences (all) | 5 | 0 | |
| Cardiac disorders | | | |
| Atrial fibrillation | | | |
| subjects affected / exposed | 5 / 93 (5.38%) | 1 / 100 (1.00%) | |
| occurrences (all) | 5 | 1 | |
| Nervous system disorders | | | |

| | | | |
|---|---|---|---|
| Headache | | | |
| subjects affected / exposed | 10 / 93 (10.75%) | 9 / 100 (9.00%) | |
| occurrences (all) | 14 | 9 | |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 16 / 93 (17.20%) | 16 / 100 (16.00%) | |
| occurrences (all) | 19 | 17 | |
| Neutropenia | | | |
| subjects affected / exposed | 15 / 93 (16.13%) | 0 / 100 (0.00%) | |
| occurrences (all) | 22 | 0 | |
| Leukopenia | | | |
| subjects affected / exposed | 8 / 93 (8.60%) | 1 / 100 (1.00%) | |
| occurrences (all) | 14 | 1 | |
| Thrombocytopenia | | | |
| subjects affected / exposed | 6 / 93 (6.45%) | 1 / 100 (1.00%) | |
| occurrences (all) | 8 | 1 | |
| Gastrointestinal disorders | | | |
| Diarrhoea | | | |
| subjects affected / exposed | 21 / 93 (22.58%) | 22 / 100 (22.00%) | |
| occurrences (all) | 24 | 25 | |
| Nausea | | | |
| subjects affected / exposed | 11 / 93 (11.83%) | 6 / 100 (6.00%) | |
| occurrences (all) | 13 | 7 | |
| Abdominal pain | | | |
| subjects affected / exposed | 9 / 93 (9.68%) | 7 / 100 (7.00%) | |
| occurrences (all) | 9 | 7 | |
| Vomiting | | | |
| subjects affected / exposed | 10 / 93 (10.75%) | 6 / 100 (6.00%) | |
| occurrences (all) | 12 | 7 | |
| Abdominal pain upper | | | |
| subjects affected / exposed | 6 / 93 (6.45%) | 2 / 100 (2.00%) | |
| occurrences (all) | 8 | 3 | |
| Gastrooesophageal reflux disease | | | |
| subjects affected / exposed | 5 / 93 (5.38%) | 2 / 100 (2.00%) | |
| occurrences (all) | 6 | 2 | |
| Renal and urinary disorders | | | |

| | | | |
|---|---|---|---|
| Acute kidney injury | | | |
| subjects affected / exposed | 8 / 93 (8.60%) | 5 / 100 (5.00%) | |
| occurrences (all) | 9 | 5 | |
| Proteinuria | | | |
| subjects affected / exposed | 5 / 93 (5.38%) | 8 / 100 (8.00%) | |
| occurrences (all) | 5 | 8 | |
| Renal impairment | | | |
| subjects affected / exposed | 7 / 93 (7.53%) | 6 / 100 (6.00%) | |
| occurrences (all) | 7 | 6 | |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 6 / 93 (6.45%) | 4 / 100 (4.00%) | |
| occurrences (all) | 7 | 5 | |
| Back pain | | | |
| subjects affected / exposed | 6 / 93 (6.45%) | 4 / 100 (4.00%) | |
| occurrences (all) | 6 | 4 | |
| Muscle spasms | | | |
| subjects affected / exposed | 5 / 93 (5.38%) | 4 / 100 (4.00%) | |
| occurrences (all) | 5 | 5 | |
| Infections and infestations | | | |
| COVID-19 | | | |
| subjects affected / exposed | 28 / 93 (30.11%) | 30 / 100 (30.00%) | |
| occurrences (all) | 31 | 31 | |
| Urinary tract infection | | | |
| subjects affected / exposed | 12 / 93 (12.90%) | 6 / 100 (6.00%) | |
| occurrences (all) | 21 | 9 | |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 8 / 93 (8.60%) | 5 / 100 (5.00%) | |
| occurrences (all) | 8 | 6 | |
| Herpes zoster | | | |
| subjects affected / exposed | 6 / 93 (6.45%) | 2 / 100 (2.00%) | |
| occurrences (all) | 6 | 2 | |
| Nasopharyngitis | | | |
| subjects affected / exposed | 5 / 93 (5.38%) | 11 / 100 (11.00%) | |
| occurrences (all) | 6 | 13 | |
| Metabolism and nutrition disorders | | | |

| | | | |
|---|---|---|---|
| Hyperkalaemia | | | |
| subjects affected / exposed | 12 / 93 (12.90%) | 13 / 100 (13.00%) | |
| occurrences (all) | 14 | 18 | |
| Hyperlipidaemia | | | |
| subjects affected / exposed | 2 / 93 (2.15%) | 9 / 100 (9.00%) | |
| occurrences (all) | 2 | 11 | |
| Hyperglycaemia | | | |
| subjects affected / exposed | 3 / 93 (3.23%) | 5 / 100 (5.00%) | |
| occurrences (all) | 3 | 6 | |
| Hyperphosphataemia | | | |
| subjects affected / exposed | 7 / 93 (7.53%) | 1 / 100 (1.00%) | |
| occurrences (all) | 7 | 1 | |
| Metabolic acidosis | | | |
| subjects affected / exposed | 5 / 93 (5.38%) | 3 / 100 (3.00%) | |
| occurrences (all) | 5 | 3 | |
| Iron deficiency | | | |
| subjects affected / exposed | 1 / 93 (1.08%) | 5 / 100 (5.00%) | |
| occurrences (all) | 1 | 5 | |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|---|---|
| 07 December 2018 | • Allowed therapies for required Pneumocystis jiroveci pneumonia (PJP) prophylaxis was broadened.<br>• Instructions regarding the determination of DSA eligibility criteria were further clarified and expanded.<br>• The section on biomarkers and pharmacogenomics research was expanded. |
| 06 February 2019 | • The target dose of IP was reduced from 25 mg SC Q4W to 12.5 mg SC Q4W.<br>• The exclusion of participants with prior exposure to clazakizumab was expanded.<br>• The risks and precautions section was updated to reflect updates from the most recent Investigator brochure.<br>• Treatment options for managing hypogammaglobulinemia were added.<br>• The concomitant medications section was updated to reflect changing clinical practice.<br>• The duration of protocol-specified PJP prophylaxis was reduced to the first year of the study. |
| 29 October 2019 | • Inclusion and exclusion criteria were updated.<br>• Due to the potential confounding long-term effects of proteasome inhibitors on the immune system, participants with any prior exposure to proteasome inhibitors were to be excluded from the study.<br>• The requirement for participants to use "highly effective methods of contraception" was amended.<br>• Throughout the protocol, the terminology for discontinuation of IP was clarified so that the term "discontinuation" now refers to permanent discontinuation and the term "withholding" refers to temporary discontinuation.<br>• The dose modification guidelines were clarified and expanded throughout the protocol.<br>• Recommendations regarding concomitant background immunosuppression were clarified.<br>• The first planned formal safety review by the Data Safety and Monitoring Board (DSMB) was changed to occur after 50 participants (instead of 100 participants) had been randomized and received at least 1 dose of IP.<br>• The guidelines for participants with severe hypogammaglobulinemia were amended to add a 4-week waiting period after reduction of background immunosuppression followed by a recheck of IgG levels before implementing treatment with IV immunoglobulin.<br>• Home health visits were added.<br>• Changes were made to clarify the process for reporting pre-existing medical conditions that met the definition of a SAE. • The appearance of Clazakizumab Drug Product in 12.5 mg/mL vials was corrected to state "clear, colorless solution. |
| 11 December 2019 | • Exclusion criteria was amended to allow for participants with fully excised ulcerative colitis to enter the study.<br>• The protocol was revised to include COVID-19 PCR testing at Screening and an additional exclusion criteria was added to exclude participants with an active COVID-19 infection. Serologic blood tests were not required during the study.<br>• The schedule of mandatory in-clinic visits was amended.<br>• The rescreening procedures were amended.<br>• The prohibited medications section was amended. |
| 04 February 2021 | • Inclusion and exclusion criteria were updated.<br>• The definition, End of treatment (EOT) was added to the schedule of events (SOE) and throughout the protocol, and the definition of end of study (EOS) was updated.<br>• A PK/PD sub-study was added to better capture clazakizumab exposures and relate these to IL-6 and hsCRP levels.<br>• Patient-reported outcome assessments were added to the protocol to assess Health-related quality of life (HRQoL). |

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| 30 April 2021 | • Clarified the required timing of the biopsy required to determine study eligibility.<br>• Corrected table to reflect administration of subcutaneous clazakizumab.<br>• Removed an exploratory healthcare utilization objective and endpoint.<br>• Outlined that patient-reported outcome assessments would not have been performed for participants randomized prior to the deployment of an electronic clinical outcome assessment solution. |
| 12 July 2022 | • The overall study design and treatment duration was changed.<br>• The frequency of procedures in Years 2 to End of Study was decreased.<br>• The study procedures were updated based upon the changes to the Schedule of Events in Years 2 to End of Study.<br>• Added a new secondary objective.<br>• A corresponding new secondary endpoint was added to the study.<br>• A description of the common treatment end date (CTED) criteria was added throughout the protocol.<br>• Text that was currently described in the Investigator Brochure was removed from the protocol.<br>• Access to study product after the end of the study would now be available at the discretion of the treating physician and offered to participants as agreed upon in their respective country.<br>• Participants who received Intravenous immunoglobulin (IVIG) underwent PK assessments.<br>• The inclusion and exclusion criteria were modified to increase the number of participants.<br>• Text from the Clinical Trials Facilitation and Coordination Group was added to the adequate contraception language.<br>• Participants who permanently discontinue IP remained in the study until the common treatment end date.<br>• Text regarding unblinding procedures was amended to provide clear directions in the case of a suspected unexpected serious adverse reaction (SUSAR).<br>• Text describing dose, administration, storage, accountability, and destruction of IP was deleted.<br>• Text regarding allowed concomitant medication was updated.<br>• Recommendations for immunizations within 6 weeks prior to the start of Screening was added to the protocol.<br>•A detailed description of EOS procedures was provided for participants who completed the study, participants who permanently discontinued IP, participants who withdrew from the study, and participants who were on treatment when the primary endpoint of the study was reached. |

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| 10 July 2023 | • The primary objective and endpoint and associated footnote were revised.<br>• The "EOS visit terminology was revised to the "Safety Follow-up Visit (SFV)" or the "Common treatment end visit (CTEV)", where applicable.<br>• Testing methodology for COVID-19 was expanded to include rapid antigen testing.<br>• Protocol text under the synopsis subsection was modified.<br>• "Secondary Safety Endpoints" was revised to "Safety Endpoints".<br>• Protocol text was revised to outline the sequence of assessments and also for managing study participants who remain in the study after permanently discontinuing IP.<br>• Text describing calcineurin inhibitor (CNI) monitoring was revised.<br>• "Acceptable" methods of contraception were removed.<br>• Secondary objectives were revised to include the previous primary efficacy objective as the first secondary objective.<br>• Added statement regarding how to manage study participants who reach the endpoint of "a sustained (>= 60 days) 40% decline in eGFR from Baseline".<br>• Sites increased to 155.<br>• Inclusion and exclusion criteria revised.<br>• Administration of live vaccines was revised to prohibited during the study.<br>• Revised dose range of mycophenolate mofetil (MMF) and mycophenolic acid (MPA) (allowed concomitant medications).<br>• Study schema, Schedule of events table, and footnotes updated.<br>• Revised protocol text: -regarding participants who discontinue IP due to pregnancy. -withholding or discontinuing IP due to AE, abnormal LFTs, neutropenia and / or thrombocytopenia, and BKV, CMV, or EBV viral infection. -emergency unblinding of IP.<br>• Drug product description was updated.<br>• Added statement to refer the reader to the CSL300 Investigator's Brochure.<br>• Protocol text for procedures and visit schedule were updated.<br>• The timing of the DSA analysis and renal biopsy was revised.<br>• Allowed participant to rescreen for administrative reason. |

Notes:

## Interruptions (globally)

Were there any global interruptions to the trial? No

## Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

The study was terminated due to futility after the planned interim analysis based on the change in eGFR from baseline to Week 52 and analysis was conducted where feasible using the data collected by the time of study termination.

Notes: