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	v1
This version publication date	19 April 2025
First version publication date	19 April 2025

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	Intravenous 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	Intravenous 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 Units: Subjects			
Age continuous Units: years			
arithmetic mean	46.3	47.0	
standard deviation	± 11.87	± 12.24	-
Gender categorical Units: Subjects			
Female	29	26	55
Male	65	74	139
Ethnicity 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) 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 analyses have not been specified because only descriptive analyses were planned for safety endpoints.

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 analyses have not been specified because only descriptive analyses were planned for safety endpoints.

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 analyses have not been specified because only descriptive analyses were planned for safety endpoints.

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 analyses have not been specified because only descriptive analyses were planned for safety endpoints.

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 analyses have not been specified because only descriptive analyses were planned for safety endpoints.

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 analyses have not been specified because only descriptive analyses were planned for safety endpoints.

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 analyses have not been specified because only descriptive analyses were planned for safety endpoints.

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 analyses have not been specified because only descriptive analyses were planned for safety endpoints.

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 (total cumulative duration of sustained eGFR < 15 mL/min/1.73 m^2 AND / OR dialysis >= 60 days)
- return to dialysis
- allograft nephrectomy
- retransplantation, or
- death from any cause.

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:

Up 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 (total cumulative duration of sustained eGFR < 15 mL/min/1.73 m^2 AND / OR dialysis >= 60 days)
- return to dialysis
- allograft nephrectomy
- retransplantation, or
- death from any cause

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:

Up 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:

This secondary endpoint assessment was not performed as planned because of early study termination due to futility (at Interim Analysis).

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	0[12]	0[13]		
Units: participants				

Notes:

[12] - This secondary endpoint assessment was not performed as planned due to early study termination.
[13] - This secondary endpoint assessment was not performed as planned due to early study termination.

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:

This secondary endpoint assessment was not performed as planned because of early study termination due to futility (at Interim Analysis).

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	0[14]	0[15]		
Units: percentage of participants				
number (not applicable)				

Notes:

[14] - This secondary endpoint assessment was not performed as planned due to early study termination.

[15] - This secondary endpoint assessment was not performed as planned due to early study termination.

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. Here, 'overall number of participants analyzed' = participants with available data for this outcome measure and 'number analyzed', 'n' = participants with available data for each specified category

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	39	45		
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:

This secondary endpoint assessment was not performed as planned because of early study termination due to futility (at Interim Analysis).

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	0[16]	0[17]		
Units: score on a scale				
number (not applicable)				

Notes:

[16] - This secondary endpoint assessment was not performed as planned due to early study termination.

[17] - This secondary endpoint assessment was not performed as planned due to early study termination.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Acute Rejection Episodes of T Cell-mediated

Rejection (TCMR) and Antibody-mediated Rejection (ABMR)

End point title	Change From Baseline in Acute Rejection Episodes of T Cell-mediated Rejection (TCMR) and Antibody-mediated Rejection (ABMR)

End point description:

This secondary endpoint assessment was not performed as planned because of early study termination due to futility (at Interim Analysis).

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	0[18]	0[19]		
Units: rejections				
arithmetic mean (standard deviation)	()	()		

Notes:

[18] - This secondary endpoint assessment was not performed as planned due to early study termination.
[19] - This secondary endpoint assessment was not performed as planned due to early study termination.

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Participant Survival

End point title	Overall Participant Survival

End point description:

This secondary endpoint assessment was not performed as planned because of early study termination due to futility (at Interim Analysis).

End point type	Secondary

End point timeframe:

Up to approximately 4 years

End point values	Clazakizumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[20]	0[21]		
Units: participants				

Notes:

[20] - This secondary endpoint assessment was not performed as planned due to early study termination.
[21] - This secondary endpoint assessment was not performed as planned due to early study termination.

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:

[22] - 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:

[23] - 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[24]

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:

[24] - 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[25]

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:

[25] - 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%)	10 / 100 (10.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 12	
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. • Instructions regarding the determination of DSA eligibility criteria were further clarified and expanded. • 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. • The exclusion of participants with prior exposure to clazakizumab was expanded. • The risks and precautions section was updated to reflect updates from the most recent Investigator brochure. • Treatment options for managing hypogammaglobulinemia were added. • The concomitant medications section was updated to reflect changing clinical practice. • 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. • 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. • The requirement for participants to use "highly effective methods of contraception" was amended. • 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. • The dose modification guidelines were clarified and expanded throughout the protocol. • Recommendations regarding concomitant background immunosuppression were clarified. • 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. • 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. • Home health visits were added. • 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. • 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. • The schedule of mandatory in-clinic visits was amended. • The rescreening procedures were amended. • The prohibited medications section was amended.
04 February 2021	• Inclusion and exclusion criteria were updated. • 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. • A PK/PD sub-study was added to better capture clazakizumab exposures and relate these to IL-6 and hsCRP levels. • Patient-reported outcome assessments were added to the protocol to assess Health-related quality of life (HRQoL).

30 April 2021	• Clarified the required timing of the biopsy required to determine study eligibility. • Corrected table to reflect administration of subcutaneous clazakizumab. • Removed an exploratory healthcare utilization objective and endpoint. • 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. • The frequency of procedures in Years 2 to End of Study was decreased. • The study procedures were updated based upon the changes to the Schedule of Events in Years 2 to End of Study. • Added a new secondary objective. • A corresponding new secondary endpoint was added to the study. • A description of the common treatment end date (CTED) criteria was added throughout the protocol. • Text that was currently described in the Investigator Brochure was removed from the protocol. • 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. • Participants who received Intravenous immunoglobulin (IVIG) underwent PK assessments. • The inclusion and exclusion criteria were modified to increase the number of participants. • Text from the Clinical Trials Facilitation and Coordination Group was added to the adequate contraception language. • Participants who permanently discontinue IP remained in the study until the common treatment end date. • Text regarding unblinding procedures was amended to provide clear directions in the case of a suspected unexpected serious adverse reaction (SUSAR). • Text describing dose, administration, storage, accountability, and destruction of IP was deleted. • Text regarding allowed concomitant medication was updated. • Recommendations for immunizations within 6 weeks prior to the start of Screening was added to the protocol. •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.

10 July 2023	• The primary objective and endpoint and associated footnote were revised. • The "EOS visit terminology was revised to the "Safety Follow-up Visit (SFV)" or the "Common treatment end visit (CTEV)", where applicable. • Testing methodology for COVID-19 was expanded to include rapid antigen testing. • Protocol text under the synopsis subsection was modified. • "Secondary Safety Endpoints" was revised to "Safety Endpoints". • 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. • Text describing calcineurin inhibitor (CNI) monitoring was revised. • "Acceptable" methods of contraception were removed. • Secondary objectives were revised to include the previous primary efficacy objective as the first secondary objective. • Added statement regarding how to manage study participants who reach the endpoint of "a sustained (>= 60 days) 40% decline in eGFR from Baseline". • Sites increased to 155. • Inclusion and exclusion criteria revised. • Administration of live vaccines was revised to prohibited during the study. • Revised dose range of mycophenolate mofetil (MMF) and mycophenolic acid (MPA) (allowed concomitant medications). • Study schema, Schedule of events table, and footnotes updated. • 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. • Drug product description was updated. • Added statement to refer the reader to the CSL300 Investigator's Brochure. • Protocol text for procedures and visit schedule were updated. • The timing of the DSA analysis and renal biopsy was revised. • 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: