Clinical trial results:
A Phase 1b/2 Study to Evaluate the Safety, Pharmacokinetics, and Preliminary Efficacy of Isatuximab (SAR650984) in Patients Awaiting Kidney Transplantation

Summary

EudraCT number	2019-004154-28
Trial protocol	ES
Global end of trial date	02 May 2022

Results information

Result version number	v1
This version publication date	17 May 2023
First version publication date	17 May 2023

Trial information

Trial identification

Sponsor protocol code	TED16414

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04294459
WHO universal trial number (UTN)	U1111-1238-9716
Other trial identifiers	IND: 143523

Notes:

Sponsors

Sponsor organisation name	Sanofi-Aventis Recherche & Développement
Sponsor organisation address	1 Avenue Pierre Brossolette, Chilly-Mazarin, France, 91380
Public contact	Trial Transparency Team, Sanofi Aventis Recherche & Développement, Contact-US@sanofi.com
Scientific contact	Trial Transparency Team, Sanofi Aventis Recherche & Développement, Contact-US@sanofi.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	28 November 2022
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	02 May 2022
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

- Phase 1: To characterise the safety and tolerability of isatuximab in kidney transplant candidates.
- Phase 2: To evaluate the efficacy of isatuximab in desensitisation of subjects awaiting kidney transplantation.

Protection of trial subjects:

Subjects were fully informed of all pertinent aspects of the clinical trial as well as the possibility to discontinue at any time in language and terms appropriate for the subject and considering the local culture. During the course of the trial, subjects were provided with individual subject cards indicating the nature of the trial the subject is participating, contact details and any information needed in the event of a medical emergency. Collected personal data and human biological samples were processed in compliance with the Sanofi-Aventis Group Personal Data Protection Charter ensuring that the Group abides by the laws governing personal data protection in force in all countries in which it operates.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	18 June 2020
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Spain: 11
Country: Number of subjects enrolled	United States: 12
Worldwide total number of subjects	23
EEA total number of subjects	11

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)	21
From 65 to 84 years	2
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Study was conducted at 6 active sites in 2 countries. A total of 23 subjects were enrolled between 18 Jun 2020 and 02 Nov 2021 and received isatuximab monotherapy. Study was planned to be conducted in 2 parts: Phase 1 (safety run-in) & Phase 2 (efficacy).

Pre-assignment

Screening details:

Sponsor decided to terminate study for non-safety reasons on 02 May 2022 after interim analysis. It was determined that enrolment of remaining subjects was unlikely to have any significant impact on study results & hence trial was stopped. Subject disposition, baseline, endpoints & safety data were presented for combined Phase 1 and 2 population.

Period 1

Period 1 title	Overall study (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Cohort A: Subjects With cPRA >=99.90%

Arm description:

Subjects with calculated panel reactive antibodies (cPRA) greater than or equal to (>=) 99.90 percent (%) (indicating active candidates on kidney transplant waitlist) received isatuximab 10 milligrams per kilogram (mg/kg), intravenous (IV) infusion, once weekly (QW) for 4 weeks (i.e., on Day 1, Day 8, Day 15 and Day 22 of Cycle 1) and then every 2 weeks (Q2W) for subsequent treatment cycles (each cycle of 28 days) until unacceptable adverse events (AEs) or subject’s decision to stop the treatment (maximum treatment duration:13 weeks).

Arm type	Experimental
Investigational medicinal product name	Isatuximab
Investigational medicinal product code	SAR650984
Other name	Sarclisa
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Isatuximab 10 mg/kg, IV infusion, QW for 4 weeks (i.e., on Day 1, Day 8, Day 15 and Day 22 of Cycle 1) and then Q2W for subsequent treatment cycles (each cycle of 28 days).

Arm title	Cohort B: Subjects With cPRA 80.00% to 99.89%

Arm description:

Subjects with cPRA between 80.00% to 99.89% (indicating active candidates on kidney transplant waitlist with no living donor cleared for donation) received isatuximab 10 mg/kg, IV infusion, QW for 4 weeks (i.e., on Day 1, Day 8, Day 15 and Day 22 of Cycle 1) and then Q2W for subsequent treatment cycles (each cycle of 28 days) until unacceptable AEs or subject’s decision to stop the treatment (maximum treatment duration: 13 weeks).

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Investigational medicinal product name	Isatuximab
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Other name	Sarclisa
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Isatuximab 10 mg/kg, IV infusion, QW for 4 weeks (i.e., on Day 1, Day 8, Day 15 and Day 22 of Cycle 1) and then Q2W for subsequent treatment cycles (each cycle of 28 days).

Number of subjects in period 1	Cohort A: Subjects With cPRA >=99.90%	Cohort B: Subjects With cPRA 80.00% to 99.89%
Started	12	11
Completed	12	10
Not completed	0	1
Adverse event	-	1

Baseline characteristics

Reporting groups	
Reporting group title	Cohort A: Subjects With cPRA >=99.90%
Reporting group description:	
Subjects with calculated panel reactive antibodies (cPRA) greater than or equal to (>=) 99.90 percent (%) (indicating active candidates on kidney transplant waitlist) received isatuximab 10 milligrams per kilogram (mg/kg), intravenous (IV) infusion, once weekly (QW) for 4 weeks (i.e., on Day 1, Day 8, Day 15 and Day 22 of Cycle 1) and then every 2 weeks (Q2W) for subsequent treatment cycles (each cycle of 28 days) until unacceptable adverse events (AEs) or subject's decision to stop the treatment (maximum treatment duration:13 weeks).	
Reporting group title	Cohort B: Subjects With cPRA 80.00% to 99.89%
Reporting group description:	
Subjects with cPRA between 80.00% to 99.89% (indicating active candidates on kidney transplant waitlist with no living donor cleared for donation) received isatuximab 10 mg/kg, IV infusion, QW for 4 weeks (i.e., on Day 1, Day 8, Day 15 and Day 22 of Cycle 1) and then Q2W for subsequent treatment cycles (each cycle of 28 days) until unacceptable AEs or subject's decision to stop the treatment (maximum treatment duration: 13 weeks).	

Reporting group values	Cohort A: Subjects With cPRA >=99.90%	Cohort B: Subjects With cPRA 80.00% to 99.89%	Total
Number of subjects	12	11	23
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	49.7	48.2	
standard deviation	± 11.9	± 12.3	-
Gender categorical Units: Subjects			
Female	6	2	8
Male	6	9	15
Race Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	2	0	2
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	3	1	4
White	4	9	13
More than one race	0	0	0
Unknown or Not Reported	3	1	4

End points

End points reporting groups

Reporting group title	Cohort A: Subjects With cPRA >=99.90%

Reporting group description:

Subjects with calculated panel reactive antibodies (cPRA) greater than or equal to (>=) 99.90 percent (%) (indicating active candidates on kidney transplant waitlist) received isatuximab 10 milligrams per kilogram (mg/kg), intravenous (IV) infusion, once weekly (QW) for 4 weeks (i.e., on Day 1, Day 8, Day 15 and Day 22 of Cycle 1) and then every 2 weeks (Q2W) for subsequent treatment cycles (each cycle of 28 days) until unacceptable adverse events (AEs) or subject's decision to stop the treatment (maximum treatment duration:13 weeks).

Reporting group title	Cohort B: Subjects With cPRA 80.00% to 99.89%

Reporting group description:

Subjects with cPRA between 80.00% to 99.89% (indicating active candidates on kidney transplant waitlist with no living donor cleared for donation) received isatuximab 10 mg/kg, IV infusion, QW for 4 weeks (i.e., on Day 1, Day 8, Day 15 and Day 22 of Cycle 1) and then Q2W for subsequent treatment cycles (each cycle of 28 days) until unacceptable AEs or subject's decision to stop the treatment (maximum treatment duration: 13 weeks).

Primary: Number of Subjects With Treatment-Emergent Adverse Events (TEAEs) and Treatment-Emergent Serious Adverse Events (TESAEs)

End point title	Number of Subjects With Treatment-Emergent Adverse Events (TEAEs) and Treatment-Emergent Serious Adverse Events (TESAEs)[1]

End point description:

An AE was defined as any untoward medical occurrence in a subject who received study drug and did not necessarily had to have a causal relationship with the treatment. Serious adverse events (SAEs) were any untoward medical occurrence that at any dose: resulted in death, was life-threatening, required inpatient hospitalisation or prolongation of existing hospitalisation, resulted in persistent or significant disability/incapacity, was a congenital anomaly/birth defect, was a medically important event. TEAEs were defined as AEs that developed, worsened or became serious during the TEAE period (defined as the time from the first dose of study drug until study cut-off date). Analysis was performed on all treated population which included all subjects who received at least one dose of isatuximab. Data was planned to be collected and analysed for the combined Phase 1 and 2 population.

End point type	Primary

End point timeframe:

From first dose of study drug until study cut-off date (maximum duration: up to 97.7 weeks)

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: As the endpoint was descriptive in nature, no statistical analysis was reported.

End point values	Cohort A: Subjects With cPRA >=99.90%	Cohort B: Subjects With cPRA 80.00% to 99.89%		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	11		
Units: subjects				
TEAEs	3	4		
TESAEs	0	0		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Hematological Abnormalities

End point title	Number of Subjects With Hematological Abnormalities[2]

End point description:

Abnormal hematological parameters assessed were anemia, platelet count decreased, neutrophil count decreased, lymphocyte count decreased and monocytes. The hematological abnormality grades were based on National Cancer Institute Common Terminology Criteria for Adverse Events (NCI-CTCAE) Version 5.0, where Grade 1 = Mild; Grade 2 = Moderate; Grade 3 = Severe; Grade 4 = Potentially Life Threatening. Grade refers to the severity of the AEs. Monocytes were assessed as per potentially clinically significant abnormality (PCSA) criteria defined as: greater than (>) 0.7*10^9/Litre. Analysis was performed on all treated population. Here, "n" = subjects with available data for each specified category. Data was planned to be collected and analysed for the combined Phase 1 and 2 population.

End point type	Primary

End point timeframe:

From first dose of study drug until study cut-off date (maximum duration: up to 97.7 weeks)

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: As the endpoint was descriptive in nature, no statistical analysis was reported.

End point values	Cohort A: Subjects With cPRA >=99.90%	Cohort B: Subjects With cPRA 80.00% to 99.89%		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	11		
Units: subjects				
Anemia: Grade 1 (n=12,11)	6	8		
Anemia: Grade 2 (n=12,11)	3	2		
Anemia: Grade 3 (n=12,11)	0	0		
Anemia: Grade 4 (n=12,11)	0	0		
Platelet count decreased: Grade 1 (n=12,11)	2	6		
Platelet count decreased: Grade 2 (n=12,11)	0	0		
Platelet count decreased: Grade 3 (n=12,11)	0	0		
Platelet count decreased: Grade 4 (n=12,11)	0	0		
Neutrophil count decreased: Grade 1 (n=9,7)	0	0		
Neutrophil count decreased: Grade 2 (n=9,7)	0	0		
Neutrophil count decreased: Grade 3 (n=9,7)	0	0		
Neutrophil count decreased: Grade 4 (n=9,7)	0	0		
Lymphocyte count decreased: Grade 1 (n=9,7)	4	2		
Lymphocyte count decreased: Grade 2 (n=9,7)	1	1		
Lymphocyte count decreased: Grade 3 (n=9,7)	1	0		
Lymphocyte count decreased: Grade 4 (n=9,7)	0	0		

Monocytes (PCSA) >0.7x10^9/L (n=9,7)	3	3		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Renal Function Abnormalities

End point title	Number of Subjects With Renal Function Abnormalities[3]

End point description:

Abnormal renal parameters assessed were creatinine increased and estimated Glomerular Filtration Rate (eGFR). The renal function abnormality grades were based on NCI-CTCAE, Version 5.0, where Grade 1 = Mild; Grade 2 = Moderate; Grade 3 = Severe; Grade 4 = Potentially Life Threatening. Grade refers to the severity of the AEs. eGFR was assessed as per PCSA criteria: 60 less than or equal to (<=) to less than (<) 90 millilitres per minute per 1.73 square metre (mL/min/1.73m^2) (Mild), 30<= to <60 mL/min/1.73m^2 (Moderate), 15<=to <30 mL/ min/1.73m^2 (Severe), <15 mL/min/1.73m^2 (End Stage Renal Disease). Analysis was performed on all treated population. Data was planned to be collected and analysed for the combined Phase 1 and 2 population.

End point type	Primary

End point timeframe:

From first dose of study drug until study cut-off date (maximum duration: up to 97.7 weeks)

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: As the endpoint was descriptive in nature, no statistical analysis was reported.

End point values	Cohort A: Subjects With cPRA >=99.90%	Cohort B: Subjects With cPRA 80.00% to 99.89%		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	11		
Units: subjects				
Creatinine increased: Grade 1	0	0		
Creatinine increased: Grade 2	0	0		
Creatinine increased: Grade 3	1	3		
Creatinine increased: Grade 4	11	8		
eGFR: 60<= - <90 mL/min/1.73m^2	0	0		
eGFR: 30<= - <60 mL/min/1.73m^2	0	0		
eGFR: 15<= - <30 mL/min/1.73m^2	0	0		
eGFR: <15 mL/min/1.73m^2	12	11		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Abnormal Electrolytes Parameters

End point title	Number of Subjects With Abnormal Electrolytes Parameters[4]

End point description:

Abnormal electrolyte parameters assessed were hypernatremia, hyponatremia, hyperkalemia, hypokalemia, hypercalcemia, hypocalcemia, blood bicarbonate decreased, hypermagnesemia, hypomagnesemia, chloride. The abnormal grades were based on NCI-CTCAE, Version 5.0, where Grade 1 = Mild; Grade 2 = Moderate; Grade 3 = Severe; Grade 4 = Potentially Life Threatening. Grade refers to the severity of the AEs. Chloride was estimated as per PCSA criteria: < 80 millimoles/litre [mmol/L] and > 115 mmol/L. Analysis was performed on all treated population. Here, "n" = subjects with available data for each specified category and "99999" is used as a space filler which signifies that none of the subjects were available for assessment. Data was planned to be collected and analysed for the combined Phase 1 and 2 population.

End point type	Primary

End point timeframe:

From first dose of study drug until study cut-off date (maximum duration: up to 97.7 weeks)

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: As the endpoint was descriptive in nature, no statistical analysis was reported.

End point values	Cohort A: Subjects With cPRA >=99.90%	Cohort B: Subjects With cPRA 80.00% to 99.89%		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	11		
Units: subjects				
Hypernatremia: Grade 1 (n=12,11)	0	0		
Hypernatremia: Grade 2 (n=12,11)	0	0		
Hypernatremia: Grade 3 (n=12,11)	0	0		
Hypernatremia: Grade 4 (n=12,11)	0	0		
Hyponatremia: Grade 1 (n=12,11)	4	1		
Hyponatremia: Grade 2 (n=12,11)	0	0		
Hyponatremia: Grade 3 (n=12,11)	0	0		
Hyponatremia: Grade 4 (n=12,11)	0	0		
Hyperkalemia: Grade 1 (n=12,11)	2	6		
Hyperkalemia: Grade 2 (n=12,11)	3	1		
Hyperkalemia: Grade 3 (n=12,11)	1	2		
Hyperkalemia: Grade 4 (n=12,11)	0	0		
Hypokalemia: Grade 1 (n=12,11)	0	0		
Hypokalemia: Grade 2 (n=12,11)	0	0		
Hypokalemia: Grade 3 (n=12,11)	0	0		
Hypokalemia: Grade 4 (n=12,11)	1	0		
Hypercalcemia: Grade 1 (n=12,11)	0	1		
Hypercalcemia: Grade 2 (n=12,11)	1	0		
Hypercalcemia: Grade 3 (n=12,11)	0	0		
Hypercalcemia: Grade 4 (n=12,11)	0	0		
Hypocalcemia: Grade 1 (n=12,11)	6	5		
Hypocalcemia: Grade 2 (n=12,11)	0	2		
Hypocalcemia: Grade 3 (n=12,11)	0	0		
Hypocalcemia: Grade 4 (n=12,11)	0	0		
Blood bicarbonate decreased: Grade 1 (n=0,0)	99999	99999		
Blood bicarbonate decreased: Grade 2 (n=0,0)	99999	99999		
Blood bicarbonate decreased: Grade 3 (n=0,0)	99999	99999		

Blood bicarbonate decreased: Grade 4 (n=0,0)	99999	99999		
Hypermagnesemia: Grade 1 (n=12,11)	2	0		
Hypermagnesemia: Grade 2 (n=12,11)	0	0		
Hypermagnesemia: Grade 3 (n=12,11)	0	0		
Hypermagnesemia: Grade 4 (n=12,11)	0	0		
Hypomagnesemia: Grade 1 (n=12,11)	3	3		
Hypomagnesemia: Grade 2 (n=12,11)	0	0		
Hypomagnesemia: Grade 3 (n=12,11)	0	0		
Hypomagnesemia: Grade 4 (n=12,11)	0	0		
Chloride (PCSA): <80 mmol/L (n=12,11)	0	0		
Chloride (PCSA): >115 mmol/L (n=12,11)	0	0		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Abnormal Metabolism Parameters

End point title	Number of Subjects With Abnormal Metabolism Parameters[5]

End point description:

Abnormal metabolism parameters assessed were hypoglycemia, hypoalbuminemia and glycated Hemoglobin A1c (HbA1c). The abnormal grades were based on NCI-CTCAE, Version 5.0, where Grade 1 = Mild; Grade 2 = Moderate; Grade 3 = Severe; Grade 4 = Potentially Life Threatening. Grade refers to the severity of the AEs. HbA1c >8% was estimated as per PCSA criteria. Analysis was performed on all treated population. Here, "n" = subjects with available data for each specified category and “99999” is used as a space filler which signifies that none of the subjects were available for assessment. Data was planned to be collected and analysed for the combined Phase 1 and 2 population.

End point type	Primary

End point timeframe:

From first dose of study drug until study cut-off date (maximum duration: up to 97.7 weeks)

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: As the endpoint was descriptive in nature, no statistical analysis was reported.

End point values	Cohort A: Subjects With cPRA >=99.90%	Cohort B: Subjects With cPRA 80.00% to 99.89%		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	11		
Units: subjects				
Hypoglycemia: Grade 1 (n=12,11)	1	2		
Hypoglycemia: Grade 2 (n=12,11)	1	0		
Hypoglycemia: Grade 3 (n=12,11)	0	0		
Hypoglycemia: Grade 4 (n=12,11)	0	0		
Hypoalbuminemia: Grade 1 (n=12,11)	3	0		
Hypoalbuminemia: Grade 2 (n=12,11)	2	2		
Hypoalbuminemia: Grade 3 (n=12,11)	0	0		
Hypoalbuminemia: Grade 4 (n=12,11)	0	0		
HbA1c (PCSA) (n=0,0)	99999	99999		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Liver Function Abnormalities

End point title	Number of Subjects With Liver Function Abnormalities[6]

End point description:

Abnormal liver function parameters assessed were Alanine aminotransferase (ALT) increased, Aspartate aminotransferase (AST) increased, Alkaline phosphatase (ALP) increased, and Total bilirubin (TB) increased. The abnormal grades were based on NCI-CTCAE, Version 5.0, where Grade 1 = Mild; Grade 2 = Moderate; Grade 3 = Severe; Grade 4 = Potentially Life Threatening. Grade refers to the severity of the AEs. Analysis was performed on all treated population. Data was planned to be collected and analysed for the combined Phase 1 and 2 population.

End point type	Primary

End point timeframe:

From first dose of study drug until study cut-off date (maximum duration: up to 97.7 weeks)

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: As the endpoint was descriptive in nature, no statistical analysis was reported.

End point values	Cohort A: Subjects With cPRA >=99.90%	Cohort B: Subjects With cPRA 80.00% to 99.89%		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	11		
Units: subjects				
ALT increased: Grade 1	1	1		
ALT increased: Grade 2	0	0		
ALT increased: Grade 3	0	0		
ALT increased: Grade 4	0	0		
AST increased: Grade 1	1	0		
AST increased: Grade 2	0	0		
AST increased: Grade 3	0	0		
AST increased: Grade 4	0	0		
ALP increased: Grade 1	3	2		
ALP increased: Grade 2	0	0		
ALP increased: Grade 3	0	0		
ALP increased: Grade 4	0	0		
TB increased: Grade 1	0	0		
TB increased: Grade 2	0	0		
TB increased: Grade 3	0	0		
TB increased: Grade 4	0	0		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With Response

End point title	Percentage of Subjects With Response[7]

End point description:

Response was defined as the percentage of subjects meeting at least one of the predefined desensitisation efficacy criteria as measured by single antigen bead (SAB) assay as follows: reduction in cPRA resulting in at least 100% increase of likelihood of finding a compatible donor; reduction in antibody titer (greater than or equal to [>=]75% reduction from Baseline) to achieve target cPRA; elimination of >=1 human leukocyte antigen (HLA) antibody (i.e., mean fluorescence intensity (MFI) reduced to <2000) as measured by SAB assay, for antibodies with Baseline MFI >=3000. Analysis performed on efficacy evaluable population which included all subjects who received at least 1 dose of isatuximab, with an evaluable Baseline and at least 1 evaluable post-baseline efficacy assessment and received >=75% of planned cumulative doses. Data was planned to be collected and analysed for the combined Phase 1 and 2 population.

End point type	Primary

End point timeframe:

From first dose of study drug until end of follow-up period (maximum duration: up to 39.1 weeks)

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: As the endpoint was descriptive in nature, no statistical analysis was reported.

End point values	Cohort A: Subjects With cPRA >=99.90%	Cohort B: Subjects With cPRA 80.00% to 99.89%		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	11		
Units: percentage of subjects				
number (confidence interval 95%)	83.3 (51.6 to 97.9)	81.8 (48.2 to 97.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacokinetics (PK) Parameters: Concentration Observed at the End of Intravenous Infusion (Ceoi) of Isatuximab

End point title	Pharmacokinetics (PK) Parameters: Concentration Observed at the End of Intravenous Infusion (Ceoi) of Isatuximab

End point description:

Ceoi is the plasma concentration observed at the end of IV infusion of isatuximab. Analysis was performed on pharmacokinetic (PK) population which included all subjects who received at least 1 dose of isatuximab, with at least 1 available concentration result post treatment. Here, "number of subjects analysed" = subjects with available data for this endpoint. Data was planned to be collected and analysed for the combined Phase 1 and 2 population.

End point type	Secondary

End point timeframe:

At End of infusion on Cycle 1, Day 1

End point values	Cohort A: Subjects With cPRA >=99.90%	Cohort B: Subjects With cPRA 80.00% to 99.89%		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	11		
Units: micrograms per millilitre (mcg/mL)				
arithmetic mean (standard deviation)	290 (± 128)	270 (± 101)		

Statistical analyses

No statistical analyses for this end point

Secondary: PK Parameters: Maximum Concentration Observed (Cmax) After the First Infusion of Isatuximab

End point title	PK Parameters: Maximum Concentration Observed (Cmax) After the First Infusion of Isatuximab

End point description:

Cmax was defined as the maximum concentration observed after the first administration, calculated using the non-compartmental analysis after the IV infusion of isatuximab. Analysis was performed on PK population. Here, "number of subjects analysed" = subjects with available data for this endpoint. Data was planned to be collected and analysed for the combined Phase 1 and 2 population.

End point type	Secondary

End point timeframe:

At Start of infusion (SOI), End of infusion (EOI), EOI+1-hour post-dose on Day 1 of Cycle 1

End point values	Cohort A: Subjects With cPRA >=99.90%	Cohort B: Subjects With cPRA 80.00% to 99.89%		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	11		
Units: mcg/mL				
arithmetic mean (standard deviation)	295 (± 128)	285 (± 94)		

Statistical analyses

No statistical analyses for this end point

Secondary: PK Parameters: Time Taken to Reach Cmax (Tmax) After the First infusion of of Isatuximab

End point title	PK Parameters: Time Taken to Reach Cmax (Tmax) After the First infusion of of Isatuximab

End point description:

Tmax was defined as the time to reach Cmax, calculated using the non-compartmental analysis after the IV infusion of isatuximab. Analysis was performed on PK population. Here, "number of subjects analysed" = subjects with available data for this endpoint. Data was planned to be collected and analysed for the combined Phase 1 and 2 population.

End point type	Secondary

End point timeframe:

At SOI, EOI, EOI+1-hour post-dose on Day 1 of Cycle 1

End point values	Cohort A: Subjects With cPRA >=99.90%	Cohort B: Subjects With cPRA 80.00% to 99.89%		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	11		
Units: hours				
median (full range (min-max))	3.67 (2.00 to 6.03)	3.40 (2.25 to 4.63)		

Statistical analyses

No statistical analyses for this end point

Secondary: PK Parameters: Last Concentration Observed Above the Lower Limit of Quantification (Clast) After the First Infusion of Isatuximab

End point title	PK Parameters: Last Concentration Observed Above the Lower Limit of Quantification (Clast) After the First Infusion of Isatuximab

End point description:

Clast was defined as the last concentration of isatuximab observed above the lower limit of quantification, calculated using non-compartmental analysis after the first infusion of isatuximab. Analysis was performed on PK population. Here, "number of subjects analysed" = subjects with available data for this endpoint. Data was planned to be collected and analysed for the combined Phase 1 and 2 population.

End point type	Secondary

End point timeframe:

At SOI, EOI, EOI+1-hour post-dose on Day 1 of Cycle 1

End point values	Cohort A: Subjects With cPRA >=99.90%	Cohort B: Subjects With cPRA 80.00% to 99.89%		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	11		
Units: mcg/mL				
arithmetic mean (standard deviation)	104 (± 41.7)	76.3 (± 21.3)		

Statistical analyses

No statistical analyses for this end point

Secondary: PK Parameters: Time of Clast (Tlast) After First Infusion of Isatuximab

End point title	PK Parameters: Time of Clast (Tlast) After First Infusion of Isatuximab

End point description:

Tlast was defined as the time of last concentration observed above the lower limit of quantification, calculated using the non-compartmental analysis after the intravenous infusion of isatuximab. Analysis was performed on PK population. Here, "number of subjects analysed" = subjects with available data for this endpoint. Data was planned to be collected and analysed for the combined Phase 1 and 2 population.

End point type	Secondary

End point timeframe:

At SOI, EOI, EOI+1-hour post-dose on Day 1 of Cycle 1

End point values	Cohort A: Subjects With cPRA >=99.90%	Cohort B: Subjects With cPRA 80.00% to 99.89%		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	11		
Units: hours				
median (full range (min-max))	166.00 (49.60 to 169.00)	167.00 (78.80 to 168.00)		

Statistical analyses

No statistical analyses for this end point

Secondary: PK Parameters: Trough Plasma Concentrations (Ctrough) of Isatuximab

End point title	PK Parameters: Trough Plasma Concentrations (Ctrough) of Isatuximab

End point description:

Ctrough was the plasma concentration of isatuximab observed just before (pre-dose) treatment administration. Analysis was performed on PK population. Here "number of subjects analysed" = subjects with available data for this endpoint. Data was planned to be collected and analysed for the combined Phase 1 and 2 population.

End point type	Secondary

End point timeframe:

Pre-dose on Cycle 2 Day 1

End point values	Cohort A: Subjects With cPRA >=99.90%	Cohort B: Subjects With cPRA 80.00% to 99.89%		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	10		
Units: mcg/mL				
arithmetic mean (standard deviation)	308 (± 79.4)	246 (± 60.6)		

Statistical analyses

No statistical analyses for this end point

Secondary: PK Parameters: Area Under the Plasma Concentration Versus Time Curve From Time 0 to 168 hr Over the Dosing Interval (AUC0-168 hr) After First Infusion of Isatuximab

End point title	PK Parameters: Area Under the Plasma Concentration Versus Time Curve From Time 0 to 168 hr Over the Dosing Interval (AUC0-168 hr) After First Infusion of Isatuximab

End point description:

AUC0-168 hr was defined as the area under the plasma concentration versus time curve from time 0 to 168 hours post dose calculated using trapezoidal after first infusion of isatuximab. Analysis was performed on PK population. Here, "number of subjects analysed" = subjects with available data for this endpoint. Data was planned to be collected and analysed for the combined Phase 1 and 2 population.

End point type	Secondary

End point timeframe:

At SOI, EOI, EOI+1-hour, 72 hours and 168 hours post-dose on Day 1 of Cycle 1

End point values	Cohort A: Subjects With cPRA >=99.90%	Cohort B: Subjects With cPRA 80.00% to 99.89%		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	11		
Units: micrograms*hours/millilitre (mcg*h/ mL)				
arithmetic mean (standard deviation)	29400 (± 7400)	20000 (± 5240)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Anti-drug Antibodies (ADA) Against

Isatuximab

End point title	Number of Subjects With Anti-drug Antibodies (ADA) Against Isatuximab

End point description:

ADA responses were categorised as treatment boosted ADA and treatment-induced ADA. Treatment boosted ADA was defined as pre-existing ADAs with a significant increase in the ADA titer during the study compared to the Baseline titer. Treatment-induced ADA was defined as ADA that developed at any time during the ADA on-study observation period in subjects without pre-existing ADA. Analysis was performed on anti-drug antibodies (ADA) population which included all subjects who received at least 1 dose of isatuximab, with at least 1 available ADA result post-treatment. Data was planned to be collected and analysed for the combined Phase 1 and 2 population.

End point type	Secondary

End point timeframe:

From first dose of study drug until study cut-off date (maximum duration: up to 97.7 weeks)

End point values	Cohort A: Subjects With cPRA >=99.90%	Cohort B: Subjects With cPRA 80.00% to 99.89%		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	11		
Units: subjects				
Treatment-induced ADA	0	0		
Treatment boosted ADA	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response (DOR)

End point title	Duration of Response (DOR)

End point description:

Time from lab sample collection date used to determine responder subject (meeting at least 1 predefined desensitisation efficacy criteria: reduction (red) in cPRA resulting in at least 100% increase of likelihood of finding compatible donor; red in antibody titer [>=75% red from Baseline] to achieve target cPRA; elimination of >=1 anti-HLA antibody i.e. MFI reduced to <2000 [SAB assay], for antibodies with Baseline MFI >=3000) when subject confirmed as no longer meeting any response criterion (non-responder)/date of death, whichever 1st. Kaplan-Meier method. Analysed on responder population: subjects who received at least 1 dose of isatuximab, with evaluable Baseline & at least 1 evaluable post-baseline efficacy assessment & received >=75% of planned cumulative dose. "Number of subjects analysed" = subjects with available data, '99999' = space filler denotes median & upper limit of 95 % confidence interval not estimable due to less subjects with event. Combined Phase 1 & 2 population.

End point type	Secondary

End point timeframe:

From first dose of study drug until end of follow-up period (maximum duration: up to 39.1 weeks)

End point values	Cohort A: Subjects With cPRA >=99.90%	Cohort B: Subjects With cPRA 80.00% to 99.89%		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	9		
Units: weeks				
median (confidence interval 95%)	99999 (4.857 to 99999)	99999 (4.143 to 99999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects Achieving Target cPRA

End point title	Number of Subjects Achieving Target cPRA

End point description:

Target calculated panel reactive antibodies (cPRA) was defined as the reduction of cPRA required to achieve at least 100% increase of likelihood of compatible donor (LCD). Number of subjects who achieved target cPRA assessed using the Organ Procurement and Transplantation Network (OPTN) calculator during the specified timepoint were reported in this endpoint. Subjects who retained their target cPRA values were censored at the date of the last available laboratory assessment achieving their target cPRA. Analysis was performed on efficacy evaluable population. Here, "number of subjects analysed" = subjects with available data for this endpoint. Data was planned to be collected and analysed for the combined Phase 1 and 2 population.

End point type	Secondary

End point timeframe:

From first dose of study drug until end of follow-up period (maximum duration: up to 97.7 weeks)

End point values	Cohort A: Subjects With cPRA >=99.90%	Cohort B: Subjects With cPRA 80.00% to 99.89%		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7	6		
Units: subjects	4	2		

Statistical analyses

No statistical analyses for this end point

Secondary: Duration for Achieving Target cPRA

End point title	Duration for Achieving Target cPRA

End point description:

Duration of achieving target cPRA was defined as time (in weeks) from laboratory sample collection date of achieving target cPRA (defined as reduction of cPRA required to achieve at least 100% increase of LCD) the first time up to laboratory sample collection date when no longer achieving target cPRA calculated using OPTN calculator or date of death due to any cause, whichever occurs first. Duration of achieving target cPRA was assessed using Kaplan-Meier method. Analysis was performed on efficacy

evaluable population. Here, "number of subjects analysed" = subjects with available data for this endpoint and '99999' was used as space filler that denotes that median & upper limit of 95% confidence interval (CI) were not estimable due to insufficient number of subjects with events & '-9999' space filler denotes lower limit of 95% CI not estimable due to insufficient number of subjects with events. Data was planned to be collected and analysed for combined Phase 1 and 2 population.

End point type	Secondary

End point timeframe:

From first dose of study drug until end of follow-up period (maximum duration: up to 97.7 weeks)

End point values	Cohort A: Subjects With cPRA >=99.90%	Cohort B: Subjects With cPRA 80.00% to 99.89%		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	2		
Units: weeks				
median (confidence interval 95%)	99999 (3.429 to 99999)	7.29 (-9999 to 99999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Anti-Human Leukocyte Antigen (HLA)-Antibody Reduction

End point title	Number of Subjects With Anti-Human Leukocyte Antigen (HLA)-Antibody Reduction

End point description:

Number of subjects with anti-HLA-antibody (Baseline MFI >=3000) reduced to <2000 as measured using a SAB assay per central laboratory assessment was reported in this endpoint. Subjects were categorised in various categories of number of antibodies which were reduced as: none, 1-5, >5-10, >10-15, and >15. If multiple visits had the same number of total anti-HLA antibody reduction, the last visit data was summarised. Analysis was performed on efficacy evaluable population. Data was planned to be collected and analysed for the combined Phase 1 and 2 population.

End point type	Secondary

End point timeframe:

From first dose of study drug until end of follow-up period (maximum duration: up to 39.1 weeks)

End point values	Cohort A: Subjects With cPRA >=99.90%	Cohort B: Subjects With cPRA 80.00% to 99.89%		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	11		
Units: subjects				
None	2	2		
1-5 antibodies	4	4		
>5-10 antibodies	4	4		
>10-15 antibodies	1	0		

>15 antibodies	1	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Time to First Transplant Offer

End point title	Time to First Transplant Offer

End point description:

Time to first transplant offer was defined as time (in days) from date of first study treatment dose up to date of first kidney transplant offer. Data on transplant status were collected and followed up until study cut-off date. Analysis was performed on efficacy-evaluable population. Here, "number of subjects analysed" = subjects with available data for this endpoint. Data was planned to be collected and analysed for the combined Phase 1 and 2 population.

End point type	Secondary

End point timeframe:

From first dose of study drug until study cut-off date (maximum duration: up to 97.7 weeks)

End point values	Cohort A: Subjects With cPRA >=99.90%	Cohort B: Subjects With cPRA 80.00% to 99.89%		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	3		
Units: days				
median (full range (min-max))	373 (248 to 517)	156 (117 to 402)		

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Transplant

End point title	Time to Transplant

End point description:

Time to transplant was defined as time (in days) from date of first study treatment dose up to date of kidney transplant. Data on transplant status were collected and followed up until study cut-off date. Analysis was performed on efficacy evaluable population. Here, "number of subjects analysed" = subjects with available data for this endpoint and included only subjects who accepted transplant offer. Data was planned to be collected and analysed for the combined Phase 1 and 2 population.

End point type	Secondary

End point timeframe:

From first dose of study drug until study cut-off date (maximum duration: up to 97.7 weeks)

End point values	Cohort A: Subjects With cPRA >=99.90%	Cohort B: Subjects With cPRA 80.00% to 99.89%		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2	2		
Units: days				
median (full range (min-max))	445 (373 to 517)	259.5 (117 to 402)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Kidney Transplant Offers

End point title	Number of Kidney Transplant Offers

End point description:

Number of kidney transplants offers received for each subject was reported in the endpoint. Data on transplant offers were collected and followed up until study cut-off date. Analysis was performed on efficacy evaluable population. Data was planned to be collected and analysed for the combined Phase 1 and 2 population.

End point type	Secondary

End point timeframe:

From first dose of study drug until study cut-off date (maximum duration: up to 97.7 weeks)

End point values	Cohort A: Subjects With cPRA >=99.90%	Cohort B: Subjects With cPRA 80.00% to 99.89%		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	11		
Units: transplant offers				
number (not applicable)	3	3		

Statistical analyses

No statistical analyses for this end point

Secondary: Time to First Antibody Mediated Rejection (AMR) Episode

End point title	Time to First Antibody Mediated Rejection (AMR) Episode

End point description:

Time to first AMR was defined as time (in days) from date of first study treatment dose up to date of biopsy with first AMR (defined as the graft rejection due to generation of antibodies against the graft).

Transplanted subjects without any AMR were censored at the subject's last assessment or contact date collected in the study or at the analysis cut-off date, whichever was earlier. Data for this endpoint was not collected and analysed as no subjects experienced a kidney transplant graft loss due to an AMR episode as of study terminated date.

End point type	Secondary

End point timeframe:

From first dose of study drug until study cut-off date (maximum duration: up to 97.7 weeks)

End point values	Cohort A: Subjects With cPRA >=99.90%	Cohort B: Subjects With cPRA 80.00% to 99.89%		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[8]	0[9]		
Units: days				
number (not applicable)				

Notes:

[8] - No subjects experienced kidney transplant graft loss due to AMR episodes.

[9] - No subjects experienced kidney transplant graft loss due to AMR episodes.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Who Experienced Any Antibody Mediated Rejection (AMR)

End point title	Percentage of Subjects Who Experienced Any Antibody Mediated Rejection (AMR)

End point description:

Antibody mediated rejection was defined as the graft rejection due to generation of antibodies against the graft. The number of subjects with AMR field checked as 'yes' based on the graft rejection biopsy in the electronic case report form was considered. Data for this endpoint was not collected and analysed as no subjects experienced a kidney transplant graft loss due to an AMR episode, as of study terminated date.

End point type	Secondary

End point timeframe:

From first dose of study drug until study cut-off date (maximum duration: up to 97.7 weeks)

End point values	Cohort A: Subjects With cPRA >=99.90%	Cohort B: Subjects With cPRA 80.00% to 99.89%		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[10]	0[11]		
Units: percentage of subjects				
number (not applicable)				

Notes:

[10] - No subjects experienced kidney transplant graft loss due to AMR episodes.

[11] - No subjects experienced kidney transplant graft loss due to AMR episodes.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Graft Survival at 6 Months Post-Transplant

End point title	Number of Subjects With Graft Survival at 6 Months Post-Transplant

End point description:

Number of subjects with graft survival status as functioning at 6-months post-transplant was reported in this endpoint. Analysis was performed on efficacy evaluable population. Here, "number of subjects analysed" = subjects with evaluable data for this endpoint.

End point type	Secondary

End point timeframe:

At 6 Months post-transplant

End point values	Cohort A: Subjects With cPRA >=99.90%	Cohort B: Subjects With cPRA 80.00% to 99.89%		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1	1		
Units: subjects	1	0		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From first dose of study drug until study cut-off date (maximum duration: up to 97.7 weeks)

Adverse event reporting additional description:

Analysis was performed on all treated population.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	25.0

Reporting groups

Reporting group title	Cohort A: Subjects With cPRA >=99.90%

Reporting group description:

Subjects with cPRA >=99.90% (indicates active candidates on kidney transplant waitlist) received isatuximab 10 mg/kg, IV infusion, QW for 4 weeks (i.e., on Day 1, Day 8, Day 15 and Day 22 of Cycle 1) and then Q2W for subsequent treatment cycles (each cycle of 28 days) until unacceptable AEs or subject's decision to stop the treatment (maximum treatment duration: 13 weeks).

Reporting group title	Cohort B: Subjects With cPRA 80.00% to 99.89%

Reporting group description:

Subjects with cPRA between 80.00% to 99.89% (indicating active candidates on kidney transplant waitlist with no living donor cleared for donation) received isatuximab 10 mg/kg, IV infusion, QW for 4 weeks (i.e., on Day 1, Day 8, Day 15 and Day 22 of Cycle 1) and then Q2W for subsequent treatment cycles (each cycle of 28 days) until unacceptable AEs or subject’s decision to stop the treatment (maximum treatment duration: 13 weeks).

Serious adverse events	Cohort A: Subjects With cPRA >=99.90%	Cohort B: Subjects With cPRA 80.00% to 99.89%	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 12 (0.00%)	0 / 11 (0.00%)	
number of deaths (all causes)	1	0	
number of deaths resulting from adverse events			

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

Non-serious adverse events	Cohort A: Subjects With cPRA >=99.90%	Cohort B: Subjects With cPRA 80.00% to 99.89%	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 12 (25.00%)	4 / 11 (36.36%)	
Injury, poisoning and procedural complications			
Infusion Related Reaction			

subjects affected / exposed occurrences (all)	2 / 12 (16.67%) 3	3 / 11 (27.27%) 3	
Cardiac disorders Tachycardia subjects affected / exposed occurrences (all)	 1 / 12 (8.33%) 1	 0 / 11 (0.00%) 0	
Nervous system disorders Headache subjects affected / exposed occurrences (all)	 1 / 12 (8.33%) 1	 0 / 11 (0.00%) 0	
General disorders and administration site conditions Chills subjects affected / exposed occurrences (all)	 1 / 12 (8.33%) 1	 0 / 11 (0.00%) 0	
Gastrointestinal disorders Nausea subjects affected / exposed occurrences (all)	 1 / 12 (8.33%) 1	 0 / 11 (0.00%) 0	
Respiratory, thoracic and mediastinal disorders Nasal Congestion subjects affected / exposed occurrences (all)	 1 / 12 (8.33%) 1	 0 / 11 (0.00%) 0	
Musculoskeletal and connective tissue disorders Temporomandibular Joint Syndrome subjects affected / exposed occurrences (all) Myalgia subjects affected / exposed occurrences (all)	 1 / 12 (8.33%) 1 1 / 12 (8.33%) 2	 0 / 11 (0.00%) 0 0 / 11 (0.00%) 0	
Infections and infestations Covid-19 subjects affected / exposed occurrences (all) Nasopharyngitis subjects affected / exposed occurrences (all)	 0 / 12 (0.00%) 0 1 / 12 (8.33%) 1	 1 / 11 (9.09%) 1 0 / 11 (0.00%) 0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
23 July 2020	Following changes were made: Provided option to adapt the premedication depending on individual situation; Clarified monitoring and risks related to viral reactivation; Added indirect Coombs tests after treatment period during Site Visit follow-up period (FUP) if Cycle (C)2Day (D)1 was positive; Ensured a post-treatment sample was collected in case C3D1 sample was not collected or if subject discontinued treatment prior to C3D1; Modified sample collection timepoint to reduce wait time/burden for study subjects; Provided flexibility and potentially reduced site visit for study subjects; Updated isatuximab approval status and number of treated subjects; Updated infusion rates based on fixed volume infusion method; Corrected typographical error; Added obinutuzumab to require 6 months washout period; Included flexibility and ease of continuation of study during regional or national emergency such as Covid-19; Updated management guideline on Grade 2 and 3 IR including permanent discontinuation of study treatment at third infusion reactions (IR); "AE or" was added to the sentence: "However, if either of the following conditions applies, then the event must be recorded and reported as an AE or SAE (instead of a disease related event [DRE]):"; Pregnancy test frequency was corrected to be consistent with Schedule of Activities; Minor editorial and format changes.
01 February 2022	Following changes were made: Criteria for cPRA reduction was corrected from "at least 50% increase of likelihood" to "at least 100% increase of likelihood"; Editorial changes were made to clarify that history of active or latent tuberculosis was relevant if within 24 weeks prior to IMP initiation, and "(peritoneal, etc.)" were specific to the "deep tissue/space infection"; Clarified on need for individual serology and viral load tests; minor editorial and format changes were done.

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.

Study was terminated for non-safety reasons on 02 May 2022. It was determined that enrolment of remaining subjects was unlikely to have any significant impact on results. All 23 subjects enrolled were followed-up per protocol until termination date.

Notes: