Clinical trial results:
A Randomized, Open-Label, Multi-Centre, Active Control Study Investigating the Efficacy and Safety of Imlifidase in Eliminating Donor Specific Anti-HLA Antibodies in the Treatment of Active Antibody-Mediated Rejection in Kidney Transplant Patients

Summary

EudraCT number	2018-000022-66
Trial protocol	FR AT DE
Global end of trial date	16 November 2022

Results information

Result version number	v1 (current)
This version publication date	17 February 2024
First version publication date	17 February 2024

Trial information

Trial identification

Sponsor protocol code	16-HMedIdeS-12

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03897205
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Hansa Biopharma AB
Sponsor organisation address	Scheelevägen 22, Lund, Sweden, 223 63
Public contact	Clinical contact information, Hansa Biopharma AB, +46 046165670, clinicalstudyinfo@hansabiopharma.com
Scientific contact	Clinical contact information, Hansa Biopharma AB, +46 046165670, clinicalstudyinfo@hansabiopharma.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	09 October 2023
Is this the analysis of the primary completion data?	Yes
Primary completion date	28 May 2022
Global end of trial reached?	Yes
Global end of trial date	16 November 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Investigate the efficacy of imlifidase compared with plasma exchange (PE) in removal of donor specific antibodies (DSA) in patients who are experiencing an active or chronic active AMR episode after kidney transplantation

Protection of trial subjects:

Details of the goals of the research and the risk and benefits of the protocol were reviewed with each potential study subject.
In the event of adverse events from the study, full resources of the hospital were available to intervene as medically necessary.
Physicians expert in the care of patients with AMR were responsible for the patients' care at each site.
To mitigate the risk of infections all patients received a standard regimen of antibiotics according to local clinical practice, starting before the first treatment and continuing until IgG levels had returned to acceptable values, as judged by the investigator.
All patients in the imlifidase arm received antihistamine before administration of imlifidase and all patients in both treatment arms
were treated in accordance with the study protocol with the background therapy described below.

Background therapy:

All patients received pulse methylprednisolone Day 1 to Day 3, followed by a tapering schedule with prednisolone/prednisone.
Patients randomised to imlifidase received their first dose of methylprednisolone before imlifidase was administered. The patients
did also receive high dose intravenous immunoglobulin (IVIg) 3 days after imlifidase treatment or directly after the last PE. In
addition a single dose of rituximab was given 5 days after completed IVIg infusion.

Evidence for comparator: -

Actual start date of recruitment	06 August 2019
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
Long term follow-up duration	3 Years
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Austria: 4
Country: Number of subjects enrolled	France: 13
Country: Number of subjects enrolled	Germany: 8
Country: Number of subjects enrolled	United States: 3
Country: Number of subjects enrolled	Australia: 1

Worldwide total number of subjects	29
EEA total number of subjects	25

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)	25
From 65 to 84 years	4
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Patients were recruited between 06-AUG-2019 and 20-MAY-2022.

Pre-assignment

Screening details:

A total of 34 patients were screened, 30 were randomised, and 29 were included in the study.

Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Blinding implementation details:

Blinding was not feasible due to the nature of the standard of care treatment.

Arms

Are arms mutually exclusive?	Yes
Arm title	Imlifidase

Arm description:

Patients treated with imlifidase

Arm type	Experimental
Investigational medicinal product name	Imlifidase
Investigational medicinal product code	
Other name	IdeS, IgG endopeptidase
Pharmaceutical forms	Powder for concentrate for solution for infusion
Routes of administration	Infusion

Dosage and administration details:

One intravenous dose of imlifidase, 0.25 mg/kg, administered over 15 minutes.

Arm title	Plasma exchange (PE)

Arm description:

Patients treated with SOC, i.e. PE

Arm type	Medical procedure-Active comparato
Investigational medicinal product name	Plasma exchange
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Pharmaceutical dose form not applicable
Routes of administration	Route of administration not applicable

Dosage and administration details:

Plasma exchange is a medicinal procedure

Number of subjects in period 1	Imlifidase	Plasma exchange (PE)
Started	19	10
Completed	17	10
Not completed	2	0
Adverse event, serious fatal	1	-
Lost to follow-up	1	-

Baseline characteristics

Reporting groups	
Reporting group title	Imlifidase
Reporting group description: Patients treated with imlifidase	
Reporting group title	Plasma exchange (PE)
Reporting group description: Patients treated with SOC, i.e. PE	

Reporting group values	Imlifidase	Plasma exchange (PE)	Total
Number of subjects	19	10	29
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	17	8	25
From 65-84 years	2	2	4
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	43.7	52.8	
standard deviation	± 13.7	± 16.4	-
Gender categorical Units: Subjects			
Female	8	5	13
Male	11	5	16

End points

End points reporting groups

Reporting group title	Imlifidase
Reporting group description:	
Patients treated with imlifidase	
Reporting group title	Plasma exchange (PE)
Reporting group description:	
Patients treated with SOC, i.e. PE	
Subject analysis set title	PK analysis set
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
PK analysis set includes patients receiving any amount of imlifidase.	

Primary: Maximum Reduction in Donor Specific Antibodies (DSA) Level During the 5 Days Following the Start of Treatment

End point title	Maximum Reduction in Donor Specific Antibodies (DSA) Level During the 5 Days Following the Start of Treatment[1]
End point description:	
Maximum reduction (%) in the sum of DSA at any time point during the 5 days following the start of treatment. Only DSA with ≥1000 mean fluorescence intensity (MFI) at pre-treatment were included in the calculations.	
End point type	Primary
End point timeframe:	
Start of treatment until 5 days following start of treatment	

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: Due to the exploratory nature of this trial, no formal hypothesis was tested.

End point values	Imlifidase	Plasma exchange (PE)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	18[2]	8[3]		
Units: Maximum reduction (%)				
arithmetic mean (standard deviation)	94 (± 4)	36 (± 26)		

Notes:

[2] - 1 patient excluded did not have MFIs above 1000

[3] - 2 patients excluded did not have MFI above 1000

Statistical analyses

No statistical analyses for this end point

Secondary: Reduction in DSA Levels After Treatment

End point title	Reduction in DSA Levels After Treatment
End point description:	
DSA levels were assessed at all visits throughout the study. The results are presented as reduction (%) from baseline. A negative value represents an increase from baseline.	
End point type	Secondary
End point timeframe:	
Screening until Day 180	

End point values	Imlifidase	Plasma exchange (PE)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	18	8		
Units: Reduction from baseline (%)				
arithmetic mean (standard deviation)				
2 hours	91 (± 7)	-2 (± 28)		
6 hours	94 (± 4)	-2 (± 33)		
24 hours	92 (± 5)	0 (± 25)		
48 hours	89 (± 10)	18 (± 34)		
72 hours	83 (± 24)	10 (± 32)		
96 hours	58 (± 32)	22 (± 26)		
Day 6	41 (± 42)	31 (± 23)		
Day 8	33 (± 45)	39 (± 20)		
Day 11	35 (± 34)	22 (± 34)		
Day 15	31 (± 43)	28 (± 36)		
Day 22	28 (± 46)	23 (± 34)		
Day 29	35 (± 30)	30 (± 14)		
Day 64	30 (± 38)	32 (± 34)		
Day 90	25 (± 41)	41 (± 33)		
Day 180	29 (± 38)	35 (± 32)		

Statistical analyses

No statistical analyses for this end point

Secondary: Estimated Glomerular Filtration Rate (eGFR) Levels

End point title	Estimated Glomerular Filtration Rate (eGFR) Levels

End point description:

eGFR as calculated from p-creatinine is a measure of kidney function. eGFR was assessed at all visits throughout the study.

End point type	Secondary

End point timeframe:

Screening until Day 180

End point values	Imlifidase	Plasma exchange (PE)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19[4]	10		
Units: mL/min/1.73m2				
arithmetic mean (standard deviation)				
Pre-dose	28.0 (± 14.0)	21.0 (± 8.1)		
24 hours	25.8 (± 13.8)	23.5 (± 11.0)		

48 hours	26.2 (± 14.5)	25.7 (± 9.4)		
72 hours	27.6 (± 15.9)	27.2 (± 10.8)		
96 hours	30.6 (± 19.5)	30.5 (± 13.8)		
Day 6	30.3 (± 18.6)	31.2 (± 12.9)		
Day 8	33.4 (± 21.1)	36.2 (± 18.2)		
Day 11	32.2 (± 18.9)	34.0 (± 16.6)		
Day 15	32.1 (± 19.3)	31.1 (± 15.4)		
Day 22	29.8 (± 16.7)	31.9 (± 14.8)		
Day 29	27.5 (± 15.3)	31.7 (± 14.5)		
Day 64	29.4 (± 14.9)	34.6 (± 14.5)		
Day 90	27.2 (± 16.7)	31.6 (± 12.8)		
Day 180	29.9 (± 15.5)	32.5 (± 17.8)		

Notes:

[4] - Some patients had missing values at sporadic occasions throughout the trial

Statistical analyses

No statistical analyses for this end point

Secondary: Urine albumin/creatinine

End point title	Urine albumin/creatinine

End point description:

The albumin/creatinine ratio in urine is a measure of kidney function.

End point type	Secondary

End point timeframe:

Pre-dose until Day 180

End point values	Imlifidase	Plasma exchange (PE)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19[5]	10[6]		
Units: Ratio				
arithmetic mean (standard deviation)				
Pre-dose	626 (± 972)	134 (± 165)		
Day 90	669 (± 964)	119 (± 166)		
Day 180	815 (± 1018)	242 (± 295)		

Notes:

[5] - Some patients had missing values at different occasions during the study.

[6] - Some patients had missing values at different occasions during the study.

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of Patients With Graft Loss Within 180 Days of Treatment

End point title	Proportion of Patients With Graft Loss Within 180 Days of Treatment

End point description:

Information on patients who experienced graft loss was collected throughout the study.

End point type	Secondary

End point timeframe:

Screening until Day 180

End point values	Imlifidase	Plasma exchange (PE)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19	10		
Units: Number of patients				
number (not applicable)	5	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of Patients With Signs or no Signs of Transplant Glomerulopathy at Day 180

End point title	Proportion of Patients With Signs or no Signs of Transplant Glomerulopathy at Day 180

End point description:

Biopsies collected 180 days after treatment were analysed for signs of glomerulopathy.

End point type	Secondary

End point timeframe:

Day 180

End point values	Imlifidase	Plasma exchange (PE)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19	10		
Units: Number of patients				
number (not applicable)				
No signs of transplant glomerulopathy	7	4		
Signs of transplant glomerulopathy	8	6		
No biopsy result or no evaluable biopsy result	4	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of Patients With Resolved AMR as Assessed by Messenger Ribonucleic Acid (mRNA) Levels

End point title	Proportion of Patients With Resolved AMR as Assessed by

	Messenger Ribonucleic Acid (mRNA) Levels

End point description:

Kidney biopsies were taken at screening, Day 29, and Day 180. Changes from baseline in mRNA levels were assessed as evidence of resolved AMR.

End point type	Secondary

End point timeframe:

Screening, Day 29, and Day 180

End point values	Imlifidase	Plasma exchange (PE)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19	10		
Units: Number of patients				
number (not applicable)				
Day 29	0	0		
Day 180	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Administered Plasma Exchange (PE) and Immunoadsorption (IA) Sessions

End point title	Number of Administered Plasma Exchange (PE) and Immunoadsorption (IA) Sessions

End point description:

Total number of administered PE and IA sessions to each treatment group are presented during the complete trial (Day 1 to Day 180) and for the time period: start of IVIg administration to Day 180.

End point type	Secondary

End point timeframe:

Day 1 to Day 180

End point values	Imlifidase	Plasma exchange (PE)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19	10		
Units: Number of sessions				
number (not applicable)				
Number of PE from Day 1 to Day 180	20	70		
Number of PE administered after start of IVIg	18	11		
Number of IA from Day 1 to Day 180	0	23		
Number of IA administered after start of IVIg	0	23		

Statistical analyses

No statistical analyses for this end point

Secondary: Total Serum Immunoglobulin G (IgG) Levels Until Administration of Intravenous Immunoglobulin (IVIg)

End point title	Total Serum Immunoglobulin G (IgG) Levels Until Administration of Intravenous Immunoglobulin (IVIg)

End point description:

Total serum IgG levels over time following treatment until administration of IVIg.
Please observe, IVIg was initiated on Day 4 (before 96 h measurement) for the imlifidase group.

End point type	Secondary

End point timeframe:

Pre-dose until Day 6

End point values	Imlifidase	Plasma exchange (PE)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19	10		
Units: mg/mL				
arithmetic mean (standard deviation)				
Pre-dose	8.6 (± 6.1)	7.9 (± 5.5)		
2 hours	0.2 (± 0.1)	4.3 (± 3.5)		
6 hours	0.2 (± 0.1)	4.6 (± 3.6)		
24 hours	0.2 (± 0.2)	5.2 (± 3.7)		
48 hours	0.2 (± 0.2)	4.6 (± 4.3)		
72 hours	0.5 (± 0.8)	4.8 (± 4.3)		
96 hours	11.7 (± 5.4)	4.1 (± 4.3)		
Day 6	20.0 (± 8.4)	4.2 (± 4.5)		

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of Patients With Intact IgG Following Treatment Until Administration of IVIg

End point title	Proportion of Patients With Intact IgG Following Treatment Until Administration of IVIg

End point description:

Presence of IgG, scIgG, and F(ab')2 was analysed using sodium dodecyl-sulphate polyacrylamide gel electrophoresis (SDS-PAGE)/western blot.
Of note, IVIg was administered on Day 4 (before 96 h measurement) to patients treated with imlifidase.

Hence no analyses beyond this timepoint were performed for this group.

End point type	Secondary

End point timeframe:

Start of treatment (Day 1) up to administration of IVIg on Day 4 (imlifidase group) and until administration of IVIg within Day 15 (PE group)

End point values	Imlifidase	Plasma exchange (PE)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19[7]	10[8]		
Units: Number of patients				
number (not applicable)				
Baseline	19	10		
2 hours	0	10		
6 hours	0	10		
24 hours	0	9		
48 hours	0	8		
72 hours	0	10		
96 hours	0	9		
Day 6	0	10		
Day 8	0	8		
Day 11	0	5		
Day 15	0	1		

Notes:

[7] - 19 patients analysed up to 72 hours then 0 patients at all following timepoints

[8] - 10 patients analysed up to Day 6, then 8 at Day 8, 5 at Day 11, and 2 at Day 15

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of Patients With Mixed Intact IgG and scIgG Following Treatment Until Administration of IVIg

End point title	Proportion of Patients With Mixed Intact IgG and scIgG Following Treatment Until Administration of IVIg

End point description:

Presence of IgG, scIgG, and F(ab')2 was analysed using sodium dodecyl-sulphate polyacrylamide gel electrophoresis (SDS-PAGE)/western blot.
Of note, IVIg was administered on Day 4 (before 96 h measurement) to patients treated with imlifidase. Hence no analyses beyond this timepoint were performed for this group.

End point type	Secondary

End point timeframe:

Start of treatment (Day 1) up to administration of IVIg on Day 4 (imlifidase group) and until administration of IVIg within Day 15 (PE group)

End point values	Imlifidase	Plasma exchange (PE)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19[9]	10[10]		
Units: Number of patients				
number (not applicable)				
Baseline	0	0		
2 hours	0	0		
6 hours	0	0		
24 hours	0	0		
48 hours	0	0		
72 hours	2	0		
96 hours	0	0		
Day 6	0	0		
Day 8	0	0		
Day 11	0	0		
Day 15	0	0		

Notes:

[9] - 19 patients analysed up to 72 hours and 0 patients at all following timepoints.

[10] - 10 patients up to Day 6, 8 at Day 8, 5 at Day 11, and 2 at Day 15

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of Patients With Only scIgG Following Treatment Until Administration of IVIg

End point title	Proportion of Patients With Only scIgG Following Treatment Until Administration of IVIg

End point description:

Presence of IgG, scIgG, and F(ab')2 was analysed using sodium dodecyl-sulphate polyacrylamide gel electrophoresis (SDS-PAGE)/western blot.
Of note, IVIg was administered on Day 4 (before 96 h measurement) to patients treated with imlifidase. Hence no analyses beyond this timepoint were performed for this group.

End point type	Secondary

End point timeframe:

Start of treatment (Day 1) up to administration of IVIg on Day 4 (imlifidase group) and until administration of IVIg within Day 15 (PE group)

End point values	Imlifidase	Plasma exchange (PE)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19[11]	10[12]		
Units: Number of patients				
number (not applicable)				
Baseline	0	0		
2 hours	0	0		
6 hours	0	0		
24 hours	0	0		
48 hours	0	0		
72 hours	0	0		

96 hours	0	0		
Day 6	0	0		
Day 8	0	0		
Day 11	0	0		
Day 15	0	0		

Notes:

[11] - 19 patient were analysed up to 72 hours thereafter 0 patients at all following timepoints

[12] - 10 patients up to Day 6, 8 at Day 8, 5 at Day 11 and 2 at Day 15

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of Patients With Mixed scIgG and F(ab')2 Fragments Following Treatment Until Administration of IVIg

End point title	Proportion of Patients With Mixed scIgG and F(ab')2 Fragments Following Treatment Until Administration of IVIg

End point description:

Presence of IgG, scIgG, and F(ab')2 was analysed using sodium dodecyl-sulphate polyacrylamide gel electrophoresis (SDS-PAGE)/western blot.
Of note, IVIg was administered on Day 4 (before 96 h measurement) to patients treated with imlifidase. Hence no analyses beyond this timepoint were performed for this group.

End point type	Secondary

End point timeframe:

Start of treatment (Day 1) up to administration of IVIg on Day 4 (imlifidase group) and until administration of IVIg within Day 15 (PE group)

End point values	Imlifidase	Plasma exchange (PE)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19[13]	10[14]		
Units: Number of patients				
number (not applicable)				
Baseline	0	0		
2 hours	2	0		
6 hours	0	0		
24 hours	0	0		
48 hours	1	0		
72 hours	1	0		
96 hours	0	0		
Day 6	0	0		
Day 8	0	0		
Day 11	0	0		
Day 15	0	0		

Notes:

[13] - 19 patients analysed up to 72 hours thereafter 0 patients at all following timepoints

[14] - 10 patients analysed up to Day 6, 8 at Day 8, 5 at Day 11, and 2 at Day 15

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of Patients With Only F(ab')2 Fragments Following Treatment Until Administration of IVIg

End point title	Proportion of Patients With Only F(ab')2 Fragments Following Treatment Until Administration of IVIg

End point description:

Presence of IgG, scIgG, and F(ab')2 was analysed using sodium dodecyl-sulphate polyacrylamide gel electrophoresis (SDS-PAGE)/western blot.
Of note, IVIg was administered on Day 4 (before 96 h measurement) to patients treated with imlifidase. Hence no analyses beyond this timepoint were performed for this group.

End point type	Secondary

End point timeframe:

Start of treatment (Day 1) up to administration of IVIg on Day 4 (imlifidase group) and until administration of IVIg within Day 15 (PE group)

End point values	Imlifidase	Plasma exchange (PE)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19[15]	10[16]		
Units: Number of patients				
number (not applicable)				
Baseline	0	0		
2 hours	17	0		
6 hours	19	0		
24 hours	19	0		
48 hours	18	0		
72 hours	16	0		
96 hours	0	0		
Day 6	0	0		
Day 8	0	0		
Day 11	0	0		
Day 15	0	0		

Notes:

[15] - 19 patients analysed up to 72 hours and thereafter 0 at all following timepoints

[16] - 10 patients analysed up to Day 6, 8 at Day 8, 5 at Day 11, and 2 at Day 15

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of Patients With No Intact IgG, scIgG, or F(ab')2 Fragments Following Treatment Until Administration of IVIg

End point title	Proportion of Patients With No Intact IgG, scIgG, or F(ab')2 Fragments Following Treatment Until Administration of IVIg

End point description:

Presence of IgG, scIgG, and F(ab')2 was analysed using sodium dodecyl-sulphate polyacrylamide gel electrophoresis (SDS-PAGE)/western blot.
Of note, IVIg was administered on Day 4 (before 96 h measurement) to patients treated with imlifidase. Hence no analyses beyond this timepoint were performed for this group.

End point type	Secondary

End point timeframe:

Start of treatment (Day 1) up to administration of IVIg on Day 4 (imlifidase group) and until administration of IVIg within Day 15 (PE group)

End point values	Imlifidase	Plasma exchange (PE)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19[17]	10[18]		
Units: Number of patients				
number (not applicable)				
Baseline	0	0		
2 hours	0	0		
6 hours	0	0		
24 hours	0	1		
48 hours	0	2		
72 hours	0	0		
96 hours	0	1		
Day 6	0	0		
Day 8	0	0		
Day 11	0	0		
Day 15	0	1		

Notes:

[17] - 19 patients were analysed up to 72 hours thereafter 0 patients at all following timepoints

[18] - 10 patients were analysed up to Day 6, 8 at Day 8, 5 at Day 11, and 2 at Day 15

Statistical analyses

No statistical analyses for this end point

Secondary: DSA Functionality Determined by C1q Analysis Pre- and Post-treatment

End point title	DSA Functionality Determined by C1q Analysis Pre- and Post-treatment

End point description:

An MFI value above 6000 is indicative of complement fixation. Analysis of DSA functionality assessed as mean MFI levels was done before and after treatment.

End point type	Secondary

End point timeframe:

Screening until Day 6

End point values	Imlifidase	Plasma exchange (PE)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19[19]	10[20]		
Units: MFI counts				
arithmetic mean (standard deviation)				
Pre-dose	19827 (± 11910)	18848 (± 9958)		
Day 2	319 (± 432)	15576 (± 12008)		
Day 6	5065 (± 9768)	11926 (± 13076)		

Notes:

[19] - 11 patients were evaluable pre-dose, Day 2 and 10 patients Day 6

[20] - 6 patients were evaluable pre-dose, Day 2, and Day 6

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacokinetics of Imlifidase

End point title	Pharmacokinetics of Imlifidase

End point description:

Cmax = Maximum observed plasma concentration of imlifidase following dosing
Tmax = Time point for maximum observed plasma concentration of imlifidase following dosing
t1/2 = Terminal half-life of imlifidase (alpha t1/2 corresponds to the initial phase and beta t1/2 corresponds to the elimination phase)
AUC = Area under the imlifidase plasma concentration vs time curve
CL = Clearance of imlifidase means the volume of blood cleared of imlifidase per unit of time
Vss = Volume of distribution associated with steady state
VZ = Volume of distribution associated with the elimination phase

End point type	Secondary

End point timeframe:

Start of treatment until Day 15

End point values	PK analysis set			
Subject group type	Subject analysis set			
Number of subjects analysed	19[21]			
Units: Result				
median (full range (min-max))				
Cmax (µg/mL)	4.2 (2.8 to 5.7)			
Tmax (h)	0.6 (0.4 to 2.3)			
alpha-t1/2 (h)	2.7 (1.4 to 6.0)			
beta-t1/2 (h)	39.7 (23.5 to 128.0)			
AUC (h×µg/mL)	127.0 (37.2 to 325.5)			
CL (mL/h/kg)	1.87 (0.77 to 6.72)			
Vss (L/kg)	0.20 (0.10 to 9.85)			
Vz (L/kg)	0.18 (0.11 to 8.41)			

Notes:

[21] - 16 patients were evaluable for AUC, beta-t1/2, CL, Vss, and Vz and 13 for alpha-t1/2

Statistical analyses

No statistical analyses for this end point

Secondary: Concentration of Anti-drug Antibodies (ADAs)

End point title	Concentration of Anti-drug Antibodies (ADAs)

End point description:

Samples were collected and analysed for presence of anti-imlifidase IgG throughout the study. Imlifidase is an IgG-degrading enzyme of Streptococcus pyogenes. Patients who have been exposed to Streptococcus prior to participating in this trial tested positive for ADA also before exposure to imlifidase.

End point type	Secondary

End point timeframe:

Screening until Day 180

End point values	PK analysis set			
Subject group type	Subject analysis set			
Number of subjects analysed	19			
Units: mg/L				
geometric mean (geometric coefficient of variation)				
Pre-dose	6.7 (± 70)			
24 hours	2.0 (± 0)			
Day 8	15 (± 66)			
Day 11	20 (± 149)			
Day 15	49 (± 275)			
Day 22	73 (± 300)			
Day 29	87 (± 398)			
Day 64	122 (± 496)			
Day 90	135 (± 536)			
Day 180	100 (± 725)			

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of Patients With Different Types of Kidney Histopathology at Screening

End point title	Proportion of Patients With Different Types of Kidney Histopathology at Screening

End point description:

Kidney biopsies were assessed according to the Banff (2017 or 2019) criteria at screening (baseline), Day 29, and Day 180.

End point type	Secondary

End point timeframe:

Screening

End point values	Imlifidase	Plasma exchange (PE)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19	10		
Units: Patients				
number (not applicable)				
Active AMR	7	4		
Active AMR + Borderline CMR	0	1		
Active AMR + CMR	5	1		
Chronic Active AMR + Borderline CMR	3	1		
Chronic Active AMR + CMR	1	2		
Chronic Active AMR	3	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of Patients With Different Types of Kidney Histopathology at Day 29

End point title	Proportion of Patients With Different Types of Kidney Histopathology at Day 29

End point description:

Kidney biopsies were assessed according to the Banff (2017 or 2019) criteria at screening (baseline), Day 29, and Day 180.

End point type	Secondary

End point timeframe:

Day 29

End point values	Imlifidase	Plasma exchange (PE)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19	10		
Units: Patients				
number (not applicable)				
Active AMR	4	3		
Active AMR + Borderline CMR	0	1		
Active AMR + CMR	1	1		
Chronic Active AMR + Borderline CMR	1	1		
Chronic Active AMR + CMR	1	0		
Chronic Active AMR	4	2		
Borderline CMR	0	1		
CMR	1	0		
No rejection	5	1		
Missing data	2	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of Patients With Different Types of Kidney Histopathology at Day 180

End point title	Proportion of Patients With Different Types of Kidney Histopathology at Day 180

End point description:

Kidney biopsies were assessed according to the Banff (2017 or 2019) criteria at screening (baseline), Day 29, and Day 180.

End point type	Secondary

End point timeframe:

Day 180

End point values	Imlifidase	Plasma exchange (PE)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19	10		
Units: Patients				
number (not applicable)				
Active AMR	2	2		
Active AMR + CMR	1	0		
Chronic Active AMR + Borderline CMR	2	0		
Chronic Active AMR + CMR	1	0		
Chronic Active AMR	5	5		
CMR	0	1		
No rejection	2	2		
Missing data	6	0		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

AEs were collected for 6 months (from signed ICF until end of study including the follow-up period). AEs after start of trial treatment and within the time of residual drug effect i.e. 28 days are classified as treatment emergent AEs (TEAEs).

Adverse event reporting additional description:

AEs were obtained if spontaneously reported, if reported in response to an open question, or if revealed by observation.
The reported non-serious AEs consists of TEAEs irrespective of relationship to treatment.
The reported SAEs covers the whole study. 6 SAEs were treatment related. The SAE with fatal outcome occurred Day 176.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	21.1

Reporting groups

Reporting group title	Imlifidase - Safety Analysis Set

Reporting group description:

The safety analysis dataset comprises data from all treated patients and was analysed according to the actual treatment received.

Reporting group title	PE - Safety Analysis Set

Reporting group description:

The safety analysis dataset comprises data from all treated patients and was analysed according to the actual treatment received.

Serious adverse events	Imlifidase - Safety Analysis Set	PE - Safety Analysis Set	
Total subjects affected by serious adverse events			
subjects affected / exposed	13 / 19 (68.42%)	8 / 10 (80.00%)	
number of deaths (all causes)	1	0	
number of deaths resulting from adverse events	1	0	
Injury, poisoning and procedural complications			
Arteriovenous fistula site complication			
subjects affected / exposed	1 / 19 (5.26%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Complications of transplanted kidney			
subjects affected / exposed	1 / 19 (5.26%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal lymphocele			

subjects affected / exposed	1 / 19 (5.26%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Shunt thrombosis			
subjects affected / exposed	1 / 19 (5.26%)	0 / 10 (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			
Leukocytosis			
subjects affected / exposed	0 / 19 (0.00%)	1 / 10 (10.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephrogenic anaemia			
subjects affected / exposed	0 / 19 (0.00%)	1 / 10 (10.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Death			
subjects affected / exposed	1 / 19 (5.26%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Device related thrombosis			
subjects affected / exposed	1 / 19 (5.26%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	0 / 19 (0.00%)	1 / 10 (10.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Kidney transplant rejection			
subjects affected / exposed	1 / 19 (5.26%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Renal transplant failure			
subjects affected / exposed	1 / 19 (5.26%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transplant rejection			
subjects affected / exposed	1 / 19 (5.26%)	1 / 10 (10.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 19 (5.26%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	1 / 19 (5.26%)	1 / 10 (10.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulum intestinal haemorrhagic			
subjects affected / exposed	1 / 19 (5.26%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal haemorrhage			
subjects affected / exposed	1 / 19 (5.26%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	5 / 19 (26.32%)	1 / 10 (10.00%)	
occurrences causally related to treatment / all	1 / 5	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bladder tamponade			
subjects affected / exposed	0 / 19 (0.00%)	1 / 10 (10.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Postrenal failure			
subjects affected / exposed	1 / 19 (5.26%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal impairment			
subjects affected / exposed	0 / 19 (0.00%)	1 / 10 (10.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary retention			
subjects affected / exposed	0 / 19 (0.00%)	1 / 10 (10.00%)	
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			
Muscle haemorrhage			
subjects affected / exposed	0 / 19 (0.00%)	1 / 10 (10.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Bacterial pyelonephritis			
subjects affected / exposed	1 / 19 (5.26%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Corona virus infection			
subjects affected / exposed	1 / 19 (5.26%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Escherichia pyelonephritis			
subjects affected / exposed	1 / 19 (5.26%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Escherichia urinary tract infection			
subjects affected / exposed	0 / 19 (0.00%)	1 / 10 (10.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Gastroenteritis			
subjects affected / exposed	0 / 19 (0.00%)	1 / 10 (10.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis viral			
subjects affected / exposed	0 / 19 (0.00%)	1 / 10 (10.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis			
subjects affected / exposed	1 / 19 (5.26%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	1 / 19 (5.26%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urosepsis			
subjects affected / exposed	1 / 19 (5.26%)	0 / 10 (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	Imlifidase - Safety Analysis Set	PE - Safety Analysis Set	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	17 / 19 (89.47%)	10 / 10 (100.00%)	
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 19 (5.26%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Hypotension			
subjects affected / exposed	0 / 19 (0.00%)	2 / 10 (20.00%)	
occurrences (all)	0	2	
General disorders and administration site conditions			

Asthenia			
subjects affected / exposed	0 / 19 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Catheter site haemorrhage			
subjects affected / exposed	1 / 19 (5.26%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Catheter site pain			
subjects affected / exposed	1 / 19 (5.26%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Chest pain			
subjects affected / exposed	1 / 19 (5.26%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Fatigue			
subjects affected / exposed	3 / 19 (15.79%)	0 / 10 (0.00%)	
occurrences (all)	3	0	
Gait disturbance			
subjects affected / exposed	1 / 19 (5.26%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Malaise			
subjects affected / exposed	1 / 19 (5.26%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Non-cardiac chest pain			
subjects affected / exposed	0 / 19 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Oedema peripheral			
subjects affected / exposed	3 / 19 (15.79%)	1 / 10 (10.00%)	
occurrences (all)	3	1	
Pyrexia			
subjects affected / exposed	0 / 19 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Immune system disorders			
Transplant rejection			
subjects affected / exposed	1 / 19 (5.26%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Respiratory, thoracic and mediastinal disorders			

Bronchospasm			
subjects affected / exposed	1 / 19 (5.26%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Dyspnoea			
subjects affected / exposed	1 / 19 (5.26%)	1 / 10 (10.00%)	
occurrences (all)	1	1	
Pulmonary congestion			
subjects affected / exposed	1 / 19 (5.26%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Psychiatric disorders			
Anxiety			
subjects affected / exposed	1 / 19 (5.26%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Depressed mood			
subjects affected / exposed	1 / 19 (5.26%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Feeling of despair			
subjects affected / exposed	1 / 19 (5.26%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Panic attack			
subjects affected / exposed	0 / 19 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Sleep disorder			
subjects affected / exposed	0 / 19 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Investigations			
Acid base balance abnormal			
subjects affected / exposed	1 / 19 (5.26%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Antibody test positive			
subjects affected / exposed	1 / 19 (5.26%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
BK polyomavirus test positive			
subjects affected / exposed	0 / 19 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Blood creatinine increased			

subjects affected / exposed	3 / 19 (15.79%)	1 / 10 (10.00%)	
occurrences (all)	3	3	
Blood glucose fluctuation			
subjects affected / exposed	0 / 19 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Blood triglycerides increased			
subjects affected / exposed	2 / 19 (10.53%)	0 / 10 (0.00%)	
occurrences (all)	2	0	
C-reactive protein increased			
subjects affected / exposed	0 / 19 (0.00%)	2 / 10 (20.00%)	
occurrences (all)	0	2	
Immunosuppressant drug level increased			
subjects affected / exposed	1 / 19 (5.26%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Injury, poisoning and procedural complications			
Infusion related reaction			
subjects affected / exposed	1 / 19 (5.26%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Overdose			
subjects affected / exposed	1 / 19 (5.26%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Renal lymphocele			
subjects affected / exposed	1 / 19 (5.26%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Cardiac disorders			
Tachycardia			
subjects affected / exposed	1 / 19 (5.26%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Nervous system disorders			
Dysgeusia			
subjects affected / exposed	1 / 19 (5.26%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Headache			
subjects affected / exposed	2 / 19 (10.53%)	1 / 10 (10.00%)	
occurrences (all)	4	1	
Tremor			

subjects affected / exposed occurrences (all)	0 / 19 (0.00%) 0	1 / 10 (10.00%) 1	
Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all) Leukocytosis subjects affected / exposed occurrences (all) Leukopenia subjects affected / exposed occurrences (all) Lymphopenia subjects affected / exposed occurrences (all) Thrombocytopenia subjects affected / exposed occurrences (all) Thrombotic microangiopathy subjects affected / exposed occurrences (all)	 2 / 19 (10.53%) 2 1 / 19 (5.26%) 1 1 / 19 (5.26%) 1 1 / 19 (5.26%) 1 4 / 19 (21.05%) 5 1 / 19 (5.26%) 1	 0 / 10 (0.00%) 0 0 / 10 (0.00%) 0 1 / 10 (10.00%) 1 0 / 10 (0.00%) 0 1 / 10 (10.00%) 1 0 / 10 (0.00%) 0	
Ear and labyrinth disorders Ear discomfort subjects affected / exposed occurrences (all) Tinnitus subjects affected / exposed occurrences (all)	 1 / 19 (5.26%) 1 1 / 19 (5.26%) 1	 0 / 10 (0.00%) 0 0 / 10 (0.00%) 0	
Eye disorders Visual impairment subjects affected / exposed occurrences (all)	 1 / 19 (5.26%) 1	 0 / 10 (0.00%) 0	
Gastrointestinal disorders Abdominal distension subjects affected / exposed occurrences (all) Abdominal hernia	 0 / 19 (0.00%) 0	 1 / 10 (10.00%) 1	

subjects affected / exposed	1 / 19 (5.26%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Abdominal pain upper			
subjects affected / exposed	1 / 19 (5.26%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Ascites			
subjects affected / exposed	1 / 19 (5.26%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Constipation			
subjects affected / exposed	2 / 19 (10.53%)	0 / 10 (0.00%)	
occurrences (all)	2	0	
Diarrhoea			
subjects affected / exposed	1 / 19 (5.26%)	1 / 10 (10.00%)	
occurrences (all)	2	1	
Dyspepsia			
subjects affected / exposed	1 / 19 (5.26%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Flatulence			
subjects affected / exposed	1 / 19 (5.26%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Food poisoning			
subjects affected / exposed	1 / 19 (5.26%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Mouth ulceration			
subjects affected / exposed	1 / 19 (5.26%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Nausea			
subjects affected / exposed	2 / 19 (10.53%)	0 / 10 (0.00%)	
occurrences (all)	3	0	
Vomiting			
subjects affected / exposed	1 / 19 (5.26%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Hepatobiliary disorders			
Hepatocellular injury			
subjects affected / exposed	1 / 19 (5.26%)	0 / 10 (0.00%)	
occurrences (all)	1	0	

Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	0 / 19 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	1 / 19 (5.26%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Dysuria			
subjects affected / exposed	1 / 19 (5.26%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Incontinence			
subjects affected / exposed	0 / 19 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Proteinuria			
subjects affected / exposed	1 / 19 (5.26%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 19 (5.26%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Bone pain			
subjects affected / exposed	0 / 19 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Muscle spasms			
subjects affected / exposed	1 / 19 (5.26%)	1 / 10 (10.00%)	
occurrences (all)	1	1	
Myalgia			
subjects affected / exposed	1 / 19 (5.26%)	1 / 10 (10.00%)	
occurrences (all)	1	1	
Pain in extremity			
subjects affected / exposed	2 / 19 (10.53%)	0 / 10 (0.00%)	
occurrences (all)	2	0	
Infections and infestations			
Cytomegalovirus infection			

subjects affected / exposed	1 / 19 (5.26%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Sinusitis			
subjects affected / exposed	1 / 19 (5.26%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Metabolism and nutrition disorders			
Calcium deficiency			
subjects affected / exposed	0 / 19 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Dehydration			
subjects affected / exposed	1 / 19 (5.26%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Dyslipidaemia			
subjects affected / exposed	0 / 19 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Folate deficiency			
subjects affected / exposed	0 / 19 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Hypercholesterolaemia			
subjects affected / exposed	1 / 19 (5.26%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Hyperglycaemia			
subjects affected / exposed	4 / 19 (21.05%)	2 / 10 (20.00%)	
occurrences (all)	10	2	
Hyperkalaemia			
subjects affected / exposed	3 / 19 (15.79%)	4 / 10 (40.00%)	
occurrences (all)	3	4	
Hyperphosphataemia			
subjects affected / exposed	1 / 19 (5.26%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Hypertriglyceridaemia			
subjects affected / exposed	1 / 19 (5.26%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Hypokalaemia			
subjects affected / exposed	1 / 19 (5.26%)	2 / 10 (20.00%)	
occurrences (all)	1	2	

Hypomagnesaemia subjects affected / exposed occurrences (all)	1 / 19 (5.26%) 1	0 / 10 (0.00%) 0	
Metabolic acidosis subjects affected / exposed occurrences (all)	1 / 19 (5.26%) 1	0 / 10 (0.00%) 0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
03 March 2020	Amendment 1, substantial, introduced changes (Austria, Australia, France, US) • Allowed for a kidney biopsy performed within standard of care to be used for inclusion. • Clarified inclusion criteria #5 by adding chronic active AMR. • Clarified that the 3 latest creatinine values prior to the current AMR should be collected. • Extension of trial duration by 8 months. • Benefit/risk section was updated with new number for infusion reactions according to the latest version of IB.
06 October 2020	Amendment 2, substantial introduced the following changes (Austria, Australia, France, US): • Ensured that patients with asymptomatic Covid-19 were not included in the trial • Serum sickness was no longer classified as a risk • Thrombocytopenic purpura (TTP) was defined as a contraindication and exclusion criterion • Extension of trial duration by 9 months

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
07 April 2020	Due to the COVID-19 pandemic the patient recruitment was temporary halted. During the last quarter of 2020 and during 2021 and 2022 (US sites only) onsite monitoring visits were not accepted due to the Covid-19 pandemic. Source data verification was performed to the extent possible and was fully completed when monitors could visit the sites again.	01 December 2020

Notes:

Limitations and caveats

None reported