Clinical trial results:
A prospective, observational long-term follow-up trial of kidney transplant patients treated with imlifidase or plasma exchange after an active/chronic active antibody-mediated rejection episode

Summary

EudraCT number	2020-004777-49
Trial protocol	FR AT DE
Global end of trial date	30 March 2023

Results information

Result version number	v1 (current)
This version publication date	12 March 2025
First version publication date	12 March 2025

Trial information

Trial identification

Sponsor protocol code	20-HMedIdeS-18

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04711850
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 Operation Department, Hansa Biopharma AB, +46 046165670, info@hansabiopharma.com
Scientific contact	Clinical Operation Department, Hansa Biopharma AB, +46 046165670, info@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	22 November 2023
Is this the analysis of the primary completion data?	Yes
Primary completion date	30 March 2023
Global end of trial reached?	Yes
Global end of trial date	30 March 2023
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this trial is to evaluate kidney graft survival in subjects that have been treated with imlifidase or plasma exchange in association with AMR in trial 16-HMedIdeS-12 (referred to as the feeder trial).

Protection of trial subjects:

No treatment was administered during this follow-up study. Administration of imlifidase was done during the feeder trial 16-HMedIdeS-12.
Details of the goals of the research and the risk and benefits of the trial protocol were reviewed with each potential trial subject.
Physicians expert in the care of patients with AMR were responsible for the patients' care at each site.

Background therapy:

N/A this is a long-term follow-up study.

Evidence for comparator:

N/A this is a long-term follow-up study.

Actual start date of recruitment	20 January 2021
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	France: 10
Country: Number of subjects enrolled	Germany: 4
Country: Number of subjects enrolled	Austria: 4
Worldwide total number of subjects	18
EEA total number of subjects	18

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)	15
From 65 to 84 years	3
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Patients were recruited between 20-JAN-2021 and 11-NOV-2022

Pre-assignment

Screening details:

All 18 patients who were screened were enrolled in the trial.

Period 1

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

Blinding implementation details:

N/A

Arms

Are arms mutually exclusive?	Yes
Arm title	Imlifidase

Arm description:

Patients in this arm received imlifidase in the feeder study 16-HMedIdeS-12

Arm type	Experimental
Investigational medicinal product name	Imlifidase
Investigational medicinal product code	
Other name	IdeS, IgG endopeptidase
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Imlifidase was not administered in this long-term follow-up trial.
Subjects randomized to imlifidase treatment in the feeder study 16-HMedIdeS-12 received one intravenous dose of imlifidase, 0.25 mg/kg, administered over 15 minutes.

Arm title	PLEX

Arm description:

Subjects randomized to plasma exchange (PLEX) treatment in the feeder study 16-HMedIdes-12 received 5-10 sessions of PLEX, as judged by the investigator. Immunoadsorption (IA) could replace PE, at the discretion of the investigator.

Arm type	PLEX

No investigational medicinal product assigned in this arm

Number of subjects in period 1	Imlifidase	PLEX
Started	11	7
Completed	3	1
Not completed	8	6
Patient not eligible - no AMR in feeder study	1	-
Graft loss	2	1
Sponsor decision	-	2

Trial terminated by Sponsor	5	3

Baseline characteristics

Reporting groups	
Reporting group title	Imlifidase
Reporting group description:	
Patients in this arm received imlifidase in the feeder study 16-HMedIdeS-12	
Reporting group title	PLEX
Reporting group description:	
Subjects randomized to plasma exchange (PLEX) treatment in the feeder study 16-HMedIdes-12 received 5-10 sessions of PLEX, as judged by the investigator. Immunoadsorption (IA) could replace PE, at the discretion of the investigator.	

Reporting group values	Imlifidase	PLEX	Total
Number of subjects	11	7	18
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)	8	7	15
From 65-84 years	3	0	3
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	45.9	48.0	
standard deviation	± 17.6	± 13.5	-
Gender categorical Units: Subjects			
Female	5	4	9
Male	6	3	9
BMI			
Body Mass Index			
Units: kg/m2			
arithmetic mean	27.1	29.0	
standard deviation	± 6.9	± 7.1	-

End points

End points reporting groups

Reporting group title	Imlifidase
Reporting group description:	
Patients in this arm received imlifidase in the feeder study 16-HMedIdeS-12	
Reporting group title	PLEX
Reporting group description:	
Subjects randomized to plasma exchange (PLEX) treatment in the feeder study 16-HMedIdes-12 received 5-10 sessions of PLEX, as judged by the investigator. Immunoadsorption (IA) could replace PE, at the discretion of the investigator.	

Primary: Overall graft survival at Year 3

End point title	Overall graft survival at Year 3[1]
End point description:	
Graft survival is defined as time from start of AMR treatment in feeder study (16-HMedIdeS-12) to graft loss. Graft loss is defined as permanent return to dialysis for at least 6 weeks, re-transplantation, or nephrectomy.	
End point type	Primary
End point timeframe:	
Three (3) years after start of AMR treatment in feeder trial 16-HMedIdeS-12.	

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 early termination of the study a large proportion of patients were censored.

End point values	Imlifidase	PLEX		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11[2]	7[3]		
Units: Patients				
Patients	9	6		

Notes:

[2] - Due to the early termination of the trial a large proportion of patients were censored prior to Y3.

[3] - Due to the early termination of the trial a large proportion of patients were censored prior to Y3.

Statistical analyses

No statistical analyses for this end point

Secondary: Overall graft survival at Year 1 and Year 2

End point title	Overall graft survival at Year 1 and Year 2
End point description:	
Graft survival is defined as time from start of AMR treatment in feeder study (16-HMedIdeS-12) to graft loss. Graft loss is defined as permanent return to dialysis for at least 6 weeks, re-transplantation, or nephrectomy.	
End point type	Secondary
End point timeframe:	
Up to 2 years after start of AMR treatment in the feeder trial (16-HMedIdes-12).	

End point values	Imlifidase	PLEX		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11[4]	7[5]		
Units: Patients				
Patients with functioning graft Year 1	9	6		
Patients with functioning graft Year 2	9	6		

Notes:

[4] - Due to the early termination of the trial a large proportion of patients were censored prior to Y2.

[5] - Due to the early termination of the trial a large proportion of patients were censored prior to Y2.

Statistical analyses

No statistical analyses for this end point

Secondary: Patient survival at Year 3

End point title	Patient survival at Year 3

End point description:

Overall patient survival is defined as time from start of AMR treatment in feeder study (16-HMedIdeS-12) to death for any cause.

End point type	Secondary

End point timeframe:

Up to 3 years after start of AMR treatment in the feeder study (16-HMedIdeS-12).

End point values	Imlifidase	PLEX		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11[6]	7[7]		
Units: Patients				
Patients alive Year 3	11	7		

Notes:

[6] - Due to the early termination of the trial a large proportion of patients were censored prior to Y3.

[7] - Due to the early termination of the trial a large proportion of patients were censored prior to Y3.

Statistical analyses

No statistical analyses for this end point

Secondary: Kidney function as evaluated by eGFR

End point title	Kidney function as evaluated by eGFR

End point description:

Estimated glomerular filtration rate (eGFR) was calculated as described by the Modification of Diet in Renal Disease Study (MDRD) equation. eGFR is a measure of kidney function.
eGFR for a kidney with normal function is 90 mL/min/1.72m2.
Kidney disease is characterised by a decreased eGFR value.

End point type	Secondary

End point timeframe:

Up to 3 years after start of AMR treatment in the feeder study (16-HMedIdes-12)

End point values	Imlifidase	PLEX		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11[8]	7[9]		
Units: mL/min/1.73m2				
arithmetic mean (standard deviation)				
Year 1	30.1 (± 20.9)	36.6 (± 12.3)		
Year 2	41.2 (± 6.4)	39.7 (± 0)		
Year 3	30.5 (± 0)	0 (± 0)		

Notes:

[8] - 8 patients Y1, 3 patients Y2, 1 patient Y3 due to early termination of trial.

[9] - 4 patients Y1, 1 patient Y2, 0 patients Y3 due to early termination of trial.

Statistical analyses

No statistical analyses for this end point

Secondary: Kidney function as evaluated by creatinine

End point title	Kidney function as evaluated by creatinine

End point description:

The creatinine in blood is a measure of kidney function.
Kidney disease is characterized by an increased creatinine level.

End point type	Secondary

End point timeframe:

Up to 3 years after start of AMR treatment in the feeder study (16-HMedIdes-12).

End point values	Imlifidase	PLEX		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11[10]	7[11]		
Units: micromole(s)/litre				
arithmetic mean (full range (min-max))				
Year 1	297 (81 to 795)	187 (102 to 288)		
Year 2	130 (107 to 161)	187 (187 to 187)		
Year 3	144 (144 to 144)	0 (0 to 0)		

Notes:

[10] - 8 patients Y1, 3 patients Y2, 1 patient Y3 due to early termination of trial.

[11] - 4 patients Y1, 1 patient Y2, 0 patients Y3 due to early termination of trial.

Statistical analyses

No statistical analyses for this end point

Secondary: AMR episodes (presumed or biopsy proven)

End point title	AMR episodes (presumed or biopsy proven)

End point description:

Information about AMR episodes was collected according to Banff 2017 or later classification.
For-cause biopsies together with contemporaneous local donor specific antibodies (DSA) analyses, kidney function parameters (creatinine, albumin/creatinine ratio in urine) and treatments (e.g. plasma exchange and IVIg) were collected to assess the rejection episodes.

End point type	Secondary

End point timeframe:

Up to 3 years after start of AMR treatment in the feeder study (16-HMedIdeS-12).

End point values	Imlifidase	PLEX		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11[12]	7[13]		
Units: Patients				
Patients with AMR episodes	9	6		

Notes:

[12] - Due to early termination of the trial a large proportion of patients were censored prior to Y3.

[13] - Due to early termination of the trial a large proportion of patients were censored prior to Y3.

Statistical analyses

No statistical analyses for this end point

Secondary: Rejection episodes other than AMR (presumed or biopsy proven)

End point title	Rejection episodes other than AMR (presumed or biopsy proven)

End point description:

Information about rejection episodes were collected according to Banff 2017 or later classification.
For-cause biopsies together with contemporaneous local donor specific antibodies (DSA) analyses, kidney function parameters (creatinine, albumin/creatinine ratio in urine) and treatments (e.g. plasma exchange and IVIg) were collected to assess the rejection episodes.

End point type	Secondary

End point timeframe:

Up to 3 years after AMR treatment in the feeder study (16-HMedIdeS-12).

End point values	Imlifidase	PLEX		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11[14]	7[15]		
Units: Patients				
Patients with rejection episodes other than AMR	3	4		

Notes:

[14] - Due to early termination of the trial a large proportion of patients were censored prior to Y3.

[15] - Due to early termination of the trial a large proportion of patients were censored prior to Y3.

Statistical analyses

No statistical analyses for this end point

Secondary: Levels of donor specific antibodies (DSA)

End point title	Levels of donor specific antibodies (DSA)

End point description:

DSA levels were measured using single antigen bead human leukocyte antigen (SAB-HLA) assay.

End point type	Secondary

End point timeframe:

Up to 3 years after start of AMR treatment in the feeder study (16-HMedIdeS-12).

End point values	Imlifidase	PLEX		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11[16]	7[17]		
Units: MFI level				
arithmetic mean (standard deviation)				
Pre-treatment in feeder study (Visit 2)	10764 (± 7603)	15794 (± 5897)		
Year 1	5964 (± 5539)	3672 (± 643)		
Year 2	2156 (± 1025)	12362 (± 0)		
Year 3	974 (± 0)	0 (± 0)		

Notes:

[16] - 10 pre-dose in 16-HMedIdeS-12, 8 patients Y1, 3 patients Y2, 1 patient Y3 due to early termination
[17] - 5 pre-dose in 16-HMedIdeS-12, 2 patients Y1, 1 patients Y2, 0 patients Y3 due to early termination

Statistical analyses

No statistical analyses for this end point

Secondary: Levels of anti-drug IgG antibodies

End point title	Levels of anti-drug IgG antibodies[18]

End point description:

The immunogenicity of imlifidase was assessed by measuring ADA levels.
Only patients exposed to imlifidase were assessed for ADA.

End point type	Secondary

End point timeframe:

Up to 3 years after start of AMR treatment in the feeder study (16-HMedIdeS-12).

Notes:

[18] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The patients in the PLEX arm were not exposed to imlifidase. Hence N/A to measure ADA for this group.

End point values	Imlifidase			
Subject group type	Reporting group			
Number of subjects analysed	11[19]			
Units: mg/L				
geometric mean (geometric coefficient of variation)				
Year 1	75 (± 405)			
Year 2	41 (± 1426)			
Year 3	15 (± 0)			

Notes:

[19] - 8 patients at Y1, 3 patients at Y2, 1 patient at Y3 due to early termination of the trial

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information[1]

Timeframe for reporting adverse events:

From inclusion until end of study (Year 3).

Adverse event reporting additional description:

Only AEs related to trial procedure or related to IMP administered in feeder trial were to be collected.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	23.1

Reporting groups

Reporting group title	Imlifidase treatment in the feeder study (16-HMedIdeS-12)

Reporting group description:

All patients treated with imlifidase in the feeder study 16-HMedIdes-12.
No treatment was administered in this long-term follow-up trial.

Reporting group title	PLEX treatment in the feeder study (16-HMedIdeS-12)

Reporting group description:

All patients treated with PLEX in the feeder study.
No treatment was administered in this long-term follow-up study.

Serious adverse events	Imlifidase treatment in the feeder study (16-HMedIdeS-12)	PLEX treatment in the feeder study (16-HMedIdeS-12)	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	

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

Non-serious adverse events	Imlifidase treatment in the feeder study (16-HMedIdeS-12)	PLEX treatment in the feeder study (16-HMedIdeS-12)	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.
Justification: Only AEs related to trial procedure or related to IMP administered in feeder trial were to be collected. No such events were reported.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

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.

Early termination leading to small number of subjects analysed.

Notes: