



## Clinical trial results:

**An open-label, single arm, multi-centre, phase II study investigating safety, tolerability, efficacy, pharmacodynamics and pharmacokinetics of imlifidase (IdeS) in patients with Guillain-Barré Syndrome (GBS), in comparison with matched control patients**

### Summary

EudraCT number	2018-001059-12
Trial protocol	GB NL
Global end of trial date	27 February 2024

### 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	15-HMedIdeS-09
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#### Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03943589
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 46165670, info@hansabiopharma.com
Scientific contact	Clinical Operation Department, Hansa Biopharma AB, 46 46165670, 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	03 July 2024
Is this the analysis of the primary completion data?	Yes
Primary completion date	27 February 2024
Global end of trial reached?	Yes
Global end of trial date	27 February 2024
Was the trial ended prematurely?	No

Notes:

## General information about the trial

Main objective of the trial:

Assess safety and tolerability of imlifidase in combination with standard IVIg treatment in GBS subjects

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 GBS were responsible for the patients' care at each site.

To mitigate the risk of infections all patients received prophylactic treatment with antibiotics administered orally once daily for 14 days starting before imlifidase infusion on Day 1.

In order to reduce the risk of infusion reaction, a phenomenon that may occur with infusion of proteins, premedication with methylprednisolone (IV) and antihistamine (oral) were given to all patients before the imlifidase infusion.

As participation in the trial delayed the commencement of standard IVIg treatment, a patient could, if the GBS symptoms worsened very quickly during the first 24 hours after imlifidase administration, be given PLEX to manage the rapid progression of GBS and to remove any remaining imlifidase before initiating IVIg treatment according to standard of care. This decision was made at the discretion of the investigator.

Background therapy:

Standard of care IVIg infusions for 5 consecutive days at 0.4 g/kg, starting on Day 3. IVIg was given at least 48 hours after imlifidase administration and within 14 days of onset of weakness. Premedication before first dose of IVIg was given according to local clinical standard.

Evidence for comparator:

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Actual start date of recruitment	12 November 2019
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

## Population of trial subjects

### Subjects enrolled per country

Country: Number of subjects enrolled	Netherlands: 1
Country: Number of subjects enrolled	United Kingdom: 3
Country: Number of subjects enrolled	France: 26
Worldwide total number of subjects	30
EEA total number of subjects	27

Notes:

<b>Subjects enrolled per age group</b>	
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)	18
From 65 to 84 years	12
85 years and over	0

## Subject disposition

### Recruitment

Recruitment details:

Patients were recruited between 12-NOV-2019 and 02-MAR-2023.

### Pre-assignment

Screening details:

A total of 31 patients were screened. Thirty (30) patients were enrolled and dosed with imlifidase.

### 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

Arm title	All patients intended to be treated
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Arm description: -

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:

A dose of 0.25 mg/kg was administered as an IV infusion over 30 minutes.

<b>Number of subjects in period 1</b>	All patients intended to be treated
Started	30
Completed	28
Not completed	2
Adverse event, serious fatal	1
Diagnosed with encephalomyelitis	1

## Baseline characteristics

### Reporting groups

Reporting group title	Overall trial
Reporting group description: -	

Reporting group values	Overall trial	Total	
Number of subjects	30	30	
Age categorical			
Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	18	18	
From 65-84 years	12	12	
85 years and over	0	0	
Age continuous			
Units: years			
arithmetic mean	55.6		
standard deviation	± 18.5	-	
Gender categorical			
Units: Subjects			
Female	14	14	
Male	16	16	

### Subject analysis sets

Subject analysis set title	FAS
Subject analysis set type	Full analysis

Subject analysis set description:

All dosed patients having a confirmed GBS diagnosis, i.e., patients re-evaluated and having change in diagnosis (incorrectly diagnosed with GBS at trial entry) were excluded.

Used for presentation of efficacy endpoints.

Subject analysis set title	PK/PD
Subject analysis set type	Sub-group analysis

Subject analysis set description:

All dosed patients, with at least one PK or PD data point available post-baseline.

Used for presentation of PK and PD endpoints.

Subject analysis set title	Safety analysis set
Subject analysis set type	Safety analysis

Subject analysis set description:

All dosed patients.

Used for presentation of safety endpoints

Reporting group values	FAS	PK/PD	Safety analysis set
Number of subjects	27	30	30
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	18	18
From 65-84 years	10	12	12
85 years and over	0	0	0
Age continuous			
Units: years			
arithmetic mean	54.8	55.6	55.6
standard deviation	± 19.3	± 18.5	± 18.5
Gender categorical			
Units: Subjects			
Female	13	14	14
Male	14	16	16

## End points

### End points reporting groups

Reporting group title	All patients intended to be treated
Reporting group description: -	
Subject analysis set title	FAS
Subject analysis set type	Full analysis
Subject analysis set description:	
All dosed patients having a confirmed GBS diagnosis, i.e., patients re-evaluated and having change in diagnosis (incorrectly diagnosed with GBS at trial entry) were excluded.	
Used for presentation of efficacy endpoints.	
Subject analysis set title	PK/PD
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
All dosed patients, with at least one PK or PD data point available post-baseline.	
Used for presentation of PK and PD endpoints.	
Subject analysis set title	Safety analysis set
Subject analysis set type	Safety analysis
Subject analysis set description:	
All dosed patients.	
Used for presentation of safety endpoints	

### Primary: GBS disability score - Able to walk independently

End point title	GBS disability score - Able to walk independently <sup>[1]</sup>
End point description:	
End point type	Primary
End point timeframe:	
From Baseline to Day 360	

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: Not applicable, this was a single arm study.

End point values	FAS			
Subject group type	Subject analysis set			
Number of subjects analysed				
Units: Patients				
Baseline	0			
Day 2	4			
Day 3	5			
Day 4	9			
Day 5	9			
Day 6	9			
Day 7	10			
Day 8	10			
Day 15	13			
Day 29	14			
Day 57	18			
Day 92	20			
Day 180	23			
Day 360	24			

## Statistical analyses

No statistical analyses for this end point

### Primary: GBS disability score - Able to run

End point title	GBS disability score - Able to run <sup>[2]</sup>
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End point description:

End point type	Primary
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End point timeframe:

From Baseline to Day 360

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: Not applicable, this was a single arm study.

End point values	FAS			
Subject group type	Subject analysis set			
Number of subjects analysed	27			
Units: Patients				
Baseline	0			
Day 2	0			
Day 3	0			
Day 4	0			
Day 5	1			
Day 6	1			
Day 7	2			
Day 8	4			
Day 15	5			
Day 29	9			
Day 57	11			
Day 92	15			
Day 180	17			
Day 360	18			

## Statistical analyses

No statistical analyses for this end point

### Primary: GBS DS - Time to improve by at least 1 grade

End point title	GBS DS - Time to improve by at least 1 grade <sup>[3]</sup>
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**End point description:**

The GBS disability score is a scoring system used to assess the status of the patients with GBS. The score consists of the following grades: 0=Healthy, 1= Minor symptoms and capable of running, 2=Able to walk independently 10 meters of more but unable to run, 3=Able to walk more than 10 meters across an open space with help, 4=Beridden or chair bound, 5=Needing mechanical ventilation, 6=Dead

End point type	Primary
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**End point timeframe:**

From Baseline to Day 360

**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: Not applicable, this was a single arm study.

End point values	FAS			
Subject group type	Subject analysis set			
Number of subjects analysed	27			
Units: Days				
median (full range (min-max))				
Time to improve by at least 1 grade	6.0 (3.0 to 16.0)			

**Statistical analyses**

No statistical analyses for this end point

**Primary: MRC sum score over time**

End point title	MRC sum score over time <sup>[4]</sup>
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**End point description:**

The Medical Research Council (MRC) scale is a commonly used tool for assessing muscle strength. The resulting MRC sum score ranges from 60 (normal) to 0 (quadriplegic).

End point type	Primary
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**End point timeframe:**

From Baseline to Day 180

**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: Not applicable, this was a single arm study.

End point values	FAS			
Subject group type	Subject analysis set			
Number of subjects analysed				
Units: Score				
arithmetic mean (standard deviation)				
Baseline	39.1 (± 13.9)			
Day 2	42.0 (± 14.7)			
Day 4	47.5 (± 14.6)			
Day 6	49.7 (± 13.7)			
Day 8	50.0 (± 13.8)			
Day 15	51.8 (± 12.1)			
Day 29	49.1 (± 17.4)			

Day 57	49.0 (± 18.4)			
Day 92	51.8 (± 16.2)			
Day 180	54.1 (± 12.4)			

## Statistical analyses

No statistical analyses for this end point

### Primary: Change in MRC sum sore over time

End point title	Change in MRC sum sore over time <sup>[5]</sup>
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End point description:

The Medical Research Council (MRC) scale is a commonly used tool for assessing muscle strength. The resulting MRC sum score ranges from 60 (normal) to 0 (quadriplegic).

End point type	Primary
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End point timeframe:

Change from Baseline to Different visits up to Day 180

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: Not applicable, this was a single arm study.

End point values	FAS			
Subject group type	Subject analysis set			
Number of subjects analysed	27 <sup>[6]</sup>			
Units: Score				
arithmetic mean (standard deviation)				
Day 2	2.9 (± 8.2)			
Day 4	8.4 (± 9.2)			
Day 6	10.3 (± 9.8)			
Day 8	10.7 (± 10.2)			
Day 15	11.2 (± 10.4)			
Day 29	10.0 (± 13.0)			
Day 57	9.9 (± 14.6)			
Day 92	12.7 (± 13.0)			
Day 180	15.0 (± 10.6)			

Notes:

[6] - 26 patients analysed at Day 6 and Day 8

25 patients analysed at Day 15

## Statistical analyses

No statistical analyses for this end point

### Primary: R-ODS over time

End point title	R-ODS over time <sup>[7]</sup>
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End point description:

The patients have rated their ability to perform different common activities using the Rasch-built overall disability score (R-ODS) questionnaire.

The resulting R-ODS ranges from 0 (most severe disability) to 100 (no disability at all).

End point type	Primary
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End point timeframe:

Baseline to Day 360

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: Not applicable, this was a single arm study.

End point values	FAS			
Subject group type	Subject analysis set			
Number of subjects analysed	27 <sup>[8]</sup>			
Units: R-ODS				
arithmetic mean (standard deviation)				
Baseline	23.7 (± 15.3)			
Day 8	41.9 (± 28.0)			
Day 15	46.2 (± 26.9)			
Day 29	52.6 (± 33.1)			
Day 57	57.2 (± 34.5)			
Day 92	63.5 (± 32.5)			
Day 180	70.0 (± 29.2)			
Day 360	73.8 (± 24.4)			

Notes:

[8] - 26 patients analysed at Day 8, Day 57, Day 92, and Day 360

24 patients analysed at Day 15

## Statistical analyses

No statistical analyses for this end point

## Primary: Change in R-ODS over time

End point title	Change in R-ODS over time <sup>[9]</sup>
End point description:	
The patients have rated their ability to perform different common activities using the Rasch-built overall disability score (R-ODS) questionnaire.	
The resulting R-ODS ranges from 0 (most severe disability) to 100 (no disability at all). This endpoint presents the change from baseline. A positive value indicates improvement.	
End point type	Primary
End point timeframe:	
From Baseline to Day 360	

Notes:

[9] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Not applicable, this was a single arm study.

End point values	FAS			
Subject group type	Subject analysis set			
Number of subjects analysed	27 <sup>[10]</sup>			
Units: R-ODS				
arithmetic mean (standard deviation)				
Day 8	17.2 (± 22.3)			
Day 15	20.8 (± 21.4)			
Day 29	28.8 (± 25.3)			
Day 57	34.5 (± 26.5)			
Day 92	40.8 (± 24.6)			

Day 180	46.3 ( $\pm$ 22.7)			
Day 360	50.5 ( $\pm$ 19.3)			

Notes:

[10] - 26 patients analysed at Day 8, Day 57, Day 92, and Day 360

24 patients analysed at Day 15

## Statistical analyses

No statistical analyses for this end point

### Primary: Days in Hospital

End point title	Days in Hospital <sup>[11]</sup>
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End point description:

End point type	Primary
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End point timeframe:

Baseline to Day 360

Notes:

[11] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Not applicable, this was a single arm study.

End point values	Safety analysis set			
Subject group type	Subject analysis set			
Number of subjects analysed	30			
Units: Days				
arithmetic mean (standard deviation)	32.5 ( $\pm$ 43.5)			

## Statistical analyses

No statistical analyses for this end point

### Primary: Time in an ICU

End point title	Time in an ICU <sup>[12]</sup>
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End point description:

End point type	Primary
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End point timeframe:

From Screening to Day 180

Notes:

[12] - 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: Not applicable, this was a single arm study.

End point values	Safety analysis set			
Subject group type	Subject analysis set			
Number of subjects analysed	30			
Units: Patients				
Admitted 0 days	18			
Admitted 2-11 days	9			
Admitted 106-113 days	2			
Admitted 172 days	1			

## Statistical analyses

No statistical analyses for this end point

## Primary: Need for mechanical ventilation

End point title	Need for mechanical ventilation <sup>[13]</sup>
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End point description:

End point type	Primary
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End point timeframe:

Screening to Day 180

Notes:

[13] - 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: Not applicable, this was a single arm study.

End point values	Safety analysis set			
Subject group type	Subject analysis set			
Number of subjects analysed	30			
Units: Patients				
Screening	0			
Day 1 to Day 90	1			
Day 5 to Day 102	1			
Day 9 to Day 90 and Day 103 to Day 180	1			

## Statistical analyses

No statistical analyses for this end point

## Primary: Quality of Life over time

End point title	Quality of Life over time <sup>[14]</sup>
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End point description:

The EQ-5D-5L questionnaire was completed by the patients. It consists of descriptive statements pertaining to 5 individual dimensions (mobility, self care, usual activities, pain/discomfort and anxiety/depression). The patient was asked to indicate his/her health state by ticking the box next to the most appropriate statement in each of the five dimensions. The EQ VAS records the patient's self-rated health on a vertical visual analogue scale where the endpoints are labelled 'The best health you

can image' and 'The worst health you can image'.

End point type	Primary
End point timeframe:	
From Day 8 to Day 360	
Notes:	
[14] - 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: Not applicable, this was a single arm study.	

End point values	FAS			
Subject group type	Subject analysis set			
Number of subjects analysed	30 <sup>[15]</sup>			
Units: EQ-5D-5L VAS score				
arithmetic mean (standard deviation)				
Day 8	49.7 (± 23.7)			
Day 15	61.3 (± 24.8)			
Day 29	67.3 (± 21.0)			
Day 57	68.8 (± 25.1)			
Day 92	75.2 (± 23.9)			
Day 180	78.6 (± 20.6)			
Day 360	79.4 (± 18.6)			

Notes:

[15] - 27 replied at D92 and D180

26 replied at D8 and D360

25 replied at D29 and D57

24 replied at D15

## Statistical analyses

No statistical analyses for this end point

## Primary: GBS DS - Time to improve by at least 2 grades

End point title	GBS DS - Time to improve by at least 2 grades <sup>[16]</sup>
End point description:	
The GBS disability score is a scoring system used to assess the status of the patients with GBS. The score consists of the following grades: 0=Healthy, 1= Minor symptoms and capable of running, 2=Able to walk independently 10 meters or more but unable to run, 3=Able to walk more than 10 meters across an open space with help, 4=Bedridden or chair bound, 5=Needing mechanical ventilation, 6=Dead	
End point type	Primary
End point timeframe:	
Baseline to Day 360	
Notes:	
[16] - 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: Not applicable, this was a single arm study.	

End point values	FAS			
Subject group type	Subject analysis set			
Number of subjects analysed	27			
Units: Days				
median (full range (min-max))				
Time to improve by at least 2 grades	16.0 (8.0 to 92.0)			

## Statistical analyses

No statistical analyses for this end point

## Secondary: Pharmacokinetics (PK) - C<sub>max</sub>, AUC, t<sub>1/2</sub> (alfa), t<sub>1/2</sub> (beta), CL, V<sub>ss</sub>, and V<sub>z</sub>

End point title	Pharmacokinetics (PK) - C <sub>max</sub> , AUC, t <sub>1/2</sub> (alfa), t <sub>1/2</sub> (beta), CL, V <sub>ss</sub> , and V <sub>z</sub>
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End point description:

C<sub>max</sub>=Maximum observed plasma concentration of imlifidase following dosing

AUC=Area under the plasma concentration of imlifidase versus time curve

t<sub>1/2</sub>α=Half-life initial phase

t<sub>1/2</sub>β=Half-life terminal phase

CL=Clearance is a measure of the ability of the body to clear imlifidase from plasma

V<sub>z</sub>=Volume of distribution of imlifidase during the elimination phase

V<sub>ss</sub>=Volume of distribution at steady state

End point type	Secondary
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End point timeframe:

From dosing until Day 15

End point values	PK/PD			
Subject group type	Subject analysis set			
Number of subjects analysed	16 <sup>[17]</sup>			
Units: See below:				
geometric mean (geometric coefficient of variation)				
C <sub>max</sub> (µg/mL)	5.5 (± 17.0)			
AUC (h×µg/mL)	45.0 (± 54.9)			
t <sub>1/2</sub> (h) initial phase (α)	1.73 (± 0)			
t <sub>1/2</sub> (h) terminal phase (β)	30.6 (± 0)			
CL (mL/h/kg)	5.6 (± 54.9)			
V <sub>z</sub> (L/kg)	0.3 (± 40.7)			
V <sub>ss</sub> (L/kg)	0.2 (± 41.1)			

Notes:

[17] - C<sub>max</sub> for all 16. All other for 9 who could be fitted to 2-compart model. Harmonic mean for t<sub>1/2</sub>s.

## Statistical analyses

No statistical analyses for this end point

## Secondary: Pharmacodynamics - IgG level in serum over time

End point title	Pharmacodynamics - IgG level in serum over time
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End point description:

The pharmacodynamic (PD) effect of imlifidase is assessed as the elimination of IgG. IgG is cleaved by

imlifidase in two steps, the first cut generates single-cleaved IgG (scIgG), and the second cut generates one F(ab')<sub>2</sub> fragment and one Fc fragment. The IgG concentration measured in serum using the MSD technology is the sum of intact IgG and scIgG and a decrease in the measured IgG concentration therefore represents complete cleavage of the IgG molecule to Fc and F(ab')<sub>2</sub> fragments. For the first 16 patients included in the trial a more frequent PD sampling schedule was conducted. After amending the protocol a less frequent PD sampling schedule was applied.

End point type	Secondary
End point timeframe:	
Day 1 (before dose) until Day 15	

End point values	PK/PD			
Subject group type	Subject analysis set			
Number of subjects analysed	30 <sup>[18]</sup>			
Units: mg/mL				
arithmetic mean (standard deviation)				
Day 1, pre-dose	10.8 (± 4.5)			
Day 2, 24 hours after dose	1.3 (± 3.5)			
Day 3, before IVIg administration	1.6 (± 3.5)			
Day 4, before IVIg administration	8.6 (± 2.3)			
Day 5, before IVIg administration	14.3 (± 1.9)			
Day 6, before IVIg administration	18.1 (± 4.0)			
Day 7, before IVIg administration	20.8 (± 5.5)			
Day 8	28.6 (± 9.2)			
Day 15	22.5 (± 10.0)			

Notes:

[18] - 16 patients analysed at Day 4, Day 5, Day 6, and Day 7 as described above.

## Statistical analyses

No statistical analyses for this end point

## Secondary: Immunogenicity - Anti-implifidase antibodies (ADA) over time

End point title	Immunogenicity - Anti-implifidase antibodies (ADA) over time
End point description:	
Anti-implifidase IgG antibodies (ADA) in serum.	
End point type	Secondary
End point timeframe:	
Predose until Day 180	

End point values	Safety analysis set			
Subject group type	Subject analysis set			
Number of subjects analysed	30 <sup>[19]</sup>			
Units: mg/mL				
arithmetic mean (standard deviation)				
Day 1, pre-dose	11.1 (± 17.1)			
Day 2, 24 h after dose	4.0 (± 9.6)			



Day 3, pre-IVIg	4.5 ( $\pm$ 12.2)			
Day 8	474.5 ( $\pm$ 909.0)			
Day 15	2811.9 ( $\pm$ 3772.6)			
Day 29	2120.1 ( $\pm$ 2813.7)			
Day 57	1060.3 ( $\pm$ 1086.5)			
Day 92	722.1 ( $\pm$ 806.8)			
Day 180	336.0 ( $\pm$ 318.9)			

Notes:

[19] - 28 patients have been analysed at Day 29, Day 57, Day 92, and Day 180

### Statistical analyses

No statistical analyses for this end point

### Secondary: Pharmacokinetics (PK) - Tmax

End point title	Pharmacokinetics (PK) - Tmax
End point description:	
Tmax = Time point for maximum observed plasma concentration of imlifidase following dosing	
End point type	Secondary
End point timeframe:	
From dosing until Day 15	

End point values	PK/PD			
Subject group type	Subject analysis set			
Number of subjects analysed	16			
Units: hours				
median (full range (min-max))				
Tmax (h)	0.74 (0.47 to 2.07)			

### Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Adverse events (AEs) were collected for 1 year (i.e., from the timepoint the patient signed the informed consent form (ICF) until Day 360.

Adverse event reporting additional description:

AEs were either spontaneously reported, reported in response to an open question, or revealed by observation.

A TEAE is any AE occurring after imlifidase and within 29 days. The listed non-serious AEs presents TEAEs only.

18 SAEs have been reported, 9 of which were TEAEs. All SAEs are listed.

Assessment type	Systematic
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### Dictionary used

Dictionary name	MedDRA
Dictionary version	21.1

### Reporting groups

Reporting group title	Safety Analysis Set
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Reporting group description:

All 30 patients who have received imlifidase in the trial.

25 out of 30 patients were affected by non-serious treatment emergent adverse events (TEAEs).

28 out of 30 patients were affected by non-serious AEs, including pre-treatment and post-treatment emergent events.

5 out of 30 patients were affected by treatment emergent SAEs.

7 out of 30 patients were affected by SAEs including pre-treatment and post-treatment emergent events.

Serious adverse events	Safety Analysis Set		
Total subjects affected by serious adverse events			
subjects affected / exposed	7 / 30 (23.33%)		
number of deaths (all causes)	1		
number of deaths resulting from adverse events	1		
Investigations			
False positive investigation result	Additional description: Covid false positive		
subjects affected / exposed	1 / 30 (3.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Neuropathy peripheral			
subjects affected / exposed	3 / 30 (10.00%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
Central nervous system inflammation			

subjects affected / exposed	1 / 30 (3.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Demyelination			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Gastrointestinal disorders			
Gastroduodenal ulcer			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Oesophagitis			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Respiratory failure			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pulmonary embolism			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Bronchospasm			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Adjustment disorder with depressed mood			

subjects affected / exposed	1 / 30 (3.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Escherichia bacteraemia			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumonia			
subjects affected / exposed	2 / 30 (6.67%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Influenza			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 3.3 %

<b>Non-serious adverse events</b>	Safety Analysis Set		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	25 / 30 (83.33%)		
Vascular disorders			
Hypertension			
subjects affected / exposed	6 / 30 (20.00%)		
occurrences (all)	6		
Deep vein thrombosis			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Hypotension			

subjects affected / exposed occurrences (all)	1 / 30 (3.33%) 1		
General disorders and administration site conditions Pyrexia subjects affected / exposed occurrences (all)  Chills subjects affected / exposed occurrences (all)  Pain subjects affected / exposed occurrences (all)  Vessel puncture site phlebitis subjects affected / exposed occurrences (all)	3 / 30 (10.00%) 3  1 / 30 (3.33%) 1  1 / 30 (3.33%) 1  1 / 30 (3.33%) 1		
Immune system disorders Drug hypersensitivity subjects affected / exposed occurrences (all)	1 / 30 (3.33%) 1		
Reproductive system and breast disorders Vulvovaginal pruritus subjects affected / exposed occurrences (all)	1 / 30 (3.33%) 1		
Respiratory, thoracic and mediastinal disorders Respiratory failure subjects affected / exposed occurrences (all)  Dyspnoea subjects affected / exposed occurrences (all)  Pneumonia aspiration subjects affected / exposed occurrences (all)  Pulmonary mass	1 / 30 (3.33%) 1  1 / 30 (3.33%) 1  1 / 30 (3.33%) 1  1 / 30 (3.33%) 1		

subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Rales			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Stridor			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Psychiatric disorders			
Anxiety			
subjects affected / exposed	6 / 30 (20.00%)		
occurrences (all)	6		
Insomnia			
subjects affected / exposed	2 / 30 (6.67%)		
occurrences (all)	2		
Delirium			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Hallucination			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Hallucination, visual			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	3 / 30 (10.00%)		
occurrences (all)	3		
C-reactive protein increased			
subjects affected / exposed	2 / 30 (6.67%)		
occurrences (all)	2		
Liver function test abnormal			
subjects affected / exposed	2 / 30 (6.67%)		
occurrences (all)	2		
White blood cell count increased			

subjects affected / exposed	2 / 30 (6.67%)		
occurrences (all)	3		
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Body temperature increased			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Gamma-glutamyltransferase increased			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Glomerular filtration rate decreased			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Haematocrit decreased			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Haemoglobin decreased			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Staphylococcus test positive			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Troponin I increased			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Weight decreased			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Infusion related reaction			

subjects affected / exposed occurrences (all)	1 / 30 (3.33%) 1		
Cardiac disorders			
Sinus tachycardia			
subjects affected / exposed	2 / 30 (6.67%)		
occurrences (all)	2		
Tachycardia			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Nervous system disorders			
Neuropathy peripheral			
subjects affected / exposed	3 / 30 (10.00%)		
occurrences (all)	3		
Facial paralysis			
subjects affected / exposed	2 / 30 (6.67%)		
occurrences (all)	2		
Headache			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Presyncope			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Vocal cord paresis			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Blood and lymphatic system disorders			
Lymphopenia			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Normocytic anaemia			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Eye disorders			
Vision blurred			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Vitreous floaters			



subjects affected / exposed occurrences (all)	1 / 30 (3.33%) 1		
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	9 / 30 (30.00%)		
occurrences (all)	9		
Abdominal pain upper			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Cheilitis			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Gastrointestinal motility disorder			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Intestinal pseudo-obstruction			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Hepatobiliary disorders			
Hepatocellular injury			
subjects affected / exposed	3 / 30 (10.00%)		
occurrences (all)	3		
Cholestasis			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Skin and subcutaneous tissue disorders			
Night sweats			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Prerenal failure			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Urinary retention			

subjects affected / exposed occurrences (all)	1 / 30 (3.33%) 1		
Endocrine disorders Autoimmune thyroiditis subjects affected / exposed occurrences (all)  Hypothyroidism subjects affected / exposed occurrences (all)  Inappropriate antidiuretic hormone secretion subjects affected / exposed occurrences (all)	1 / 30 (3.33%) 1   1 / 30 (3.33%) 1  1 / 30 (3.33%) 1		
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all)  Pain in extremity subjects affected / exposed occurrences (all)  Spinal pain subjects affected / exposed occurrences (all)	1 / 30 (3.33%) 1  1 / 30 (3.33%) 1  1 / 30 (3.33%) 1		
Infections and infestations Pneumonia subjects affected / exposed occurrences (all)  Urinary tract infection bacterial subjects affected / exposed occurrences (all)  Corona virus infection subjects affected / exposed occurrences (all)  Cytomegalovirus infection subjects affected / exposed occurrences (all)  Epstein-Barr virus infection	3 / 30 (10.00%) 3  2 / 30 (6.67%) 2  1 / 30 (3.33%) 1  1 / 30 (3.33%) 1		

subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Erysipelas			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Escherichia urinary tract infection			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Oral candidiasis			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Oral herpes			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Pneumonia pseudomonal			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Sepsis			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Urinary tract infection			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Urinary tract infection enterococcal			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Metabolism and nutrition disorders			
Hyponatraemia			
subjects affected / exposed	5 / 30 (16.67%)		
occurrences (all)	5		
Hypokalaemia			
subjects affected / exposed	2 / 30 (6.67%)		
occurrences (all)	2		
Folate deficiency			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		

Gout			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Hyperglycaemia			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Hypophosphataemia			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Vitamin B1 deficiency			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
14 November 2019	<ul style="list-style-type: none"><li>- Updates to the SRC composition</li><li>- Modification of 2 eligibility criteria</li><li>- More detailed guidance about IVIg treatment</li></ul>
09 October 2020	Patients with a positive PCR test for SARS-CoV-2 (Covid-19) should be excluded from the trial before restarting the trial. In addition, patients with an ongoing infection were to be excluded from the trial regardless if the infection required treatment or not.
11 June 2021	<ul style="list-style-type: none"><li>- Minor modifications to the screening procedures were introduced (SARS-CoV-2 PCR test results if done at hospital admission could be used), thus minimising the risk of unnecessary delay of GBS treatment.</li></ul>
31 January 2022	<ul style="list-style-type: none"><li>- PK sampling and ECG data collection were removed from the protocol as available data were deemed sufficient.</li><li>- A less frequent sampling schedule was introduced</li><li>- Addition of safety sections describing overdose and adverse events of special interest (AESIs).</li><li>- Change in CRO responsible for SAE/suspected unexpected serious adverse reaction (SUSAR) reporting.</li><li>- Prohibited therapies updated and clarified.</li></ul>
27 June 2023	<ul style="list-style-type: none"><li>- To avoid delay in the reporting of the results of the single arm trial, the planned comparison to an externally matched cohort of GBS subjects will be outlined in a separate study protocol</li><li>- To ensure comparison of relevant endpoints in the non-interventional study (matched cohort of GBS subjects) some endpoints were updated or added to the trial protocol. The objective, endpoints, and statistical sections were updated to reflect these changes.</li><li>- To ensure the trial results can be properly evaluated and clinically interpreted, additional baseline and disease characteristic data were added to the protocol. These data were to be collected from the patient's medical records.</li></ul>

Notes:

### Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
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01 March 2020	<p>This trial started in November 2019 and was completed in February 2024, which included the period during which the Covid-19 pandemic was ongoing in the countries with participating trial sites. In March 2020 the SRC recommended Hansa Biopharma to temporarily halt the enrolment of new patients into the trial due to the pandemic. The already included patients in the trial at the timepoint for halt of enrolment continued in the trial according to protocol.</p> <p>In September 2020, an ad-hoc SRC meeting was held to discuss restart of enrolment into the trial. The SRC members agreed that recruitment of patients in the trial could restart on a site-by-site basis after discussion with and confirmation by each principal investigator after amending the protocol to exclude patients with a positive PCR test for SARS-CoV-2 (Covid-19).</p>	30 September 2020
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Notes:

## Limitations and caveats

None reported