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

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:

-

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:

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)	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

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.

Number of subjects in period 1	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[1]
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[2]

End point description:

End point type	Primary

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[3]

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

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[4]

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

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[5]

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

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[6]			
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[7]

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

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[8]			
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[9]

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[10]			
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 (± 22.7)			
Day 360	50.5 (± 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[11]

End point description:

End point type	Primary

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 (± 43.5)			

Statistical analyses

No statistical analyses for this end point

Primary: Time in an ICU

End point title	Time in an ICU[12]

End point description:

End point type	Primary

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[13]

End point description:

End point type	Primary

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[14]

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[15]			
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[16]

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

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) - Cmax, AUC, t1/2 (alfa), t1/2 (beta), CL, Vss, and Vz

End point title	Pharmacokinetics (PK) - Cmax, AUC, t1/2 (alfa), t1/2 (beta), CL, Vss, and Vz

End point description:

Cmax=Maximum observed plasma concentration of imlifidase following dosing
AUC=Area under the plasma concentration of imlifidase versus time curve
t½α=Half-life initial phase
t½β=Half-life terminal phase
CL=Clearance is a measure of the ability of the body to clear imlifidase from plasma
Vz=Volume of distribution of imlifidase during the elimination phase
Vss=Volume of distribution at steady state

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[17]			
Units: See below:				
geometric mean (geometric coefficient of variation)				
Cmax (µg/mL)	5.5 (± 17.0)			
AUC (h×µg/mL)	45.0 (± 54.9)			
t½ (h) initial phase (α)	1.73 (± 0)			
t½ (h) terminal phase (β)	30.6 (± 0)			
CL (mL/h/kg)	5.6 (± 54.9)			
Vz (L/kg)	0.3 (± 40.7)			
Vss (L/kg)	0.2 (± 41.1)			

Notes:

[17] - Cmax for all 16. All other for 9 who could be fitted to 2-compart model. Harmonic mean for t1/2s.

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

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')2 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')2 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[18]			
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-imlifidase antibodies (ADA) over time

End point title	Immunogenicity - Anti-imlifidase antibodies (ADA) over time

End point description:

Anti-imlifidase 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[19]			
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 (± 12.2)			
Day 8	474.5 (± 909.0)			
Day 15	2811.9 (± 3772.6)			
Day 29	2120.1 (± 2813.7)			
Day 57	1060.3 (± 1086.5)			
Day 92	722.1 (± 806.8)			
Day 180	336.0 (± 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

Dictionary used

Dictionary name	MedDRA
Dictionary version	21.1

Reporting groups

Reporting group title	Safety Analysis Set

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 %

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

subjects affected / exposed occurrences (all)	1 / 30 (3.33%) 1		
Rales subjects affected / exposed occurrences (all)	1 / 30 (3.33%) 1		
Stridor subjects affected / exposed occurrences (all)	1 / 30 (3.33%) 1		
Psychiatric disorders Anxiety subjects affected / exposed occurrences (all)	6 / 30 (20.00%) 6		
Insomnia subjects affected / exposed occurrences (all)	2 / 30 (6.67%) 2		
Delirium subjects affected / exposed occurrences (all)	1 / 30 (3.33%) 1		
Hallucination subjects affected / exposed occurrences (all)	1 / 30 (3.33%) 1		
Hallucination, visual subjects affected / exposed occurrences (all)	1 / 30 (3.33%) 1		
Investigations Alanine aminotransferase increased subjects affected / exposed occurrences (all)	3 / 30 (10.00%) 3		
C-reactive protein increased subjects affected / exposed occurrences (all)	2 / 30 (6.67%) 2		
Liver function test abnormal subjects affected / exposed occurrences (all)	2 / 30 (6.67%) 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 occurrences (all) Tachycardia subjects affected / exposed occurrences (all)	 2 / 30 (6.67%) 2 1 / 30 (3.33%) 1		
Nervous system disorders Neuropathy peripheral subjects affected / exposed occurrences (all) Facial paralysis subjects affected / exposed occurrences (all) Headache subjects affected / exposed occurrences (all) Presyncope subjects affected / exposed occurrences (all) Vocal cord paresis subjects affected / exposed occurrences (all)	 3 / 30 (10.00%) 3 2 / 30 (6.67%) 2 1 / 30 (3.33%) 1 1 / 30 (3.33%) 1 1 / 30 (3.33%) 1		
Blood and lymphatic system disorders Lymphopenia subjects affected / exposed occurrences (all) Normocytic anaemia subjects affected / exposed occurrences (all)	 1 / 30 (3.33%) 1 1 / 30 (3.33%) 1		
Eye disorders Vision blurred subjects affected / exposed occurrences (all) Vitreous floaters	 1 / 30 (3.33%) 1 		

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

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	- Updates to the SRC composition - Modification of 2 eligibility criteria - More detailed guidance about IVIg treatment
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	- 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.
31 January 2022	- PK sampling and ECG data collection were removed from the protocol as available data were deemed sufficient. - A less frequent sampling schedule was introduced - Addition of safety sections describing overdose and adverse events of special interest (AESIs). - Change in CRO responsible for SAE/suspected unexpected serious adverse reaction (SUSAR) reporting. - Prohibited therapies updated and clarified.
27 June 2023	- 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 - 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. - 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.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date

01 March 2020	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. 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).	30 September 2020

Notes:

Limitations and caveats

None reported