



Clinical trial results:

PEACE (Pegzilarginase Effect on Arginase 1 Deficiency Clinical Endpoints): A Randomized, Double-Blind, Placebo-Controlled Phase 3 Study of the Efficacy and Safety of Pegzilarginase in Children and Adults with Arginase 1 Deficiency

Summary

EudraCT number	2018-004837-34
Trial protocol	AT DE FR GB IT
Global end of trial date	01 February 2023

Results information

Result version number	v1 (current)
This version publication date	06 November 2025
First version publication date	06 November 2025

Trial information

Trial identification

Sponsor protocol code	CAEB1102-300A
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03921541
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Aeglea BioTherapeutics, Inc.
Sponsor organisation address	221 Crescent Street, Waltham, Massachusetts, United States, 02453
Public contact	Global Integrated Evidence Generation, Immedica Pharma AB, +46 8 533 39 50, clinical@immedica.com
Scientific contact	Global Integrated Evidence Generation, Immedica Pharma AB, +46 8 533 39 50, clinical@immedica.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	15 March 2024
Is this the analysis of the primary completion data?	Yes
Primary completion date	01 February 2023
Global end of trial reached?	Yes
Global end of trial date	01 February 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To demonstrate the efficacy of pegzilarginase relative to placebo based on a statistically significant decrease in plasma arginine concentrations

Protection of trial subjects:

This trial was performed in accordance with the ethical principles that have their origin in the Declaration of Helsinki and that are consistent with the United States Food and Drug Administration regulations, the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use E6 guidelines for Good Clinical Practice, and the applicable regulatory requirements.

Furthermore, the trial adhered to the European Union Clinical Trials Directive 2001/20/EC, as well as all relevant local and national laws and regulations governing the conduct of human clinical trials were followed. I was also performed in accordance with the United Kingdom Medicines for Human Use (Clinical Trials) Regulations 2004 and Canada Drug-Part C, Division 5 of the Food and Drugs Act and Regulation. The trial was conducted by investigators experienced in the treatment of patients (children and adults) with arginase 1 deficiency (ARG1-D).

A Safety Review Committee (SRC) periodically provided independent review of the safety data during the trial.

Background therapy:

The previously prescribed individualized disease management (IDM) was continued throughout the trial.

Evidence for comparator:

A placebo-controlled study design was employed to demonstrate the efficacy of pegzilarginase in subjects with ARG1-D in the double-blind (DB) period. It is well recognized that improvements in disease parameters can occur in subjects not receiving active treatment due to changes in behavior and other factors resulting from participation in a clinical trial.

Actual start date of recruitment	01 May 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	United Kingdom: 5
Country: Number of subjects enrolled	Austria: 2
Country: Number of subjects enrolled	France: 6
Country: Number of subjects enrolled	Germany: 1
Country: Number of subjects enrolled	Italy: 3
Country: Number of subjects enrolled	United States: 14
Country: Number of subjects enrolled	Canada: 1
Worldwide total number of subjects	32
EEA total number of subjects	12

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)	18
Adolescents (12-17 years)	11
Adults (18-64 years)	3
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

44 subjects were screened. 12 subjects were screening failures. 32 subjects were randomized, 21 to receive pegzilarginase and 11 to receive placebo.

Pre-assignment

Screening details:

Patients who met all inclusion criteria and none of the exclusion criteria were eligible to participate in the trial.

Period 1

Period 1 title	Placebo-controlled 24-week DB period
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer, Assessor

Blinding implementation details:

Laboratory results of parameters who had the potential to unblind the investigator to subjects' treatment groups were not provided to the investigator or other blinded individuals, including subjects, families, sponsor personnel, or assessors, until all subjects had completed the 24-week DB period and formal unblinding had occurred. Dose modifications were implemented by an unblinded pharmacist and/or physician.

Arms

Are arms mutually exclusive?	Yes
Arm title	Pegzilarginase

Arm description:

Pegzilarginase, administered once weekly for 24 weeks.

Arm type	Experimental
Investigational medicinal product name	Pegzilarginase
Investigational medicinal product code	
Other name	AEB1102, Co-ARG1-PEG
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

The initial dose was 0.10 mg/kg. Dose adjustments were permitted based on the subject's pharmacodynamic response. The weekly dose was administered intravenously over approximately 30 minutes at the same time of day.

Arm title	Placebo
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Arm description:

Placebo, administered once weekly for 24 weeks.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

The weekly dose was administered intravenously over approximately 30 minutes at the same time of day. The volume corresponded to the pegzilarginase infusion.

Number of subjects in period 1	Pegzilarginase	Placebo
Started	21	11
Completed	20	11
Not completed	1	0
personal reasons	1	-

Period 2

Period 2 title	Long-term extension (LTE)
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Blinding implementation details:

In the first 8 weeks of the LTE period, the treatment was blinded to subject and investigator. Subjects had the option to receive open-label pegzilarginase by subcutaneous (SC) administration after that.

Arms

Arm title	Pegzilarginase
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Arm description:

Pegzilarginase, administered once weekly for up to 150 weeks.

Arm type	Experimental
Investigational medicinal product name	Pegzilarginase
Investigational medicinal product code	
Other name	AEB1102, Co-ARG1-PEG
Pharmaceutical forms	Infusion, Injection
Routes of administration	Intravenous use, Subcutaneous use

Dosage and administration details:

All subjects received pegzilarginase plus IDM during the LTE period.

During blinded 8 weeks: Subjects initially randomized to pegzilarginase received the optimized dose they received during the 24-week DB period. Subjects initially randomized to placebo during the 24-week DB period started with 0.10 mg/kg pegzilarginase, which was adjusted during the LTE period based on arginine levels. The weekly dose was administered intravenously over approximately 30 minutes at the same time of day.

During open-label LTE period after blinded 8 weeks: Subjects received weekly a SC injection of pegzilarginase. The initial mg/kg SC dose was the same as the IV dose unless dictated by the arginine level. The first 4 SC doses were given at the investigational site. Subsequent SC doses were administered outside of the investigational site by appropriately trained home health care professionals.

Number of subjects in period 2	Pegzilarginase
Started	31
Completed	31

Baseline characteristics

Reporting groups

Reporting group title	Pegzilarginase
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Reporting group description:

Pegzilarginase, administered once weekly for 24 weeks.

Reporting group title	Placebo
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Reporting group description:

Placebo, administered once weekly for 24 weeks.

Reporting group values	Pegzilarginase	Placebo	Total
Number of subjects	21	11	32
Age categorical			
Units: Subjects			
Children (2 to <6 years)	5	1	6
Children (6 to <12 years)	8	4	12
Children (12 to <18 years)	7	4	11
Adults (≥18 years)	1	2	3
Age continuous			
Units: years			
median	8	12	-
full range (min-max)	2 to 28	5 to 29	-
Gender categorical			
Units: Subjects			
Female	9	4	13
Male	12	7	19
Gross motor function classification system level			
Units: Subjects			
Level I	9	5	14
Level II	9	4	13
Level III	0	0	0
Level IV	3	2	5
Level V	0	0	0
Level of spasticity			
Units: Subjects			
None	8	3	11
Mild	7	2	9
Moderate	5	4	9
Severe	1	2	3
Age at ARG1-D diagnosis			
Units: Years			
median	0.7	4.6	-
full range (min-max)	0 to 15	0 to 11	-
Historical arginine level			
Units: µM			
median	409	454	-
full range (min-max)	173 to 724	277 to 664	-

End points

End points reporting groups

Reporting group title	Pegzilarginase
Reporting group description: Pegzilarginase, administered once weekly for 24 weeks.	
Reporting group title	Placebo
Reporting group description: Placebo, administered once weekly for 24 weeks.	
Reporting group title	Pegzilarginase
Reporting group description: Pegzilarginase, administered once weekly for up to 150 weeks.	

Primary: Change from Baseline in plasma arginine after 24 weeks of study drug

End point title	Change from Baseline in plasma arginine after 24 weeks of study drug
End point description: The primary analysis tested the change in the level of plasma arginine between baseline and completion of Week 24 assessments. The change from baseline in plasma arginine on Week 24 was compared between subjects treated with pegzilarginase and those treated with placebo. Log-transformed plasma arginine data were used. Baseline values for plasma arginine concentrations were defined as the mean of all logged values (analyzed at the designated central laboratory) obtained during the Screening/Baseline Period and before the first dose of blinded study treatment.	
End point type	Primary
End point timeframe: From Baseline (Screening/Baseline period and before the first dose of blinded study treatment) until the end of the 24-week DB period (Week 24).	

End point values	Pegzilarginase	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	21	11		
Units: μM				
geometric mean (standard deviation)	0.244 (\pm 1.635)	0.918 (\pm 1.371)		

Statistical analyses

Statistical analysis title	Change in plasma arginine after 24-week treatment
Statistical analysis description: The used mixed effect model repeated measures (MMRM) method included visit, randomized study treatment, and interaction between visit and randomized study treatment as effects and Baseline value as a covariate. Log-transformed plasma arginine data were used. The output of this model with unstructured covariance structure is shown as geometric least squares mean ratio (pegzilarginase/placebo).	
Comparison groups	Pegzilarginase v Placebo

Number of subjects included in analysis	32
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Mixed models analysis
Parameter estimate	Geometric mean ratio
Point estimate	0.233
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.165
upper limit	0.329

Secondary: Mean change from Baseline at Week 24 in the 2-minute walk test (2MWT)

End point title	Mean change from Baseline at Week 24 in the 2-minute walk test (2MWT)
End point description: The mean change from Baseline in the 2 MWT of the mobility assessments was a key secondary outcome measure. The change in distance completed in 2 minutes in meters were compared between subjects treated with pegzilarginase and those treated with placebo.	
End point type	Secondary
End point timeframe: From Baseline until the end of the 24-week DB period (Week 24).	

End point values	Pegzilarginase	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19	10		
Units: m				
arithmetic mean (standard deviation)	7.3 (± 30.64)	2.7 (± 19.66)		

Statistical analyses

Statistical analysis title	Change in 2MWT at Week 24
Statistical analysis description: The used MMRM method included visit, randomized study treatment, and interaction between visit and randomized study treatment as effects and Baseline value as a covariate. The output of this model is shown as least squares (LS) mean difference (pegzilarginase - placebo).	
Comparison groups	Placebo v Pegzilarginase

Number of subjects included in analysis	29
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5961
Method	Mixed models analysis
Parameter estimate	LS mean difference
Point estimate	5.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-15.6
upper limit	26.7

Secondary: Mean change from Baseline at Week 24 in the gross motor function measure-88 part E (GMFM-E)

End point title	Mean change from Baseline at Week 24 in the gross motor function measure-88 part E (GMFM-E)
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End point description:

The mean change from Baseline in the GMFM-E of the mobility assessments was a key secondary outcome measure. The GMFM-E assessed walking, running, and jumping. The GMFM-E is scored from 0 to 72, with a higher score representing better gross motor function. The score change was compared between subjects treated with pegzilarginase and those treated with placebo.

End point type	Secondary
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End point timeframe:

From Baseline until the end of the 24-week DB period (Week 24).

End point values	Pegzilarginase	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20	11		
Units: score(s)				
arithmetic mean (standard deviation)	4.2 (± 7.69)	-0.4 (± 6.20)		

Statistical analyses

Statistical analysis title	Change in GMFM-E score at Week 24
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Statistical analysis description:

The used MMRM method included visit, randomized study treatment, and interaction between visit and randomized study treatment as effects and Baseline value as a covariate. The output of this model is shown as LS mean difference (pegzilarginase - placebo).

Comparison groups	Pegzilarginase v Placebo
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Number of subjects included in analysis	31
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1087
Method	Mixed models analysis
Parameter estimate	LS mean difference
Point estimate	4.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.1
upper limit	10.2

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From first administration of the study drug (pegzilarginase or placebo) until Week 24 in the DB period and from first administration of pegzilarginase until up to 150 weeks in the LTE period.

Assessment type	Non-systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	24.0
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Reporting groups

Reporting group title	Pegzilarginase (DB period)
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Reporting group description:

All subjects who received pegzilarginase during the DB period.

Reporting group title	Placebo (DB period)
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Reporting group description:

All subjects who received placebo during the DB period.

Reporting group title	Pegzilarginase - pegzilarginase (LTE period)
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Reporting group description:

All subjects who received pegzilarginase during the DB and the LTE period .

Reporting group title	Placebo - pegzilarginase (LTE period)
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Reporting group description:

All subjects who received placebo during the DB period and pegzilarginase during the LTE period.

Serious adverse events	Pegzilarginase (DB period)	Placebo (DB period)	Pegzilarginase - pegzilarginase (LTE period)
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 21 (19.05%)	4 / 11 (36.36%)	5 / 20 (25.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 21 (0.00%)	0 / 11 (0.00%)	1 / 20 (5.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ammonia increased			
subjects affected / exposed	0 / 21 (0.00%)	0 / 11 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aspartate aminotransferase increased			

subjects affected / exposed	0 / 21 (0.00%)	0 / 11 (0.00%)	1 / 20 (5.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	1 / 21 (4.76%)	0 / 11 (0.00%)	1 / 20 (5.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain			
subjects affected / exposed	0 / 21 (0.00%)	0 / 11 (0.00%)	1 / 20 (5.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Constipation			
subjects affected / exposed	0 / 21 (0.00%)	0 / 11 (0.00%)	1 / 20 (5.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholecystitis acute			
subjects affected / exposed	0 / 21 (0.00%)	0 / 11 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	0 / 21 (0.00%)	0 / 11 (0.00%)	1 / 20 (5.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Gastroenteritis			
subjects affected / exposed	0 / 21 (0.00%)	0 / 11 (0.00%)	2 / 20 (10.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hand-foot-and-mouth disease			

subjects affected / exposed	0 / 21 (0.00%)	0 / 11 (0.00%)	1 / 20 (5.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Hyperammonaemia			
subjects affected / exposed	2 / 21 (9.52%)	3 / 11 (27.27%)	2 / 20 (10.00%)
occurrences causally related to treatment / all	0 / 3	0 / 4	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperammonaemic encephalopathy			
subjects affected / exposed	1 / 21 (4.76%)	1 / 11 (9.09%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Placebo - pegzilarginase (LTE period)		
Total subjects affected by serious adverse events			
subjects affected / exposed	7 / 11 (63.64%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Ammonia increased			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Vomiting			

subjects affected / exposed	3 / 11 (27.27%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
Abdominal pain			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Constipation			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Cholecystitis acute			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Gastroenteritis			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hand-foot-and-mouth disease			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Hyperammonaemia			

subjects affected / exposed	5 / 11 (45.45%)		
occurrences causally related to treatment / all	1 / 7		
deaths causally related to treatment / all	0 / 0		
Hyperammonaemic encephalopathy			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Pegzilarginase (DB period)	Placebo (DB period)	Pegzilarginase - pegzilarginase (LTE period)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	18 / 21 (85.71%)	11 / 11 (100.00%)	20 / 20 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Benign neoplasm of skin			
subjects affected / exposed	0 / 21 (0.00%)	0 / 11 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Oral papilloma			
subjects affected / exposed	0 / 21 (0.00%)	0 / 11 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Skin papilloma			
subjects affected / exposed	0 / 21 (0.00%)	0 / 11 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	4 / 21 (19.05%)	0 / 11 (0.00%)	9 / 20 (45.00%)
occurrences (all)	4	0	13
Asthenia			
subjects affected / exposed	0 / 21 (0.00%)	0 / 11 (0.00%)	2 / 20 (10.00%)
occurrences (all)	0	0	2
Fatigue			
subjects affected / exposed	0 / 21 (0.00%)	0 / 11 (0.00%)	9 / 20 (45.00%)
occurrences (all)	0	0	9
Gait disturbance			

subjects affected / exposed	0 / 21 (0.00%)	0 / 11 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Influenza like illness			
subjects affected / exposed	0 / 21 (0.00%)	0 / 11 (0.00%)	2 / 20 (10.00%)
occurrences (all)	0	0	2
Injection site pain			
subjects affected / exposed	0 / 21 (0.00%)	0 / 11 (0.00%)	2 / 20 (10.00%)
occurrences (all)	0	0	3
Pain			
subjects affected / exposed	0 / 21 (0.00%)	0 / 11 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Vaccination site pain			
subjects affected / exposed	0 / 21 (0.00%)	0 / 11 (0.00%)	2 / 20 (10.00%)
occurrences (all)	0	0	3
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	4 / 21 (19.05%)	2 / 11 (18.18%)	10 / 20 (50.00%)
occurrences (all)	4	2	16
Nasal congestion			
subjects affected / exposed	0 / 21 (0.00%)	1 / 11 (9.09%)	2 / 20 (10.00%)
occurrences (all)	0	1	3
Oropharyngeal pain			
subjects affected / exposed	0 / 21 (0.00%)	1 / 11 (9.09%)	2 / 20 (10.00%)
occurrences (all)	0	1	2
Rhinorrhoea			
subjects affected / exposed	2 / 21 (9.52%)	0 / 11 (0.00%)	5 / 20 (25.00%)
occurrences (all)	4	0	5
Catarrh			
subjects affected / exposed	0 / 21 (0.00%)	0 / 11 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Lower respiratory tract congestion			
subjects affected / exposed	0 / 21 (0.00%)	0 / 11 (0.00%)	2 / 20 (10.00%)
occurrences (all)	0	0	2
Productive cough			

subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0	0 / 11 (0.00%) 0	0 / 20 (0.00%) 0
Sinus congestion subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0	0 / 11 (0.00%) 0	0 / 20 (0.00%) 0
Psychiatric disorders			
Aggression subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0	1 / 11 (9.09%) 1	0 / 20 (0.00%) 0
Generalised anxiety disorder subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0	1 / 11 (9.09%) 1	0 / 20 (0.00%) 0
Mood altered subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0	1 / 11 (9.09%) 1	0 / 20 (0.00%) 0
Insomnia subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0	0 / 11 (0.00%) 0	0 / 20 (0.00%) 0
Investigations			
Alanine aminotransferase increased subjects affected / exposed occurrences (all)	2 / 21 (9.52%) 6	0 / 11 (0.00%) 0	4 / 20 (20.00%) 9
Ammonia increased subjects affected / exposed occurrences (all)	3 / 21 (14.29%) 5	2 / 11 (18.18%) 3	3 / 20 (15.00%) 5
Aspartate aminotransferase increased subjects affected / exposed occurrences (all)	2 / 21 (9.52%) 4	0 / 11 (0.00%) 0	4 / 20 (20.00%) 7
Blood potassium decreased subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0	1 / 11 (9.09%) 1	0 / 20 (0.00%) 0
Body temperature increased subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0	1 / 11 (9.09%) 1	0 / 20 (0.00%) 0
Cardiac murmur			

subjects affected / exposed	0 / 21 (0.00%)	1 / 11 (9.09%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Activated partial thromboplastin time prolonged			
subjects affected / exposed	0 / 21 (0.00%)	0 / 11 (0.00%)	2 / 20 (10.00%)
occurrences (all)	0	0	2
Amino acid level increased			
subjects affected / exposed	0 / 21 (0.00%)	0 / 11 (0.00%)	4 / 20 (20.00%)
occurrences (all)	0	0	6
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 21 (0.00%)	0 / 11 (0.00%)	3 / 20 (15.00%)
occurrences (all)	0	0	3
Haemoglobin decreased			
subjects affected / exposed	0 / 21 (0.00%)	0 / 11 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Insulin-like growth factor decreased			
subjects affected / exposed	0 / 21 (0.00%)	0 / 11 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Prothrombin time prolonged			
subjects affected / exposed	0 / 21 (0.00%)	0 / 11 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
SARS-CoV-2 test positive			
subjects affected / exposed	0 / 21 (0.00%)	0 / 11 (0.00%)	4 / 20 (20.00%)
occurrences (all)	0	0	6
Transaminases increased			
subjects affected / exposed	0 / 21 (0.00%)	0 / 11 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Weight decreased			
subjects affected / exposed	0 / 21 (0.00%)	0 / 11 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Weight increased			
subjects affected / exposed	0 / 21 (0.00%)	0 / 11 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			

Fall subjects affected / exposed occurrences (all)	2 / 21 (9.52%) 4	0 / 11 (0.00%) 0	3 / 20 (15.00%) 3
Contusion subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0	0 / 11 (0.00%) 0	0 / 20 (0.00%) 0
Post-traumatic pain subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0	0 / 11 (0.00%) 0	0 / 20 (0.00%) 0
Nervous system disorders Dizziness subjects affected / exposed occurrences (all)	2 / 21 (9.52%) 3	0 / 11 (0.00%) 0	0 / 20 (0.00%) 0
Headache subjects affected / exposed occurrences (all)	2 / 21 (9.52%) 3	1 / 11 (9.09%) 1	5 / 20 (25.00%) 7
Lethargy subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0	1 / 11 (9.09%) 1	0 / 20 (0.00%) 0
Blood and lymphatic system disorders Lymphadenopathy subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0	0 / 11 (0.00%) 0	0 / 20 (0.00%) 0
Ear and labyrinth disorders Ear pain subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0	0 / 11 (0.00%) 0	0 / 20 (0.00%) 0
Hypoacusis subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0	0 / 11 (0.00%) 0	0 / 20 (0.00%) 0
Gastrointestinal disorders Abdominal pain subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0	3 / 11 (27.27%) 5	3 / 20 (15.00%) 4
Constipation subjects affected / exposed occurrences (all)	3 / 21 (14.29%) 9	1 / 11 (9.09%) 1	2 / 20 (10.00%) 3

Diarrhoea			
subjects affected / exposed	0 / 21 (0.00%)	1 / 11 (9.09%)	2 / 20 (10.00%)
occurrences (all)	0	1	2
Nausea			
subjects affected / exposed	0 / 21 (0.00%)	4 / 11 (36.36%)	5 / 20 (25.00%)
occurrences (all)	0	6	7
Vomiting			
subjects affected / exposed	5 / 21 (23.81%)	3 / 11 (27.27%)	10 / 20 (50.00%)
occurrences (all)	10	8	27
Abdominal discomfort			
subjects affected / exposed	0 / 21 (0.00%)	0 / 11 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Abdominal pain upper			
subjects affected / exposed	0 / 21 (0.00%)	0 / 11 (0.00%)	3 / 20 (15.00%)
occurrences (all)	0	0	3
Dental caries			
subjects affected / exposed	0 / 21 (0.00%)	0 / 11 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Hepatobiliary disorders			
Hepatic cytolysis			
subjects affected / exposed	0 / 21 (0.00%)	1 / 11 (9.09%)	0 / 20 (0.00%)
occurrences (all)	0	2	0
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	2 / 21 (9.52%)	0 / 11 (0.00%)	0 / 20 (0.00%)
occurrences (all)	2	0	0
Rash			
subjects affected / exposed	0 / 21 (0.00%)	1 / 11 (9.09%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Skin exfoliation			
subjects affected / exposed	0 / 21 (0.00%)	1 / 11 (9.09%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Alopecia			
subjects affected / exposed	0 / 21 (0.00%)	0 / 11 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Ingrowing nail			

subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0	0 / 11 (0.00%) 0	0 / 20 (0.00%) 0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 21 (0.00%)	1 / 11 (9.09%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Osteochondrosis			
subjects affected / exposed	0 / 21 (0.00%)	1 / 11 (9.09%)	0 / 20 (0.00%)
occurrences (all)	0	2	0
Pain in extremity			
subjects affected / exposed	0 / 21 (0.00%)	1 / 11 (9.09%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Back pain			
subjects affected / exposed	0 / 21 (0.00%)	0 / 11 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Muscle spasms			
subjects affected / exposed	0 / 21 (0.00%)	0 / 11 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	2 / 21 (9.52%)	0 / 11 (0.00%)	5 / 20 (25.00%)
occurrences (all)	4	0	8
Asymptomatic COVID-19			
subjects affected / exposed	0 / 21 (0.00%)	0 / 11 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
COVID-19			
subjects affected / exposed	0 / 21 (0.00%)	0 / 11 (0.00%)	4 / 20 (20.00%)
occurrences (all)	0	0	5
Conjunctivitis			
subjects affected / exposed	0 / 21 (0.00%)	0 / 11 (0.00%)	2 / 20 (10.00%)
occurrences (all)	0	0	2
Ear infection			
subjects affected / exposed	0 / 21 (0.00%)	0 / 11 (0.00%)	3 / 20 (15.00%)
occurrences (all)	0	0	3
Gastroenteritis viral			

subjects affected / exposed	0 / 21 (0.00%)	0 / 11 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Helicobacter infection			
subjects affected / exposed	0 / 21 (0.00%)	0 / 11 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Localised infection			
subjects affected / exposed	0 / 21 (0.00%)	0 / 11 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Molluscum contagiosum			
subjects affected / exposed	0 / 21 (0.00%)	0 / 11 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Parasitic gastroenteritis			
subjects affected / exposed	0 / 21 (0.00%)	0 / 11 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Rhinitis			
subjects affected / exposed	0 / 21 (0.00%)	0 / 11 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract infection			
subjects affected / exposed	0 / 21 (0.00%)	0 / 11 (0.00%)	5 / 20 (25.00%)
occurrences (all)	0	0	5
Viral infection			
subjects affected / exposed	0 / 21 (0.00%)	0 / 11 (0.00%)	2 / 20 (10.00%)
occurrences (all)	0	0	2
Viral skin infection			
subjects affected / exposed	0 / 21 (0.00%)	0 / 11 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 21 (0.00%)	2 / 11 (18.18%)	0 / 20 (0.00%)
occurrences (all)	0	2	0
Hyperammonaemia			
subjects affected / exposed	0 / 21 (0.00%)	0 / 11 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Placebo - pegzilarginase (LTE period)		
Total subjects affected by non-serious			

adverse events			
subjects affected / exposed	11 / 11 (100.00%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Benign neoplasm of skin			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	2		
Oral papilloma			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Skin papilloma			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	5 / 11 (45.45%)		
occurrences (all)	6		
Asthenia			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences (all)	0		
Fatigue			
subjects affected / exposed	2 / 11 (18.18%)		
occurrences (all)	3		
Gait disturbance			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	2		
Influenza like illness			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Injection site pain			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Pain			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Vaccination site pain			

subjects affected / exposed	0 / 11 (0.00%)		
occurrences (all)	0		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	3 / 11 (27.27%)		
occurrences (all)	4		
Nasal congestion			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences (all)	0		
Oropharyngeal pain			
subjects affected / exposed	4 / 11 (36.36%)		
occurrences (all)	8		
Rhinorrhoea			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences (all)	0		
Catarrh			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Lower respiratory tract congestion			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences (all)	0		
Productive cough			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Sinus congestion			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Psychiatric disorders			
Aggression			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Generalised anxiety disorder			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences (all)	0		
Mood altered			

subjects affected / exposed	0 / 11 (0.00%)		
occurrences (all)	0		
Insomnia			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	3 / 11 (27.27%)		
occurrences (all)	5		
Ammonia increased			
subjects affected / exposed	4 / 11 (36.36%)		
occurrences (all)	8		
Aspartate aminotransferase increased			
subjects affected / exposed	3 / 11 (27.27%)		
occurrences (all)	4		
Blood potassium decreased			
subjects affected / exposed	2 / 11 (18.18%)		
occurrences (all)	2		
Body temperature increased			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences (all)	0		
Cardiac murmur			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences (all)	0		
Activated partial thromboplastin time prolonged			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Amino acid level increased			
subjects affected / exposed	2 / 11 (18.18%)		
occurrences (all)	4		
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences (all)	0		
Haemoglobin decreased			

subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	2		
Insulin-like growth factor decreased			
subjects affected / exposed	2 / 11 (18.18%)		
occurrences (all)	2		
Prothrombin time prolonged			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
SARS-CoV-2 test positive			
subjects affected / exposed	3 / 11 (27.27%)		
occurrences (all)	3		
Transaminases increased			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Weight decreased			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Weight increased			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences (all)	0		
Contusion			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	3		
Post-traumatic pain			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences (all)	0		
Headache			

subjects affected / exposed	2 / 11 (18.18%)		
occurrences (all)	2		
Lethargy			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Blood and lymphatic system disorders			
Lymphadenopathy			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Hypoacusis			
subjects affected / exposed	2 / 11 (18.18%)		
occurrences (all)	2		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	4 / 11 (36.36%)		
occurrences (all)	4		
Constipation			
subjects affected / exposed	2 / 11 (18.18%)		
occurrences (all)	2		
Diarrhoea			
subjects affected / exposed	2 / 11 (18.18%)		
occurrences (all)	2		
Nausea			
subjects affected / exposed	2 / 11 (18.18%)		
occurrences (all)	10		
Vomiting			
subjects affected / exposed	7 / 11 (63.64%)		
occurrences (all)	13		
Abdominal discomfort			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Abdominal pain upper			

subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0		
Dental caries subjects affected / exposed occurrences (all)	1 / 11 (9.09%) 1		
Hepatobiliary disorders Hepatic cytolysis subjects affected / exposed occurrences (all)	1 / 11 (9.09%) 1		
Skin and subcutaneous tissue disorders Pruritus subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0		
Rash subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0		
Skin exfoliation subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0		
Alopecia subjects affected / exposed occurrences (all)	1 / 11 (9.09%) 1		
Ingrowing nail subjects affected / exposed occurrences (all)	1 / 11 (9.09%) 2		
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all)	1 / 11 (9.09%) 1		
Osteochondrosis subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0		
Pain in extremity subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0		
Back pain			

subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Muscle spasms			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Asymptomatic COVID-19			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
COVID-19			
subjects affected / exposed	2 / 11 (18.18%)		
occurrences (all)	2		
Conjunctivitis			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences (all)	0		
Ear infection			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences (all)	0		
Gastroenteritis viral			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Helicobacter infection			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Localised infection			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Molluscum contagiosum			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Parasitic gastroenteritis			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		

Rhinitis			
subjects affected / exposed	2 / 11 (18.18%)		
occurrences (all)	2		
Upper respiratory tract infection			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences (all)	0		
Viral infection			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	3		
Viral skin infection			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Hyperammonaemia			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
15 January 2019	Protocol v2.0 with following changes to v1.0: <ul style="list-style-type: none">- Schedule of Assessments was updated to clarify timing, add height assessments in the LTE period, specify that mutation analysis and arginase activity in red blood cells were required for all subjects, and for other clarifications.- Clarified that interactive web/voice response system (IXRS) evaluates arginine data and sends the dose adjustments to the unblinded pharmacist and/or physician. Also formal unblinding was defined.- Questions for caregivers were clarified.- Hypersensitivity reactions and hyperammonemic episodes were specified as adverse events of special interest (AESIs), and a guidance regarding corticosteroids was given.- Definition of hyperammonemic episodes was added.
08 June 2020	Protocol v5.0 with following changes to v2.0: <ul style="list-style-type: none">- AE were to be reported from signing of informed consent continuing through the last study follow-up visit.- The objectives "compare pegzilarginase with placebo with respect to (re:) other aspects of mobility", "compare pegzilarginase with placebo re: adaptive behavior" and "compare pegzilarginase with placebo re: objective measures of neurological/neuromotor manifestations" were added; including corresponding endpoints.- Definitions were clarified and added regarding clinical response, responder and AESI.- Requirements for a stable, consistent diet through the first 8 weeks of the LTE period were added.- Measures to minimize bias were clarified.- Time period for botulinum toxin use (standard treatment for spasticity) before study treatment (exclusion criterion 8) was shortened.- Storage temperature was corrected, and description of study treatment was updated and clarified.- Initial calculation of dose was to be based on subject's weight at Baseline.- Potential for transition to SC treatment was added.- Limitations of GMFM to parts D and E and minimum clinically important differences for these parts were added.- Subject requirement to maintain dietary protein intake levels during DB period consistent with baseline was added.- AESI terms were defined. Specifications of measures to be taken in case of hypersensitivity reaction were added.- Statistical analysis was specified. Sample Size determination with new power calculations was added.- Interim analysis after completion of the DB period was added. Analyses were completed at an overall 2-sided alpha=0.05 without adjustment for multiplicity for the interim analysis.- Personnel and level of unblinding/access was clarified.- Timings of assessments were revised and adjusted.- SC dosing and administration requirements were added.- Specified that the SRC had access to full subject data/treatment assignment in case of safety concerns.

11 December 2020	<p>Protocol v6.0 with following changes to v5.0:</p> <ul style="list-style-type: none"> - Objectives, endpoints, and analyses were clarified and reprioritized based on clinical and statistical considerations. The statistical approach was changed to specify the use of continuous rather than categorical variables, and multiple comparison procedures were specified for global control of Type 1 error. - Additional changes were made to ensure continuity and safety of study subjects despite the impact of the global pandemic. A section was added addressing the impact of COVID-19. - The key secondary objective (including corresponding endpoint) was revised to be based on key mobility and/or motor function outcome measures. - Secondary objectives and endpoints and the tertiary objectives and endpoints were clarified. - For the primary endpoint analysis, the values would be log transformed before analysis. - Sensitivity analyses were added. - Contingency for action if the primary analysis is or is not statistically significant was added. - Schedule of Assessments footnotes were clarified. - Preparation/Handling/Storage/Accountability section was revised to reflect new data. - Clarification was made re: when the IXRS would be discontinued. - Specification for reporting additional follow-up SAE information was added. - Injection site reactions was defined and added as AESI. - The hyperammonemia section was revised for accuracy and clarity. - Sample size determination was adjusted to reflect inclusion of Study CAEB1102-102A preliminary data and specification of the number of units corresponding to the log scale. - Sample size was adjusted to align with the changes in statistical analyses/endpoints/objectives. - Additional details were included for the statistical analyses consistent with the change in the statistical approach.
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Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

<http://www.ncbi.nlm.nih.gov/pubmed/38292042>