Clinical trial results:
An Open-label, Multicenter Study to Evaluate the Long-Term Safety, Tolerability, and Efficacy of AEB1102 in Patients with Arginase 1 Deficiency

Summary

EudraCT number	2018-003163-67
Trial protocol	GB PT
Global end of trial date	15 December 2022

Results information

Result version number	v1 (current)
This version publication date	23 October 2025
First version publication date	23 October 2025

Trial information

Trial identification

Sponsor protocol code	CAEB1102-102A

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03378531
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	20 February 2024
Is this the analysis of the primary completion data?	Yes
Primary completion date	15 December 2022
Global end of trial reached?	Yes
Global end of trial date	15 December 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the long-term safety and tolerability of intravenous (IV) or subcutaneous (SC) pegzilarginase administered for up to 4 years in patients with arginase 1 deficiency (ARG1-D) and hyperargininemia

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. The trial was conducted by investigators experienced in the treatment of patients (children and adults) with ARG1-D. Pegzilarginase dosing outside of the clinical research unit (CRU) was to be done by appropriately qualified and trained home health care professionals.
A Data Safety Monitoring Board periodically provided independent review of the safety, tolerability, immunogenicity, pharmacokinetic (PK), and pharmacodynamic (PD) measures during the study.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	07 December 2017
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	Portugal: 2
Country: Number of subjects enrolled	United Kingdom: 1
Country: Number of subjects enrolled	United States: 8
Country: Number of subjects enrolled	Canada: 3
Worldwide total number of subjects	14
EEA total number of subjects	2

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)	6
Adolescents (12-17 years)	3
Adults (18-64 years)	5
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

All 14 subjects who completed Study CAEB1102-101A were eligible, none had a clinically significant adverse event or had experienced another unmanageable drug toxicity that precluded further dosing, and were enrolled and treated with pegzilarginase in Study CAEB1102-102A.

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	Long-term extension (LTE) (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Pegzilarginase

Arm description:

Pegzilarginase administered once weekly for up to 4 years.

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:

The pegzilarginase dose level and frequency were initially the same as received at the end of CAEB1102-101A, but the individual dose may have been adjusted based on PK/PD data or for safety and/or tolerability reasons. Dose adjustments were allowed to find a dose and regimen that maintained plasma arginine levels below 200 µM, and if achievable, in normal range of 40 to 115 µM. The maximum permitted dose was 0.33 mg/kg.
Dosing was to start approximately 4 weeks (but not sooner than 3 weeks) after subject's last dose of pegzilarginase in CAEB1102-101A. The first 24 doses were administered IV, with the first 12 doses to be given weekly at the CRU. After 24 weeks of IV dosing, subjects received a weekly SC injection, the dose of which initially was the same as the last IV dose. The first 4 SC doses were to be given at the CRU. The Investigator could switch back to IV dosing at any time if clinically indicated. Dosing outside CRU was to be done by trained home health care professionals.

Number of subjects in period 1	Pegzilarginase
Started	14
Completed	13
Not completed	1
Consent withdrawn by subject	1

Baseline characteristics

Reporting groups	
Reporting group title	Pegzilarginase
Reporting group description:	
Pegzilarginase administered once weekly for up to 4 years.	

Reporting group values	Pegzilarginase	Total	
Number of subjects	14	14	
Age categorical Units: Subjects			
Children (2 to <12 years)	6	6	
Children (12 to <18 years)	3	3	
Adults (≥18 years)	5	5	
Age continuous Units: years			
median	14		
full range (min-max)	6 to 32	-	
Gender categorical Units: Subjects			
Female	11	11	
Male	3	3	
Gross motor function classification system level Units: Subjects			
Level I	7	7	
Level II	4	4	
Level III	2	2	
Level IV	1	1	
Level of spasticity Units: Subjects			
None	4	4	
Mild	3	3	
Moderate	3	3	
Severe	4	4	
Age at ARG1-D diagnosis Units: Years			
median	1.7		
full range (min-max)	0.03 to 25.41	-	
Baseline arginine level Units: µM			
median	313.5		
full range (min-max)	186 to 503	-	

End points

End points reporting groups

Reporting group title	Pegzilarginase

Reporting group description:

Pegzilarginase administered once weekly for up to 4 years.

Primary: Safety and tolerability

End point title	Safety and tolerability[1]

End point description:

Primary safety and tolerability outcome measures included the following: treatment-emergent adverse events (TEAEs)/serious adverse events (SAEs), physical examinations, vital signs, electrocardiograms (ECGs), clinical laboratory studies (serum chemistries, hematology, coagulation, and urinalysis), clinically significant (CS) hyperammonemia, and immunogenicity safety measures (levels of anti-pegzilarginase and anti-polyethylene glycol antibodies). CS values were to be reported as TEAEs.

End point type	Primary

End point timeframe:

From the first pegzilarginase dose in Study CAEB1102-102A until the last study follow-up visit (approximately 2 weeks after the completion of the final dose of pegzilarginase; up to 4 years).

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: No statistical analysis was done for this end point.

End point values	Pegzilarginase			
Subject group type	Reporting group			
Number of subjects analysed	14			
Units: Subject(s)				
Any TEAE	14			
Study drug-related TEAE	7			
TEAE requiring dose interruption	8			
TEAE leading to discontinuation of pegzilarginase	0			
SAE	8			
Study drug-related SAE	2			
Death	0			
CS findings in physical examinations/vital signs	0			
CS abnormalities in ECG	0			
CS changes in hematology abnormalities (TEAEs)	3			
CS changes in chemistry abnormalities (TEAEs)	5			
CS liver function abnormalities (not in chemistry)	5			
Ammonia increased (TEAE, not in chemistry)	6			
Hyperammonemia (TEAE, not in chemistry)	6			
CS coagulation abnormalities (TEAEs)	1			
CS urinalysis abnormalities (TEAEs)	1			

On-pegzilarginase treatment anti-drug antibodies	0			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From the signing of consent for Study CAEB1102-102A until the last study follow-up visit (approximately 2 weeks after the completion of the final dose of pegzilarginase; up to 4 years).

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	24.0

Reporting groups

Reporting group title	Pegzilarginase (LTE period)

Reporting group description:

All subjects who received pegzilarginase during Study CAEB1102-102A.

Serious adverse events	Pegzilarginase (LTE period)		
Total subjects affected by serious adverse events			
subjects affected / exposed	8 / 14 (57.14%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Investigations			
Ammonia increased			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Post-traumatic headache			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Social circumstances			
Social problem			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Abdominal pain			

subjects affected / exposed	1 / 14 (7.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vomiting			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Gastroenteritis			
subjects affected / exposed	2 / 14 (14.29%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Respiratory syncytial virus infection			
subjects affected / exposed	2 / 14 (14.29%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Influenza			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory tract infection			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Hyperammonaemia			
subjects affected / exposed	5 / 14 (35.71%)		
occurrences causally related to treatment / all	8 / 12		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Pegzilarginase (LTE period)		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	14 / 14 (100.00%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Lip neoplasm benign			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Vascular disorders			
Thrombophlebitis superficial			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	5 / 14 (35.71%)		
occurrences (all)	10		
Fatigue			
subjects affected / exposed	3 / 14 (21.43%)		
occurrences (all)	9		
Injection site erythema			
subjects affected / exposed	2 / 14 (14.29%)		
occurrences (all)	6		
Catheter site pain			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Chills			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Gait disturbance			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Injection site bruising			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	2		
Injection site irritation			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	2		

Injection site rash subjects affected / exposed occurrences (all)	1 / 14 (7.14%) 1		
Injection site reaction subjects affected / exposed occurrences (all)	1 / 14 (7.14%) 1		
Injection site swelling subjects affected / exposed occurrences (all)	1 / 14 (7.14%) 1		
Non-cardiac chest pain subjects affected / exposed occurrences (all)	1 / 14 (7.14%) 1		
Vaccination site pain subjects affected / exposed occurrences (all)	1 / 14 (7.14%) 1		
Vaccination site urticaria subjects affected / exposed occurrences (all)	1 / 14 (7.14%) 1		
Immune system disorders Seasonal allergy subjects affected / exposed occurrences (all)	2 / 14 (14.29%) 5		
Reproductive system and breast disorders Amenorrhoea subjects affected / exposed occurrences (all)	2 / 14 (14.29%) 2		
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all)	11 / 14 (78.57%) 35		
Oropharyngeal pain subjects affected / exposed occurrences (all)	5 / 14 (35.71%) 6		
Rhinorrhoea subjects affected / exposed occurrences (all)	3 / 14 (21.43%) 3		

Sneezing subjects affected / exposed occurrences (all)	2 / 14 (14.29%) 2		
Dyspnoea subjects affected / exposed occurrences (all)	1 / 14 (7.14%) 3		
Epistaxis subjects affected / exposed occurrences (all)	1 / 14 (7.14%) 1		
Nasal congestion subjects affected / exposed occurrences (all)	1 / 14 (7.14%) 1		
Psychiatric disorders Anxiety subjects affected / exposed occurrences (all)	2 / 14 (14.29%) 2		
Aggression subjects affected / exposed occurrences (all)	1 / 14 (7.14%) 1		
Depressed mood subjects affected / exposed occurrences (all)	1 / 14 (7.14%) 1		
Depression subjects affected / exposed occurrences (all)	1 / 14 (7.14%) 1		
Obsessive-compulsive disorder subjects affected / exposed occurrences (all)	1 / 14 (7.14%) 1		
Stereotypy subjects affected / exposed occurrences (all)	1 / 14 (7.14%) 1		
Investigations Ammonia increased subjects affected / exposed occurrences (all)	5 / 14 (35.71%) 8		
Alanine aminotransferase increased			

subjects affected / exposed	3 / 14 (21.43%)			
occurrences (all)	5			
Transaminases increased				
subjects affected / exposed	3 / 14 (21.43%)			
occurrences (all)	7			
Aspartate aminotransferase increased				
subjects affected / exposed	2 / 14 (14.29%)			
occurrences (all)	4			
Blood lactate dehydrogenase increased				
subjects affected / exposed	2 / 14 (14.29%)			
occurrences (all)	3			
Blood urea decreased				
subjects affected / exposed	2 / 14 (14.29%)			
occurrences (all)	5			
Activated partial thromboplastin time prolonged				
subjects affected / exposed	1 / 14 (7.14%)			
occurrences (all)	1			
Alanine aminotransferase abnormal				
subjects affected / exposed	1 / 14 (7.14%)			
occurrences (all)	1			
Amino acid level increased				
subjects affected / exposed	1 / 14 (7.14%)			
occurrences (all)	1			
Aspartate aminotransferase abnormal				
subjects affected / exposed	1 / 14 (7.14%)			
occurrences (all)	1			
Blood iron decreased				
subjects affected / exposed	1 / 14 (7.14%)			
occurrences (all)	1			
Blood potassium decreased				
subjects affected / exposed	1 / 14 (7.14%)			
occurrences (all)	1			
Prothrombin time prolonged				

subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
White blood cells urine			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	2 / 14 (14.29%)		
occurrences (all)	2		
Procedural pain			
subjects affected / exposed	2 / 14 (14.29%)		
occurrences (all)	2		
Contusion			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Scratch			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Skin abrasion			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Congenital, familial and genetic disorders			
Usher's syndrome			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Cardiac disorders			
Palpitations			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Nervous system disorders			
Headache			
subjects affected / exposed	7 / 14 (50.00%)		
occurrences (all)	30		
Lethargy			
subjects affected / exposed	2 / 14 (14.29%)		
occurrences (all)	2		

Dizziness subjects affected / exposed occurrences (all)	1 / 14 (7.14%) 1		
Hypoaesthesia subjects affected / exposed occurrences (all)	1 / 14 (7.14%) 1		
Memory impairment subjects affected / exposed occurrences (all)	1 / 14 (7.14%) 1		
Seizure subjects affected / exposed occurrences (all)	1 / 14 (7.14%) 1		
Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all)	1 / 14 (7.14%) 1		
Ear and labyrinth disorders Ear pain subjects affected / exposed occurrences (all)	2 / 14 (14.29%) 3		
Eye disorders Eye swelling subjects affected / exposed occurrences (all)	1 / 14 (7.14%) 1		
Night blindness subjects affected / exposed occurrences (all)	1 / 14 (7.14%) 1		
Visual impairment subjects affected / exposed occurrences (all)	1 / 14 (7.14%) 1		
Gastrointestinal disorders Vomiting subjects affected / exposed occurrences (all)	8 / 14 (57.14%) 33		
Abdominal pain upper subjects affected / exposed occurrences (all)	6 / 14 (42.86%) 8		

Nausea subjects affected / exposed occurrences (all)	6 / 14 (42.86%) 21		
Constipation subjects affected / exposed occurrences (all)	5 / 14 (35.71%) 6		
Diarrhoea subjects affected / exposed occurrences (all)	3 / 14 (21.43%) 4		
Abdominal pain subjects affected / exposed occurrences (all)	2 / 14 (14.29%) 2		
Abdominal discomfort subjects affected / exposed occurrences (all)	1 / 14 (7.14%) 1		
Abdominal hernia subjects affected / exposed occurrences (all)	1 / 14 (7.14%) 1		
Abdominal pain lower subjects affected / exposed occurrences (all)	1 / 14 (7.14%) 1		
Gastrooesophageal reflux disease subjects affected / exposed occurrences (all)	1 / 14 (7.14%) 1		
Toothache subjects affected / exposed occurrences (all)	1 / 14 (7.14%) 1		
Skin and subcutaneous tissue disorders Alopecia subjects affected / exposed occurrences (all)	2 / 14 (14.29%) 2		
Hypertrichosis subjects affected / exposed occurrences (all)	2 / 14 (14.29%) 2		
Achromotrichia acquired			

subjects affected / exposed occurrences (all)	1 / 14 (7.14%) 1		
Acne subjects affected / exposed occurrences (all)	1 / 14 (7.14%) 1		
Dermatitis atopic subjects affected / exposed occurrences (all)	1 / 14 (7.14%) 2		
Dry skin subjects affected / exposed occurrences (all)	1 / 14 (7.14%) 1		
Ecchymosis subjects affected / exposed occurrences (all)	1 / 14 (7.14%) 1		
Eczema subjects affected / exposed occurrences (all)	1 / 14 (7.14%) 1		
Ingrowing nail subjects affected / exposed occurrences (all)	1 / 14 (7.14%) 1		
Skin striae subjects affected / exposed occurrences (all)	1 / 14 (7.14%) 1		
Vitiligo subjects affected / exposed occurrences (all)	1 / 14 (7.14%) 1		
Renal and urinary disorders Pollakiuria subjects affected / exposed occurrences (all)	1 / 14 (7.14%) 1		
Polyuria subjects affected / exposed occurrences (all)	1 / 14 (7.14%) 1		
Musculoskeletal and connective tissue disorders			

Arthralgia subjects affected / exposed occurrences (all)	3 / 14 (21.43%) 5		
Back pain subjects affected / exposed occurrences (all)	2 / 14 (14.29%) 2		
Bone deformity subjects affected / exposed occurrences (all)	1 / 14 (7.14%) 1		
Foot deformity subjects affected / exposed occurrences (all)	1 / 14 (7.14%) 1		
Joint stiffness subjects affected / exposed occurrences (all)	1 / 14 (7.14%) 1		
Muscle spasms subjects affected / exposed occurrences (all)	1 / 14 (7.14%) 1		
Muscular weakness subjects affected / exposed occurrences (all)	1 / 14 (7.14%) 1		
Pain in extremity subjects affected / exposed occurrences (all)	1 / 14 (7.14%) 1		
Soft tissue swelling subjects affected / exposed occurrences (all)	1 / 14 (7.14%) 2		
Infections and infestations Nasopharyngitis subjects affected / exposed occurrences (all)	7 / 14 (50.00%) 13		
COVID-19 subjects affected / exposed occurrences (all)	6 / 14 (42.86%) 6		
Upper respiratory tract infection			

subjects affected / exposed	5 / 14 (35.71%)			
occurrences (all)	10			
Gastroenteritis				
subjects affected / exposed	2 / 14 (14.29%)			
occurrences (all)	2			
Influenza				
subjects affected / exposed	1 / 14 (7.14%)			
occurrences (all)	1			
Adenoiditis				
subjects affected / exposed	1 / 14 (7.14%)			
occurrences (all)	1			
Cellulitis				
subjects affected / exposed	1 / 14 (7.14%)			
occurrences (all)	1			
Conjunctivitis				
subjects affected / exposed	1 / 14 (7.14%)			
occurrences (all)	1			
Cystitis				
subjects affected / exposed	1 / 14 (7.14%)			
occurrences (all)	1			
Helicobacter infection				
subjects affected / exposed	1 / 14 (7.14%)			
occurrences (all)	1			
Localised infection				
subjects affected / exposed	1 / 14 (7.14%)			
occurrences (all)	1			
Pharyngitis streptococcal				
subjects affected / exposed	1 / 14 (7.14%)			
occurrences (all)	1			
Pneumonia				
subjects affected / exposed	1 / 14 (7.14%)			
occurrences (all)	1			
Sinusitis				
subjects affected / exposed	1 / 14 (7.14%)			
occurrences (all)	2			
Urinary tract infection				

subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Metabolism and nutrition disorders			
Hyperammonaemia			
subjects affected / exposed	5 / 14 (35.71%)		
occurrences (all)	19		
Decreased appetite			
subjects affected / exposed	3 / 14 (21.43%)		
occurrences (all)	4		
Dehydration			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Hypokalaemia			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Hypomagnesaemia			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Iron deficiency			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Vitamin D deficiency			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
14 May 2018	Amendment v1.1 with following changes to original protocol: - Optional adjustments in dose, dosing frequency (weekly or every other week), and route of administration (IV or SC) was added - Option for dose administration and assessments at home after demonstration of sufficient safety, to reduce burden on subjects and parents/caregivers was added - Adjustment of blood sampling schedules and key PK/PD sample timepoints to accommodate every other week dosing - Alignment of neurocognitive/developmental/quality of life (QoL) instruments with Phase 3 program based on expert review - Adjustment of frequency of neurocognitive/developmental/QoL and neurological/neuromotor assessments to reflect timeframes considered more likely to show changes in this population - Optional food effect substudy was added
28 March 2019	Protocol v2.0 (US, Canada, Portugal) with following changes to v1.1 (incorporated on 08-May-2029 in Protocol v2.1 for UK): - Dosing was changed to requiring 24-week IV dosing before a change to an SC route, the option for every other week dosing was removed and the following dosing schedule was recommended: IV administration once weekly for Weeks 1 through 24; SC administration once weekly for Weeks 25 through 48; as clinically indicated thereafter for Years 2 and 3 - Replacement of "AEB1102" by the generic drug name "pegzilarginase" - Defined that initial mg/kg SC dose was to match the last IV dose the subject received - Subsequent SC doses can be administered outside of the CRU by appropriately trained home health care professionals if considered safe and appropriate by investigator and sponsor - List of examples for hypersensitivity reactions was updated and recommendations for their management and severity classification were included - Noted that the benefits and risks of corticosteroid treatment should be carefully considered, as it may cause hyperammonemia in this patient population
17 October 2019	Protocol v3.0 with following change to v2.0: - PK sampling during SC administration and the PK parameters to be evaluated were added
05 May 2020	Protocol v4.0 with the following changes to v3.0: - Optional food effect substudy was removed, as no subjects consented to participate - Short-Form 36 evaluation was removed due to no assessment in CAEB1102-101A; no Short-Form 36 data were collected in the trial prior to this protocol amendment - Frequency of assessments were adjusted to reduce subject's burden
09 October 2020	Protocol v5.0 with following changes to v4.0: - Extension of pegzilarginase treatment for up to 4 years if pegzilarginase was not commercially available or otherwise available, e.g. as part of an extended access protocol - Guidance on the COVID-19 pandemic was added

21 May 2021	Protocol v6.0 with following changes to v5.0: - Continuation of treatment with pegzilarginase for subjects who completed Year 4 was allowed, post assessments after Week 192 were added and the study period changed from "up to 4 years (192 weeks of dosing)" to "until available through other means" - Height and clinical growth assessment was added to Week 168 and physical examination to Week 168 and Week 192 to be consistent with assessments being conducted every 24 weeks - Follow-up visit was changed from 4 weeks to 2 weeks post last dose - Identity of study drug was updated to include newest vial presentation: 10-mL single use glass vials with a green cap, containing 5 mL of formulated drug product at a concentration of 5 mg/mL for SC administration - Storage temperature of study drug was changed from "at or below 65°C" to "at or below 60°C" based on stability data - PD samples were updated to include "PD analyses may also be conducted via dried blood spot by fingerstick or via alternate methods as outlined in the lab manual once they are available and will be sent to a designated central laboratory"

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/33325055