Clinical trial results:
A Single arm, Prospective, Open Label, Multicenter Study to Evaluate Efficacy and Safety of One-Year Maximum Dosage in Chinese Label of Imiglucerase Treatment in Chinese Patients who are Diagnosed as Gaucher Disease Type

Summary

EudraCT number	2024-000041-27
Trial protocol	Outside EU/EEA
Global end of trial date	12 October 2023

Results information

Result version number	v1 (current)
This version publication date	25 April 2024
First version publication date	25 April 2024

Trial information

Trial identification

Sponsor protocol code	LPS16031

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04656600
WHO universal trial number (UTN)	U1111-1244-1166

Notes:

Sponsors

Sponsor organisation name	SANOFI (CHINA) INVESTMENT CO., LTD
Sponsor organisation address	7F of HP Building, No.112 Jianguo Road, Chaoyang District, Beijing, China, 100022
Public contact	Trial Transparency Team, Sanofi aventis recherche & développement, Contact-US@sanofi.com
Scientific contact	Trial Transparency Team, Sanofi aventis recherche & développement, Contact-US@sanofi.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?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	07 December 2023
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	12 October 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the efficacy on hematologic manifestations of Cerezyme treatment in Chinese participants who were diagnosed as Gaucher disease type and to evaluate the safety profile of Cerezyme in maximum dose in the label (60 units per kilogram [U/kg], intravenous [IV] biweekly) in Chinese participants.

Protection of trial subjects:

The study was conducted by investigators experienced in the treatment of pediatric particpants. The parent(s) or guardian(s) as well as children were fully informed of all pertinent aspects of the clinical trial as well as the possibility to discontinue at any time. In addition to the consent form for the parent(s)/guardian(s), an assent form in child-appropriate language was provided and explained to the child. Repeated invasive procedures were minimised. The number of blood samples as well as the amount of blood drawn were adjusted according to age and weight. A topical anaesthesia may have been used to minimise distress and discomfort.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	02 March 2021
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	China: 12
Worldwide total number of subjects	12
EEA total number of subjects	0

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)	2
Adolescents (12-17 years)	6

Adults (18-64 years)	4
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted at 5 centers in China. A total of 13 participants were screened from 02 March 2021 to 15 September 2022, of which 1 was screen failure.

Pre-assignment

Screening details:

A total of 12 participants were enrolled in this study.

Period 1

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

Arms

Arm title	Cerezyme

Arm description:

Participants received Cerezyme 60 U/kg by IV infusion once every 2 weeks for 12 months.

Arm type	Experimental
Investigational medicinal product name	Cerezyme
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Cerezyme 60 U/kg was administered by IV infusion once every 2 weeks for 12 months.

Number of subjects in period 1	Cerezyme
Started	12
Completed	12

Baseline characteristics

Reporting groups	
Reporting group title	Cerezyme
Reporting group description:	
Participants received Cerezyme 60 U/kg by IV infusion once every 2 weeks for 12 months.	

Reporting group values	Cerezyme	Total	
Number of subjects	12	12	
Age Categorical Units: Subjects			
Age Continuous Units: years arithmetic mean standard deviation	 18.7 ± 14.10	 -	
Gender Categorical Units: Subjects			
Female Male	3 9	3 9	
Hemoglobin Units: gram per litre (g/L) arithmetic mean standard deviation	 123.7 ± 18.13	 -	
Platelet count Units: 10^9/litre (L) arithmetic mean standard deviation	 193.7 ± 157.45	 -	

End points

End points reporting groups

Reporting group title	Cerezyme

Reporting group description:

Participants received Cerezyme 60 U/kg by IV infusion once every 2 weeks for 12 months.

Primary: Number of Participants With Treatment-emergent Adverse Events (TEAEs) and Treatment-emergent Serious Adverse Events (TESAEs)

End point title	Number of Participants With Treatment-emergent Adverse Events (TEAEs) and Treatment-emergent Serious Adverse Events (TESAEs)[1]

End point description:

An adverse event (AE) is any untoward medical occurrence in a participant or clinical study participant, temporally associated with the use of study treatment, whether or not considered related to the study treatment. TEAEs were defined as the adverse events that occurred between the first dose of study drug and the end of the study. Serious adverse events (SAE): Any untoward medical occurrence that at any dose: resulted in death, was life-threatening, required inpatient hospitalization or prolongation of existing hospitalization, resulted in persistent disability/incapacity, was a congenital anomaly/birth defect, was a medically important event. Safety population included all participants who received at least 1 dose of study intervention.

End point type	Primary

End point timeframe:

From first dose of study treatment (Day 1) up to Day 30 post last dose of study treatment, approximately 13 months

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: As the endpoint is descriptive in nature, no statistical analysis is provided.

End point values	Cerezyme			
Subject group type	Reporting group			
Number of subjects analysed	12			
Units: participants				
TEAE	12			
TESAE	1			

Statistical analyses

No statistical analyses for this end point

Primary: Mean Change From Baseline in Platelet Count at Month 12

End point title	Mean Change From Baseline in Platelet Count at Month 12[2]

End point description:

The mean change in platelet count from baseline to Month 12 was assessed. Evaluable population included all participants with no critical protocol deviations. Only those participants with data available were analyzed.

End point type	Primary

End point timeframe:

Baseline and Month 12

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: As the endpoint is descriptive in nature, no statistical analysis is provided.

End point values	Cerezyme			
Subject group type	Reporting group			
Number of subjects analysed	11			
Units: 10^9/L				
arithmetic mean (standard deviation)	112.9 (± 98.09)			

Statistical analyses

No statistical analyses for this end point

Primary: Mean Change From Baseline in Hemoglobin at Month 12

End point title	Mean Change From Baseline in Hemoglobin at Month 12[3]

End point description:

The mean change in hemoglobin from baseline to Month 12 was assessed. Evaluable population included all participants with no critical protocol deviations. Only those participants with data available were analyzed.

End point type	Primary

End point timeframe:

Baseline and Month 12

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: As the endpoint is descriptive in nature, no statistical analysis is provided.

End point values	Cerezyme			
Subject group type	Reporting group			
Number of subjects analysed	11			
Units: g/L				
arithmetic mean (standard deviation)	12.8 (± 11.33)			

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change From Baseline in Liver and Spleen Volume at Month 12

End point title	Mean Change From Baseline in Liver and Spleen Volume at Month 12

End point description:

Magnetic resonance imaging (MRI) was used for volumetric measurement of liver and spleen. The mean change in liver and spleen volumes from baseline to Month 12 was assessed. Negative value signifies

reduction of volume. Evaluable population included all participants with no critical protocol deviations. Only those participants with data available were analyzed. Here 'n'= number of participants with available data for a particular category.

End point type	Secondary

End point timeframe:

Baseline and Month 12

End point values	Cerezyme			
Subject group type	Reporting group			
Number of subjects analysed	10			
Units: multiples of normal (MN)				
arithmetic mean (standard deviation)				
Spleen Volume (n=7)	-7.334 (± 4.393)			
Liver Volume (n=10)	-0.558 (± 0.445)			

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change from Baseline in Quality of life (QoL) as Assessed by SF-12v2 Health Survey (SF-12v2) at Months 3, 6, 9, and 12

End point title	Mean Change from Baseline in Quality of life (QoL) as Assessed by SF-12v2 Health Survey (SF-12v2) at Months 3, 6, 9, and 12

End point description:

The SF-12v2 was used to assess the participant's functional health and well-being. SF-12v2 transformed health domain scale total raw scores to 0–100 scores, where higher score means better level of physical and mental health. Evaluable population included all participants with no critical protocol deviations. Only adult participants were included for the analysis of this endpoint.

End point type	Secondary

End point timeframe:

Baseline and Months 3, 6, 9, and 12

End point values	Cerezyme			
Subject group type	Reporting group			
Number of subjects analysed	5			
Units: score on a scale				
arithmetic mean (standard deviation)				
Mental Health Score: Month 3	-1.42 (± 10.263)			
Mental Health Score: Month 6	2.49 (± 8.029)			
Mental Health Score: Month 9	0.55 (± 6.151)			
Mental Health Score: Month 12	2.96 (± 8.981)			
Physical Health Score: Month 3	-2.67 (± 3.067)			

Physical Health Score: Month 6	-4.64 (± 4.514)			
Physical Health Score: Month 9	-3.83 (± 2.798)			
Physical Health Score: Month 12	-4.07 (± 4.419)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in the Number of Bone Crisis at Month 12

End point title	Change From Baseline in the Number of Bone Crisis at Month 12

End point description:

The number of bone crises were recorded at baseline and up to the end of study. Bone crisis was defined as pain with acute onset which required immobilization of the affected area, narcotics for relief of pain and might be accompanied by one or more of the following: periosteal elevation, elevated white blood cell count, fever, or debilitation of >3 days. Evaluable population included all participants with no critical protocol deviations. Only those participants with data available were analyzed.

End point type	Secondary

End point timeframe:

Baseline and Month 12

End point values	Cerezyme			
Subject group type	Reporting group			
Number of subjects analysed	11			
Units: times				
arithmetic mean (standard deviation)	0.0 (± 0.0)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Severity of Bone Pain at Month 12

End point title	Change From Baseline in Severity of Bone Pain at Month 12

End point description:

The severity of bone pain was assessed at baseline and up to end of study. Numeric Rating Scale (NRS) was used to evaluate the severity of bone pain. All participants were asked the following question: 'How would you rate your bone pain?'. Score range 0-10 was used to represent the level of pain, where higher scores indicate more severe bone pain. Evaluable population included all participants with no critical protocol deviations.

End point type	Secondary

End point timeframe:

Baseline and Month 12

End point values	Cerezyme			
Subject group type	Reporting group			
Number of subjects analysed	12			
Units: score on a scale				
arithmetic mean (standard deviation)	-1.13 (± 1.625)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Duration of Bone Pain at Month 12

End point title	Change From Baseline in Duration of Bone Pain at Month 12

End point description:

The duration of bone pain was assessed at baseline and up to end of study. All participants were asked the following question: 'How long did single bone pain attack last?'. For bone pain occurring after walking or related to exertion, duration of bone pain was classified as "pain on exertion or exertion"; for intermittent, irregular and occasional bone pain, duration of bone pain was categorized as "intermittent or irregular pain"; for persistent pain, duration of bone pain was categorized as "persistent bone pain". Evaluable population included all participants with no critical protocol deviations. Only those participants with data available were analyzed.

End point type	Secondary

End point timeframe:

Baseline and Month 12

End point values	Cerezyme			
Subject group type	Reporting group			
Number of subjects analysed	7			
Units: minutes				
median (full range (min-max))	0.0 (-320 to 0)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Frequency of Bone Pain at Month 12

End point title	Change From Baseline in Frequency of Bone Pain at Month 12

End point description:

The frequency of bone pain was assessed at baseline and up to end of study. All participants were asked the following question: 'What is the frequency of your bone pain during last month?'. For bone pain occurring after walking or related to exertion, frequency of bone pain was classified as "pain on exertion or exertion"; for intermittent, irregular and occasional bone pain, frequency of bone pain was

categorized as "intermittent or irregular pain"; for persistent pain, frequency of bone pain was defined as 30 times/month. Evaluable population included all participants with no critical protocol deviations. Only those participants with data available were analyzed.

End point type	Secondary

End point timeframe:

Baseline and Month 12

End point values	Cerezyme			
Subject group type	Reporting group			
Number of subjects analysed	8			
Units: times/month				
arithmetic mean (standard deviation)	14.84 (± 47.750)			

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change from Baseline in QoL as Assessed by Measurement Model for the Pediatric Quality of Life Inventory (PedsQL) at Months 3, 6, 9, and 12

End point title	Mean Change from Baseline in QoL as Assessed by Measurement Model for the Pediatric Quality of Life Inventory (PedsQL) at Months 3, 6, 9, and 12

End point description:

The PedsQL was used to assess health-related quality of life in children. For the young child (aged 7 and below), the PedsQL was administered by their parents. Children aged 8-18 self-administered the PedsQL. Participants reported their function using a 5-point Likert scale ranging from 0 to 4. The responses were reverse scored and linearly transformed to a 0 to 100 scale, with a higher score indicating a higher QOL in pediatrics. Evaluable population included all participants with no critical protocol deviations. Only pediatric participants were included for the analysis of this endpoint. Here ’n’= number of participants with available data for a particular category.

End point type	Secondary

End point timeframe:

Baseline and Months 3, 6, 9, and 12

End point values	Cerezyme			
Subject group type	Reporting group			
Number of subjects analysed	7			
Units: score on a scale				
arithmetic mean (standard deviation)				
Mental Health Score: Month 3 (n=7)	-3.33 (± 8.156)			
Mental Health Score: Month 6 (n=7)	-3.49 (± 11.509)			
Mental Health Score: Month 9 (n=6)	-4.92 (± 6.540)			

Mental Health Score: Month 12 (n=7)	-6.70 (± 12.085)			
Physical Health Score: Month 3 (n=3)	1.34 (± 25.816)			
Physical Health Score: Month 6 (n=7)	1.33 (± 25.938)			
Physical Health Score: Month 9 (n=6)	1.05 (± 20.510)			
Physical Health Score: Month 12 (n=7)	-6.26 (± 25.060)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
From first dose of study treatment (Day 1) up to Day 30 post last dose of study treatment, approximately 13 months	
Adverse event reporting additional description:	
Safety population included all participants who received at least 1 dose of study intervention.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	26.1

Reporting groups	
Reporting group title	Cerezyme
Reporting group description:	
Participants received Cerezyme 60 U/kg by IV infusion once every 2 weeks for 12 months.	

Serious adverse events	Cerezyme		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 12 (8.33%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Injury, poisoning and procedural complications			
Humerus Fracture			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Cerezyme		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	12 / 12 (100.00%)		
Investigations			
Blood Homocysteine Increased			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Alanine Aminotransferase Increased			

subjects affected / exposed occurrences (all) Electrocardiogram T Wave Peaked subjects affected / exposed occurrences (all) Neutrophil Count Decreased subjects affected / exposed occurrences (all) Vitamin B12 Decreased subjects affected / exposed occurrences (all) Blood Folate Decreased subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1 1 / 12 (8.33%) 1 1 / 12 (8.33%) 1 1 / 12 (8.33%) 1 1 / 12 (8.33%) 1		
Injury, poisoning and procedural complications Skin Abrasion subjects affected / exposed occurrences (all) Lip Injury subjects affected / exposed occurrences (all) Face Injury subjects affected / exposed occurrences (all)	 1 / 12 (8.33%) 1 1 / 12 (8.33%) 1 2 / 12 (16.67%) 2		
Cardiac disorders Arrhythmia Supraventricular subjects affected / exposed occurrences (all) Tachycardia subjects affected / exposed occurrences (all)	 1 / 12 (8.33%) 1 1 / 12 (8.33%) 1		
Nervous system disorders Lethargy subjects affected / exposed occurrences (all) Ataxia	 1 / 12 (8.33%) 1		

subjects affected / exposed occurrences (all) Dizziness subjects affected / exposed occurrences (all) Epilepsy subjects affected / exposed occurrences (all) Generalised Tonic-Clonic Seizure subjects affected / exposed occurrences (all) Headache subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1 1 / 12 (8.33%) 1 4 / 12 (33.33%) 4 1 / 12 (8.33%) 1 1 / 12 (8.33%) 1		
General disorders and administration site conditions Fatigue subjects affected / exposed occurrences (all) Pyrexia subjects affected / exposed occurrences (all)	 1 / 12 (8.33%) 1 2 / 12 (16.67%) 2		
Eye disorders Refraction Disorder subjects affected / exposed occurrences (all) Ocular Hypertension subjects affected / exposed occurrences (all) Amblyopia subjects affected / exposed occurrences (all)	 2 / 12 (16.67%) 2 1 / 12 (8.33%) 1 1 / 12 (8.33%) 1		
Gastrointestinal disorders Diarrhoea subjects affected / exposed occurrences (all) Abdominal Pain Upper	 2 / 12 (16.67%) 2		

subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Abdominal Pain			
subjects affected / exposed	2 / 12 (16.67%)		
occurrences (all)	2		
Nausea			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Vomiting			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Rhinitis Allergic			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Productive Cough			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Sneezing			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Skin and subcutaneous tissue disorders			
Dermatitis Allergic			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Rash			
subjects affected / exposed	2 / 12 (16.67%)		
occurrences (all)	2		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	3 / 12 (25.00%)		
occurrences (all)	3		
Arthritis			

subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Bone Infarction			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Bone Pain			
subjects affected / exposed	2 / 12 (16.67%)		
occurrences (all)	2		
Pain In Extremity			
subjects affected / exposed	2 / 12 (16.67%)		
occurrences (all)	2		
Infections and infestations			
Upper Respiratory Tract Infection			
subjects affected / exposed	4 / 12 (33.33%)		
occurrences (all)	4		
Respiratory Tract Infection			
subjects affected / exposed	2 / 12 (16.67%)		
occurrences (all)	2		
Nasopharyngitis			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Covid-19			
subjects affected / exposed	2 / 12 (16.67%)		
occurrences (all)	2		
Conjunctivitis			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Herpes Virus Infection			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Metabolism and nutrition disorders			
Hyperphosphataemia			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Hypocalcaemia			

subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Hypokalaemia			
subjects affected / exposed	2 / 12 (16.67%)		
occurrences (all)	2		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
30 June 2020	The amendment of the protocol was mainly based on the communication with Center for Drug Evaluation of National Medical Products Administration of China. The major change was to include Gaucher Disease type Chinese participants instead of Gaucher Disease participants with significant change of electroencephalogram. There were also changes in inclusion and exclusion criteria based on opinions from principal investigators.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported