



Clinical trial results:

A Phase 4, Open Label, Safety and Efficacy Study of Fabrazyme® (Agalsidase Beta) as Enzyme Replacement Therapy in Chinese Subjects With Fabry Disease

Summary

EudraCT number	2023-000624-11
Trial protocol	Outside EU/EEA
Global end of trial date	09 March 2023

Results information

Result version number	v1 (current)
This version publication date	14 September 2023
First version publication date	14 September 2023

Trial information

Trial identification

Sponsor protocol code	LPS16583
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05054387
WHO universal trial number (UTN)	U1111-1255-4881

Notes:

Sponsors

Sponsor organisation name	Sanofi B.V.
Sponsor organisation address	Paasheuvelweg 25, BP Amsterdam, Netherlands, 1105
Public contact	Trial Transparency Team, Sanofi Recherche et Développement, Contact-US@sanofi.com
Scientific contact	Trial Transparency Team, Sanofi Recherche et 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	27 March 2023
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	09 March 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the safety and tolerability of Fabrazyme in Chinese fabry disease subjects.

Protection of trial subjects:

The study was conducted by investigators experienced in the treatment of adults and paediatric subjects. The parent(s) or guardian(s) as well as the 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 anesthesia may have been used to minimise distress and discomfort. Adult subjects were fully informed of all pertinent aspects of the clinical trial as well as the possibility to discontinue at any time in language and terms appropriate for the subject and considering the local culture. During the course of the trial, subjects were provided with individual subject cards indicating the nature of the trial the subject is participating, contact details and any information needed in the event of a medical emergency. Collected personal data and human biological samples were processed in compliance with the Sanofi-Aventis Group Personal Data Protection Charter ensuring that the Group abides by the laws governing personal data protection in force in all countries in which it operates.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	13 October 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: 22
Worldwide total number of subjects	22
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	0

months)	
Children (2-11 years)	2
Adolescents (12-17 years)	2
Adults (18-64 years)	18
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted at 6 centers in China between 13-October-2021 to 09-March-2023.

Pre-assignment

Screening details:

A total of 22 subjects were enrolled and treated in the study.

Period 1

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

Arms

Arm title	Fabrazyme: All Subjects
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Arm description:

Subjects received agalsidase beta (Fabrazyme) intravenous (IV) infusion at a dose of 1 milligram per kilogram (mg/kg) body weight, every other week (Q2W) for up to Week 48.

Arm type	Experimental
Investigational medicinal product name	Agalsidase beta
Investigational medicinal product code	GZ419828
Other name	Fabrazyme
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous bolus use

Dosage and administration details:

Agalsidase beta IV infusion, 1 mg/kg body weight, Q2W.

Number of subjects in period 1	Fabrazyme: All Subjects
Started	22
Completed	22

Baseline characteristics

Reporting groups

Reporting group title	Overall Period
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Reporting group description:

Subjects received agalsidase beta (Fabrazyme) IV infusion at a dose of 1 mg/kg body weight, Q2W for up to Week 48.

Reporting group values	Overall Period	Total	
Number of subjects	22	22	
Age categorical Units: Subjects			
Age continuous Units: years arithmetic mean standard deviation	29.0 ± 13.5	-	
Gender categorical Units: Subjects			
Female	4	4	
Male	18	18	

End points

End points reporting groups

Reporting group title	Fabrazyme: All Subjects
Reporting group description: Subjects received agalsidase beta (Fabrazyme) intravenous (IV) infusion at a dose of 1 milligram per kilogram (mg/kg) body weight, every other week (Q2W) for up to Week 48.	

Primary: Number of Subjects with Treatment-emergent Adverse Events (TEAEs), Serious Adverse Events (SAEs), and Adverse Events of Special Interest (AESIs)

End point title	Number of Subjects with Treatment-emergent Adverse Events (TEAEs), Serious Adverse Events (SAEs), and Adverse Events of Special Interest (AESIs) ^[1]
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End point description:

Adverse Event (AE) was defined as any untoward medical occurrence in subject who received study drug and did not necessarily had a causal relationship with treatment. TEAEs were defined as AEs that developed, worsened/became serious during treatment-emergent period (time from 1st dose of study drug to the last dose of study drug + 14 days). SAE was any AE that at any dose: resulted in death, was life-threatening, required inpatient hospitalisation or prolongation of existing hospitalisation, resulted in persistent or significant disability/incapacity, was a congenital anomaly/birth defect, was medically important event or was suspected transmission of any infectious agent via authorised medicinal product. AESI was any AE of scientific and medical concern specific to the study for which ongoing monitoring and immediate notification to the Sponsor was required. Analysis performed on exposed population which included all enrolled subjects who had taken at least one dose of study drug.

End point type	Primary
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End point timeframe:

From first dose of study drug up to 14 days after last dose of study drug (i.e., up to Week 50)

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 was descriptive in nature, no statistical analysis was provided.

End point values	Fabrazyme: All Subjects			
Subject group type	Reporting group			
Number of subjects analysed	22			
Units: Subjects				
TEAEs	22			
SAEs	2			
AESIs	8			

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects with Infusion Associated Reactions (IARs)

End point title	Number of Subjects with Infusion Associated Reactions
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End point description:

Adverse Event was defined as any untoward medical occurrence in subject who received study drug and did not necessarily had a causal relationship with treatment. Infusion Associated Reactions (IARs) were

the AEs that occurred during the infusion or within 24 hours after the start of infusion and was considered as related or possibly related to the study intervention by the Investigator or the Sponsor. An event occurring ≥ 24 hours after the start of an infusion may be deemed an IAR if a delayed reaction was considered possible by the Investigator or the Sponsor. Analysis was performed on exposed population.

End point type	Primary
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End point timeframe:

From first dose of study drug up to Week 48

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 was descriptive in nature, no statistical analysis was provided.

End point values	Fabrazyme: All Subjects			
Subject group type	Reporting group			
Number of subjects analysed	22			
Units: Subjects	8			

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute Change From Baseline in Plasma Lyso-GL-3 at Weeks 6, 12, 24 and 48

End point title	Absolute Change From Baseline in Plasma Lyso-GL-3 at Weeks 6, 12, 24 and 48
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End point description:

Change in Plasma globotriaosylsphingosine-3 (Lyso-GL-3) values in blood was evaluated by measuring level of total plasma lyso-GL-3. Blood samples were collected at Baseline, Week 6, Week 12, Week 24 and Week 48 to evaluate the absolute change in plasma lyso-GL-3 from Baseline. Analysis performed on exposed population. Here 'n' refers to the number of subjects with available data for each specified category.

End point type	Secondary
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End point timeframe:

Baseline, Week 6, 12, 24 and 48

End point values	Fabrazyme: All Subjects			
Subject group type	Reporting group			
Number of subjects analysed	22			
Units: microgram(s) per litre (mcg/L)				
arithmetic mean (standard deviation)				
Week 6 (n=16)	-45.758 (\pm 29.607)			
Week 12 (n=14)	-37.275 (\pm 31.187)			
Week 24 (n=18)	-43.241 (\pm 32.193)			
Week 48 (n=20)	-44.230 (\pm 32.934)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change From Baseline in Plasma Lyso-GL-3 at Weeks 6, 12, 24 and 48

End point title	Percent Change From Baseline in Plasma Lyso-GL-3 at Weeks 6, 12, 24 and 48
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End point description:

Change in Plasma Lyso-GL-3 values in blood was evaluated by measuring level of total plasma lyso-GL-3. Blood samples were collected at Baseline, Week 6, Week 12, Week 24 and Week 48 to evaluate the percent change in plasma lyso-GL-3 from Baseline. Percent change from Baseline was calculated as: Percent change = (post-baseline value-Baseline value)/Baseline value *100%. Analysis performed on exposed population. Here 'n' refers to the number of subjects with available data for each specified category.

End point type	Secondary
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End point timeframe:

Baseline, Week 6, 12, 24 and 48

End point values	Fabrazyme: All Subjects			
Subject group type	Reporting group			
Number of subjects analysed	22			
Units: percent change				
arithmetic mean (standard deviation)				
Week 6 (n=16)	-64.881 (± 12.684)			
Week 12 (n=14)	-58.837 (± 20.181)			
Week 24 (n=18)	-61.745 (± 18.781)			
Week 48 (n=20)	-60.320 (± 21.957)			

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute Change From Baseline in Plasma GL-3 at Weeks 6, 12, 24 and 48

End point title	Absolute Change From Baseline in Plasma GL-3 at Weeks 6, 12, 24 and 48
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End point description:

Change in plasma Globotriaosylceramide -3 (GL-3) values in blood was evaluated by measuring level of

total plasma GL-3. Blood samples were collected at Baseline, Week 6, Week 12, Week 24 and Week 48 to evaluate the absolute change in plasma GL-3 from Baseline. Analysis was performed on exposed population. Here 'n' refers to the number of subjects with available data for each specified category.

End point type	Secondary
End point timeframe:	
Baseline, Week 6, 12, 24 and 48	

End point values	Fabrazyme: All Subjects			
Subject group type	Reporting group			
Number of subjects analysed	22			
Units: milligram(s) per litre (mg/L)				
arithmetic mean (standard deviation)				
Week 6 (n=16)	-3.289 (± 1.922)			
Week 12 (n=14)	-2.693 (± 1.999)			
Week 24 (n=18)	-3.257 (± 2.173)			
Week 48 (n=20)	-2.921 (± 2.442)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change From Baseline in Plasma GL-3 at Weeks 6, 12, 24 and 48

End point title	Percent Change From Baseline in Plasma GL-3 at Weeks 6, 12, 24 and 48
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End point description:

Change in plasma GL-3 values in blood was evaluated by measuring level of total plasma GL-3. Blood samples were collected at Baseline, Week 6, Week 12, Week 24 and Week 48 to evaluate the absolute change in plasma GL-3 from Baseline. Percent change from Baseline was calculated as Percent change = (post-Baseline value-Baseline value)/Baseline value *100 %. Analysis was performed on exposed population. Here 'n' refers to the number of subjects with available data for each specified category.

End point type	Secondary
End point timeframe:	
Baseline, Week 6, 12, 24 and 48	

End point values	Fabrazyme: All Subjects			
Subject group type	Reporting group			
Number of subjects analysed	22			
Units: percent change				
arithmetic mean (standard deviation)				
Week 6 (n=16)	-41.932 (± 14.899)			

Week 12 (n=14)	-36.404 (± 19.205)			
Week 24 (n=18)	-41.458 (± 16.807)			
Week 48 (n=20)	-34.577 (± 27.356)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Abnormal Plasma GL-3 Values at Weeks 6, 12, 24 and 48

End point title	Number of Subjects With Abnormal Plasma GL-3 Values at Weeks 6, 12, 24 and 48
End point description:	Number of subjects with abnormal plasma GL-3 values per the central lab reference range were presented in this endpoint. Blood samples for the estimation of plasma GL-3 values were collected at Week 6, 12, 24 and 48. Analysis was performed on exposed population.
End point type	Secondary
End point timeframe:	At Week 6, 12, 24 and 48

End point values	Fabrazyme: All Subjects			
Subject group type	Reporting group			
Number of subjects analysed	22			
Units: Subjects				
Week 6	13			
Week 12	8			
Week 24	12			
Week 48	13			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Change From Baseline in Fabry Disease Symptoms Assessment at Week 24 and Week 48

End point title	Number of Subjects with Change From Baseline in Fabry Disease Symptoms Assessment at Week 24 and Week 48
End point description:	Fabry disease symptoms (angiokeratoma, sweating, chronic abdominal pain, level of activity, exercise tolerance and heat tolerance, headache, tinnitus) were assessed at Baseline, Week 24 and Week 48 to determine the change in the symptoms from Baseline at the specified timepoints. The disease symptoms were assessed as improved, worsened or same. Analysis was performed on exposed population. Here 'n' refers to the number of subjects with available data for each specified category.
End point type	Secondary

End point timeframe:

From Baseline up to Week 24 and Week 48

End point values	Fabrazyme: All Subjects			
Subject group type	Reporting group			
Number of subjects analysed	22			
Units: Subjects				
Week 24 - Improved (n=22)	8			
Week 24 - Worsen (n=22)	0			
Week 24 - Same (n=22)	14			
Week 48 - Improved (n=21)	13			
Week 48 - Worsen (n=21)	0			
Week 48 - Same (n=21)	8			

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute Change From Baseline in Estimated Glomerular Filtration Rate (eGFR) at Weeks 12, 24, 36 and 48

End point title	Absolute Change From Baseline in Estimated Glomerular Filtration Rate (eGFR) at Weeks 12, 24, 36 and 48			
End point description:	Estimated Glomerular Filtration Rate (eGFR) was estimated from serum creatinine using Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) formula for adults and from serum creatinine and height using Bedside Schwartz Formula for children (less than equal to 8 years of age to less than 18 years of age). Analysis was performed on exposed population. Here 'n' refers to the number of subjects with available data for each specified category.			
End point type	Secondary			
End point timeframe:	Baseline, Week 12, 24, 36 and 48			

End point values	Fabrazyme: All Subjects			
Subject group type	Reporting group			
Number of subjects analysed	22			
Units: millilitre/minute/1.73 metre square				
arithmetic mean (standard deviation)				
Week 12 (n=14)	1.5 (± 10.5)			
Week 24 (n=18)	-0.1 (± 17.8)			
Week 36 (n=15)	0.4 (± 16.1)			
Week 48 (n=20)	0.0 (± 12.4)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From first dose of study drug up to 14 days after last dose of study drug (i.e., up to Week 50)

Adverse event reporting additional description:

Analysis was performed on exposed population.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	25.1
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Reporting groups

Reporting group title	Fabrazyme
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Reporting group description:

Subjects received agalsidase beta (Fabrazyme), IV infusion at a dose of 1 mg/kg body weight, Q2W for up to Week 48.

Serious adverse events	Fabrazyme		
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 22 (9.09%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Nervous system disorders			
Tension Headache			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
End Stage Renal Disease			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Fabrazyme		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	22 / 22 (100.00%)		

General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	3 / 22 (13.64%)		
occurrences (all)	4		
Oedema Peripheral			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		
Non-Cardiac Chest Pain			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		
Asthenia			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	2		
Chest Discomfort			
subjects affected / exposed	2 / 22 (9.09%)		
occurrences (all)	2		
Chills			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	2		
Feeling Hot			
subjects affected / exposed	3 / 22 (13.64%)		
occurrences (all)	5		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		
Epistaxis			
subjects affected / exposed	2 / 22 (9.09%)		
occurrences (all)	2		
Oropharyngeal Pain			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		
Rhinorrhoea			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		
Psychiatric disorders			

Depression subjects affected / exposed occurrences (all)	1 / 22 (4.55%) 1		
Investigations Red Blood Cell Sedimentation Rate Increased subjects affected / exposed occurrences (all) C-Reactive Protein Increased subjects affected / exposed occurrences (all) Weight Decreased subjects affected / exposed occurrences (all) Weight Increased subjects affected / exposed occurrences (all)	1 / 22 (4.55%) 1 1 / 22 (4.55%) 1 2 / 22 (9.09%) 2 1 / 22 (4.55%) 1		
Nervous system disorders Dizziness subjects affected / exposed occurrences (all) Headache subjects affected / exposed occurrences (all)	3 / 22 (13.64%) 3 1 / 22 (4.55%) 1		
Blood and lymphatic system disorders Nephrogenic Anaemia subjects affected / exposed occurrences (all)	1 / 22 (4.55%) 1		
Eye disorders Vision Blurred subjects affected / exposed occurrences (all)	1 / 22 (4.55%) 2		
Gastrointestinal disorders Vomiting subjects affected / exposed occurrences (all) Toothache	2 / 22 (9.09%) 2		

<p>subjects affected / exposed occurrences (all)</p> <p>Nausea subjects affected / exposed occurrences (all)</p> <p>Diarrhoea subjects affected / exposed occurrences (all)</p> <p>Constipation subjects affected / exposed occurrences (all)</p>	<p>1 / 22 (4.55%) 1</p> <p>3 / 22 (13.64%) 4</p> <p>1 / 22 (4.55%) 1</p> <p>1 / 22 (4.55%) 1</p>		
<p>Hepatobiliary disorders Cholelithiasis subjects affected / exposed occurrences (all)</p>	<p>1 / 22 (4.55%) 1</p>		
<p>Skin and subcutaneous tissue disorders Rash subjects affected / exposed occurrences (all)</p> <p>Pruritus subjects affected / exposed occurrences (all)</p>	<p>1 / 22 (4.55%) 1</p> <p>3 / 22 (13.64%) 5</p>		
<p>Renal and urinary disorders Renal Hypertension subjects affected / exposed occurrences (all)</p>	<p>1 / 22 (4.55%) 1</p>		
<p>Endocrine disorders Hyperparathyroidism Secondary subjects affected / exposed occurrences (all)</p>	<p>1 / 22 (4.55%) 1</p>		
<p>Musculoskeletal and connective tissue disorders Pain In Extremity subjects affected / exposed occurrences (all)</p> <p>Myalgia</p>	<p>2 / 22 (9.09%) 3</p>		

subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		
Chronic Kidney Disease-Mineral And Bone Disorder			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		
Ankylosing Spondylitis			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		
Infections and infestations			
Gastroenteritis			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		
Cholecystitis Infective			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		
Covid-19			
subjects affected / exposed	14 / 22 (63.64%)		
occurrences (all)	14		
Influenza			
subjects affected / exposed	4 / 22 (18.18%)		
occurrences (all)	5		
Otitis Media			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		
Upper Respiratory Tract Infection			
subjects affected / exposed	4 / 22 (18.18%)		
occurrences (all)	7		
Urinary Tract Infection			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		
Metabolism and nutrition disorders			
Hyperhomocysteinaemia			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		
Hyperphosphataemia			

subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		
Hypoproteinaemia			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		
Hypocalcaemia			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		
Hyperuricaemia			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported