Clinical trial results:
A Phase 4, single-arm, open-label safety and efficacy study of Aldurazyme® (laronidase) as enzyme replacement therapy in participants with Mucopolysaccharidosis I (MPS I) in China

Summary

EudraCT number	2023-001027-16
Trial protocol	Outside EU/EEA
Global end of trial date	26 July 2023

Results information

Result version number	v1 (current)
This version publication date	01 February 2024
First version publication date	01 February 2024

Trial information

Trial identification

Sponsor protocol code	LPS16578

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05134571
WHO universal trial number (UTN)	U1111-1260-3947

Notes:

Sponsors

Sponsor organisation name	Sanofi B.V.
Sponsor organisation address	Paasheuvelweg 25, Amsterdam, Netherlands, 1105 BP
Public contact	Trial Transparency Team, Sanofi-Aventis Recherche & Developpement, Contact-US@sanofi.com
Scientific contact	Trial Transparency Team, Sanofi-Aventis Recherche & Developpement, 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	14 August 2023
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	26 July 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 aldurazyme in Chinese mucopolysaccharidosis I (MPS I) participants.
• To evaluate the efficacy of aldurazyme on urinary glycosaminoglycans (uGAGs) after 26 weeks of treatment in Chinese MPS I participants.

Protection of trial subjects:

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	28 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: 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)	7
Adolescents (12-17 years)	1

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 active centers in China between 28 October 2021 and 26 July 2023. A total of 12 subjects were screened in this study and there were no screening failures.

Pre-assignment

Screening details:

A total of 12 subjects were treated in the study. This was a single-arm, open-label 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	Aldurazyme

Arm description:

Subjects were treated with aldurazyme 100 units per kilogram (U/kg) of body weight intravenous (IV) infusion once weekly (QW) up to 26 weeks.

Arm type	Experimental
Investigational medicinal product name	Aldurazyme
Investigational medicinal product code	
Other name	Laronidase
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Aldurazyme 100 U/kg of body weight through IV infusion QW up to 26 weeks.

Number of subjects in period 1	Aldurazyme
Started	12
Completed	12

Baseline characteristics

Reporting groups	
Reporting group title	Aldurazyme
Reporting group description:	
Subjects were treated with aldurazyme 100 units per kilogram (U/kg) of body weight intravenous (IV) infusion once weekly (QW) up to 26 weeks.	

Reporting group values	Aldurazyme	Total	
Number of subjects	12	12	
Age categorical Units: Subjects			
Age continuous Units: years arithmetic mean standard deviation	 13.8 ± 7.7	 -	
Gender categorical Units: Subjects			
Female	4	4	
Male	8	8	

End points

End points reporting groups

Reporting group title	Aldurazyme

Reporting group description:

Subjects were treated with aldurazyme 100 units per kilogram (U/kg) of body weight intravenous (IV) infusion once weekly (QW) up to 26 weeks.

Primary: Number of Participants With Treatment Emergent Adverse Events (TEAEs) and Treatment Emergent Serious Adverse Events (SAEs)

End point title	Number of Participants With Treatment Emergent Adverse Events (TEAEs) and Treatment Emergent Serious Adverse Events (SAEs)[1]

End point description:

An adverse event (AE) is any untoward medical occurrence in a subject or clinical study subject, temporally associated with the use of study intervention, whether or not considered related to the study intervention. A SAE is any untoward medical occurrence that results: death or life-threatening or inpatient hospitalization or prolongation of existing hospitalization or persistent or significant disability or congenital anomaly or medically important event. TEAEs are defined as AEs that develop or worsen during the on-treatment period [that is, from the time of first dose of study intervention up to 7 days after the last administration of the study intervention]. Results are based on the safety analysis set which included all enrolled subjects who received at least 1 dose of study intervention.

End point type	Primary

End point timeframe:

From first dose administration (Day 1) up to Week 27

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: Only descriptive statistical analysis was performed for the primary endpoint.

End point values	Aldurazyme			
Subject group type	Reporting group			
Number of subjects analysed	12			
Units: Subjects				
any TEAE	11			
any treatment emergent SAE	1			
any TEAE leading to death	0			

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants With Potentially Clinically Significant Abnormalities in Clinical Laboratory Parameters

End point title	Number of Participants With Potentially Clinically Significant Abnormalities in Clinical Laboratory Parameters[2]

End point description:

Blood samples were collected to determine the clinical chemistry laboratory abnormalities. Results are based on the safety analysis set which included all enrolled subjects who received at least 1 dose of study intervention.

End point type	Primary

End point timeframe:

From first dose administration (Day 1) up to Week 27

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: Only descriptive statistical analysis was performed for the primary endpoint.

End point values	Aldurazyme			
Subject group type	Reporting group			
Number of subjects analysed	12			
Units: Subjects				
Hemoglobin: Decrease from baseline	1			
Platelet count: Low	2			
Eosinophils: High	1			
Lymphocytes: High	1			
Leukocyte count: Low	1			
Urea nitrogen: High	2			

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants With Potentially Clinically Significant Abnormalities in Electrocardiogram (ECG)

End point title	Number of Participants With Potentially Clinically Significant Abnormalities in Electrocardiogram (ECG)[3]

End point description:

Single 12-lead ECGs were recorded after at least 10 minutes rest in the supine position using an electrocardiographic device. The following were assessed: heart rate (HR), PR interval, QRS duration, QT interval and corrected QTc (method unspecified). Results are based on the safety analysis set which included all enrolled subjects who received at least 1 dose of study intervention. Here, n= number of subjects analyzed for each parameter.

End point type	Primary

End point timeframe:

From first dose administration (Day 1) up to Week 27

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: Only descriptive statistical analysis was performed for the primary endpoint.

End point values	Aldurazyme			
Subject group type	Reporting group			
Number of subjects analysed	12[4]			
Units: Subjects				
HR: High, >= Grade 1	2			
HR: High, >= Grade 2	1			
HR: High and increase from baseline, all Grades	2			
HR: High and increase from baseline >= Grade 1	2			

HR: High and increase from baseline >= Grade 2	1			
PR interval: High, all Grades	1			
QTc correction: High, >= Grade 1	2			
QTc correction: Increase from baseline, Grade 1	2			

Notes:

[4] - n= 4 for HR:High, >= Grade 1 and Grade 2; HR:High and increase from baseline >= Grade 1 and Grade 2.

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants With Potentially Clinically Significant Abnormalities in Vital Signs

End point title	Number of Participants With Potentially Clinically Significant Abnormalities in Vital Signs[5]

End point description:

Subjects vital signs were examined to determine the abnormalities. Vital signs included HR, systolic blood pressure (SBP) and diastolic blood pressure (DBP), weight, respiratory rate, temperature and height. Results are based on the safety analysis set which included all enrolled subjects who received at least 1 dose of study intervention. Here, n= number of subjects analyzed for each parameter.

End point type	Primary

End point timeframe:

From first dose administration (Day 1) up to Week 27

Notes:

[5] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive statistical analysis was performed for the primary endpoint.

End point values	Aldurazyme			
Subject group type	Reporting group			
Number of subjects analysed	12[6]			
Units: Subjects				
SBP: Low and decrease from baseline	3			
SBP: High and increase from baseline	1			
DBP: Low and decrease from baseline	5			
DBP: High and increase from baseline	6			
HR: High and increase from baseline	1			
Weight: Decrease from baseline	3			
Weight: Increase from baseline	2			
Respiratory rate: Low	2			
Respiratory rate: High	3			

Notes:

[6] - n= 4 for HR, weight: Increase from baseline.
n= 8 for respiratory rate.

Statistical analyses

No statistical analyses for this end point

Primary: Percent Change From Baseline in Urinary Glycosaminoglycan (uGAGs) at Week 26

End point title	Percent Change From Baseline in Urinary Glycosaminoglycan

	(uGAGs) at Week 26[7]

End point description:

Urine samples collected and performed analysis at central lab to determine the uGAG level. The missing value was imputed by carrying forward the last uGAG value [last observation carried forward (LOCF) method] observed during the on-treatment period. Results are based on the modified intent-to-treat (mITT) analysis set which included all enrolled subjects who received at least 1 dose of study intervention and with an evaluable primary efficacy endpoint.

End point type	Primary

End point timeframe:

Baseline (Day 1) and Week 26

Notes:

[7] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive statistical analysis was performed for the primary endpoint.

End point values	Aldurazyme			
Subject group type	Reporting group			
Number of subjects analysed	12			
Units: percent change				
arithmetic mean (standard deviation)	-64.61 (± 26.90)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change From Baseline in uGAGs up to Week 20

End point title	Percent Change From Baseline in uGAGs up to Week 20

End point description:

Urine samples collected and performed analysis at central lab to determine the uGAG level. Results are based on the mITT analysis set which included all enrolled subjects who received at least 1 dose of study intervention and with an evaluable primary efficacy endpoint. Here, n= number of subjects analyzed at specific time points.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and Weeks 2, 4, 8, 12 and 20

End point values	Aldurazyme			
Subject group type	Reporting group			
Number of subjects analysed	12			
Units: percent change				
arithmetic mean (standard deviation)				
Week 2 (n=10)	-32.23 (± 29.37)			
Week 4 (n=10)	-55.21 (± 30.86)			
Week 8 (n=10)	-59.79 (± 22.48)			
Week 12 (n=11)	-53.15 (± 23.48)			

Week 20 (n=11)	-60.15 (± 27.16)			

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute Change From Baseline in uGAGs up to Week 26

End point title	Absolute Change From Baseline in uGAGs up to Week 26

End point description:

Urine samples collected and performed analysis at central lab to determine the uGAG level. The missing value was imputed by carrying forward the last uGAG value (LOCF method) observed during the on-treatment period. Results are based on the mITT analysis set which included all enrolled subjects who received at least 1 dose of study intervention and with an evaluable primary efficacy endpoint. Here, n= number of subjects analyzed at specific time points.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and Weeks 2, 4, 8, 12, 20 and 26

End point values	Aldurazyme			
Subject group type	Reporting group			
Number of subjects analysed	12			
Units: absolute change				
arithmetic mean (standard deviation)				
Week 2 (n=10)	-149.93 (± 138.55)			
Week 4 (n=10)	-240.02 (± 181.58)			
Week 8 (n=10)	-216.46 (± 92.59)			
Week 12 (n=11)	-250.70 (± 194.64)			
Week 20 (n=11)	-269.77 (± 199.82)			
Week 26 (n=12)	-297.80 (± 225.55)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change From Baseline in Liver Volume at Week 26

End point title	Percent Change From Baseline in Liver Volume at Week 26

End point description:

Liver volume was measured by abdominal B type ultrasound examination. Results are based on the mITT analysis set which included all enrolled subjects who received at least 1 dose of study intervention

and with an evaluable primary efficacy endpoint.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and Week 26

End point values	Aldurazyme			
Subject group type	Reporting group			
Number of subjects analysed	12			
Units: percent change				
arithmetic mean (standard deviation)	-13.24 (± 7.86)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
TEAEs data was collected from first dose administration (Day 1) up to Week 27.	
Adverse event reporting additional description:	
Analysis was performed on the safety analysis set.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	26.0

Reporting groups	
Reporting group title	Aldurazyme
Reporting group description:	
Subjects were treated with aldurazyme 100 U/kg of body weight IV infusion QW up to 26 weeks.	

Serious adverse events	Aldurazyme		
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		
Vascular disorders			
Hypertension			
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: 0 %

Non-serious adverse events	Aldurazyme		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	11 / 12 (91.67%)		
Investigations			
Blood Pressure Increased			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Platelet Count Decreased			

subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1		
Vascular disorders Hypotension subjects affected / exposed occurrences (all)	 1 / 12 (8.33%) 2		
Nervous system disorders Dizziness subjects affected / exposed occurrences (all)	 1 / 12 (8.33%) 1		
General disorders and administration site conditions Pyrexia subjects affected / exposed occurrences (all) Face Oedema subjects affected / exposed occurrences (all) Influenza Like Illness subjects affected / exposed occurrences (all)	 1 / 12 (8.33%) 1 1 / 12 (8.33%) 1 1 / 12 (8.33%) 1		
Ear and labyrinth disorders Deafness subjects affected / exposed occurrences (all)	 1 / 12 (8.33%) 1		
Gastrointestinal disorders Abdominal Distension subjects affected / exposed occurrences (all) Diarrhoea subjects affected / exposed occurrences (all)	 1 / 12 (8.33%) 1 1 / 12 (8.33%) 1		
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all)	 3 / 12 (25.00%) 3		
Skin and subcutaneous tissue disorders			

Rash Erythematous subjects affected / exposed occurrences (all) Urticaria subjects affected / exposed occurrences (all)	 1 / 12 (8.33%) 1 1 / 12 (8.33%) 1		
Musculoskeletal and connective tissue disorders Musculoskeletal Stiffness subjects affected / exposed occurrences (all)	 1 / 12 (8.33%) 1		
Infections and infestations Covid-19 subjects affected / exposed occurrences (all) Influenza subjects affected / exposed occurrences (all) Upper Respiratory Tract Infection subjects affected / exposed occurrences (all) Suspected Covid-19 subjects affected / exposed occurrences (all)	 1 / 12 (8.33%) 1 1 / 12 (8.33%) 1 3 / 12 (25.00%) 3 2 / 12 (16.67%) 2		
Metabolism and nutrition disorders Hypercholesterolaemia subjects affected / exposed occurrences (all)	 1 / 12 (8.33%) 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