Clinical trial results:
A Single Arm, Prospective, Open-label, Multi-center Study to Evaluate Efficacy and Safety in Chinese Patients with Late Onset Pompe Disease with Alglucosidase Alfa Treatment

Summary

EudraCT number	2024-000461-24
Trial protocol	Outside EU/EEA
Global end of trial date	25 July 2024

Results information

Result version number	v1 (current)
This version publication date	01 February 2025
First version publication date	01 February 2025

Trial information

Trial identification

Sponsor protocol code	ALGMYL09010 / LPS15677

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04676373
WHO universal trial number (UTN)	U1111-1238-1267

Notes:

Sponsors

Sponsor organisation name	Sanofi China Investment Co.,Ltd
Sponsor organisation address	Floor 7, No. 112, Jianguo Road, Chaoyang District, Beijing, China,
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	11 November 2024
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	25 July 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

- To evaluate the effect of alglucosidase alfa (Myozyme) treatment on motor function (Six-minute walk test [6MWT] and lung function (predicted Forced vital capacity [FVC]) among Chinese late-onset pompe disease (LOPD) participants above 5 years old.
- To evaluate the safety of alglucosidase alfa (Myozyme) 20 milligram per kilogram (mg/kg), intravenous (IV) biweekly in Chinese LOPD participants above 3 years old.

Protection of trial subjects:

The study was conducted by investigators experienced in the treatment of pediatric participants. 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), as assent form in child-appropriate language was provided and explained to the child. Repeated invasive procedures were minimized. 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 minimize distress and discomfort.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	10 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: 41
Worldwide total number of subjects	41
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)	14

Adults (18-64 years)	25
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted at 10 centers in China. A total of 43 participants were screened from 10 March 2021 to 01 June 2023, of which 2 were screen failures. Screen failures were mainly due to not meeting the eligibility criteria.

Pre-assignment

Screening details:

A total of 41 participants with LOPD received alglucosidase alfa in the 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	Alglucosidase alfa

Arm description:

Participants received alglucosidase alfa at a dose of 20 mg/kg body weight every 2 weeks as an IV infusion for up to 52 weeks.

Arm type	Experimental
Investigational medicinal product name	Alglucosidase alfa
Investigational medicinal product code	
Other name	MYOZYME®
Pharmaceutical forms	Powder for injection
Routes of administration	Intravenous use

Dosage and administration details:

Participants received alglucosidase alfa at a dose of 20 mg/kg body weight every 2 weeks as an IV infusion using an infusion pump, over approximately 4 hours.

Number of subjects in period 1	Alglucosidase alfa
Started	41
Completed	36
Not completed	5
Consent withdrawn by subject	3
Adverse event, non-fatal	1
Coronavirus Disease-2019 (COVID-19)	1

Baseline characteristics

Reporting groups	
Reporting group title	Alglucosidase alfa
Reporting group description:	
Participants received alglucosidase alfa at a dose of 20 mg/kg body weight every 2 weeks as an IV infusion for up to 52 weeks.	

Reporting group values	Alglucosidase alfa	Total	
Number of subjects	41	41	
Age Categorical Units: Subjects			
Age Continuous Units: years			
arithmetic mean	24.2		
standard deviation	± 11.17	-	
Gender Categorical Units: Participants			
Female	21	21	
Male	20	20	
Percentage of Predicted Forced Vital Capacity (FVC)			
FVC is a measurement of pulmonary function which is defined as the volume of air that can forcibly be blown out after full inspiration. It was assessed using the spirometry system with the participant in upright seated position. Percent of predicted FVC = (actual FVC measurement)/(predicted value of FVC) x 100.			
Units: Percentage of Predicted FVC			
arithmetic mean	49.777		
standard deviation	± 14.992	-	
Six-Minute Walk Test (6MWT)			
The 6MWT is a practical simple test that measures the distance that a participant can quickly walk on a flat, hard surface in a period of 6 minutes. It evaluates the global and integrated responses of all the systems involved during exercise, including the pulmonary and cardiovascular systems, systemic circulation, peripheral circulation, blood, neuromuscular units, and muscle metabolism.			
Units: Meters			
arithmetic mean	390.282		
standard deviation	± 101.928	-	

End points

End points reporting groups

Reporting group title	Alglucosidase alfa

Reporting group description:

Participants received alglucosidase alfa at a dose of 20 mg/kg body weight every 2 weeks as an IV infusion for up to 52 weeks.

Primary: Change From Baseline in six-Minute Walk Test (6MWT) for Participants Greater Than or Equal to (>=) 5-Year old at Month 12

End point title	Change From Baseline in six-Minute Walk Test (6MWT) for Participants Greater Than or Equal to (>=) 5-Year old at Month 12[1]

End point description:

The 6MWT is a practical simple test that requires a 100-ft hallway but no exercise equipment or advanced training for technicians. This test measures the distance that a participant can quickly walk on a flat, hard surface in a period of 6 minutes. It evaluates the global and integrated responses of all the systems involved during exercise, including the pulmonary and cardiovascular systems, systemic circulation, peripheral circulation, blood, neuromuscular units, and muscle metabolism. Baseline was defined as the last available value before the treatment. The primary endpoint is estimated based on last observation carried forward (LOCF) method. Intent-to-treat (ITT) population included all enrolled participants treated with alglucosidase alfa.

End point type	Primary

End point timeframe:

Baseline (Day 1) and Month 12

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	Alglucosidase alfa			
Subject group type	Reporting group			
Number of subjects analysed	41			
Units: Meters				
arithmetic mean (confidence interval 95%)	43.637 (17.461 to 69.813)			

Statistical analyses

No statistical analyses for this end point

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

End point title	Number of Participants With Treatment-Emergent Adverse Events (TEAEs) and Treatment-Emergent Serious Adverse Events (TESAEs) for all Participants[2]

End point description:

An AE was defined as any untoward medical occurrence in a participant or clinical investigation participant administered a pharmaceutical product and which does not necessarily have to have a causal

relationship with this treatment. TEAEs were defined as the AEs that developed, worsened or became serious during the treatment-emergent period (defined as the time from first dose of study treatment [Day 1] up to 30 days after the last dose of study treatment). A serious adverse event (SAE) was defined as 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 or significant disability/incapacity, was a congenital anomaly/birth defect or was a medically important event. Safety population included all the participants who actually received at least 1 dose or part of a dose of study treatment.

End point type	Primary

End point timeframe:

From first dose of study drug (Day 1) up to 30 days after last dose, approximately 14.4 months

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	Alglucosidase alfa			
Subject group type	Reporting group			
Number of subjects analysed	41			
Units: Participants				
Any TEAE	32			
Any TESAE	7			

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline in Percent Predicted Forced Vital Capacity (%FVC) in Upright Position for Participants >=5-Year old at Month 12

End point title	Change From Baseline in Percent Predicted Forced Vital Capacity (%FVC) in Upright Position for Participants >=5-Year old at Month 12[3]

End point description:

FVC is a measurement of pulmonary function which is defined as the volume of air that can forcibly be blown out after full inspiration. It was assessed using the spirometry system with the participant in upright seated position. Percent of predicted FVC = (actual FVC measurement)/(predicted value of FVC) x 100. Baseline was defined as the last available value before the treatment. The endpoint is estimated based on LOCF method. ITT population included all enrolled participants treated with alglucosidase alfa.

End point type	Primary

End point timeframe:

Baseline (Day 1) 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 was descriptive in nature, no statistical analysis was provided.

End point values	Alglucosidase alfa			
Subject group type	Reporting group			
Number of subjects analysed	41			
Units: Percentage of Predicted FVC				
arithmetic mean (confidence interval 95%)	2.430 (-0.852 to 5.713)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Maximal Inspiratory Pressure (MIP) in Upright Position for Participants >=5-Year old at Week 52

End point title	Change From Baseline in Maximal Inspiratory Pressure (MIP) in Upright Position for Participants >=5-Year old at Week 52

End point description:

MIP is a measurement of inspiratory muscle strength which is defined as how much air pressure force a participant creates by inhaling through the mouth as hard as possible. It was assessed using the pneumography with the participant in upright seated position. Baseline was defined as the last available value before the treatment. ITT population included all enrolled participants treated with alglucosidase alfa. Only those participants with data collected at Baseline and at Week 52 are reported.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and Week 52

End point values	Alglucosidase alfa			
Subject group type	Reporting group			
Number of subjects analysed	31			
Units: centimeter of water column (cmH2O)				
least squares mean (confidence interval 95%)	2.059 (-0.582 to 4.699)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Maximal Expiratory Pressure (MEP) in Upright Position for Participants >=5-Year old at Week 52

End point title	Change From Baseline in Maximal Expiratory Pressure (MEP) in Upright Position for Participants >=5-Year old at Week 52

End point description:

MEP is a measurement of expiratory muscle strength which is defined as the greater pressure generated during maximal expiration. It was assessed using the pneumography with the participant in upright seated position. Baseline was defined as the last available value before the treatment. ITT population included all enrolled participants treated with alglucosidase alfa. Only those participants with data collected at Baseline and at Week 52 are reported.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and Week 52

End point values	Alglucosidase alfa			
Subject group type	Reporting group			
Number of subjects analysed	31			
Units: cmH2O				
least squares mean (confidence interval 95%)	0.073 (-2.921 to 3.066)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Manual Muscle Test (MMT) for Participants >=5-Year old at Week 52

End point title	Change From Baseline in Manual Muscle Test (MMT) for Participants >=5-Year old at Week 52

End point description:

MMT was assessed according to expanded Medical Research Council (MRC) scale. MMT is used to measure body strength for deltoid muscle, quadriceps femoris, iliopsoas, and neck stretch flexor. Each individual item score range: 0 to 5 points with subdivisions in + or -, where a plus sign corresponds to an increase of one-third of score point and minus sign corresponds to a decrease of one-third of score point. Total scores are a sum of each individual item score, ranging from 0 (no muscle strength) to 40 (high muscle strength) with higher scores indicating better muscle strength. Baseline was defined as the last available value before the treatment. ITT population included all enrolled participants treated with alglucosidase alfa. Only those participants with data collected at Baseline and at Week 52 are reported.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and Week 52

End point values	Alglucosidase alfa			
Subject group type	Reporting group			
Number of subjects analysed	36			
Units: Score on a scale				
least squares mean (confidence interval 95%)	2.53 (1.559 to 3.493)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Quick Motor Function Test (QMFT) Scores for Participants >=5-Year old at Week 52

End point title	Change From Baseline in Quick Motor Function Test (QMFT)

	Scores for Participants >=5-Year old at Week 52

End point description:

The QMFT is a reliable and valid test for assessing motor function in participants with Pompe's disease. QMFT comprised of 16 items specifically difficult for participants with Pompe's disease. Each item was scored separately on a 5-point ordinal scale which ranged from 0 to 4; higher scores indicated better outcomes. Total QMFT score was obtained by adding the scores of all items and ranged from 0 (unable to perform motor function tests) to 64 (normal muscle function); higher scores represented better outcomes. Baseline was defined as the last available value before the treatment. ITT population included all enrolled participants treated with alglucosidase alfa. Only those participants with data collected at Baseline and at Week 52 are reported.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and Week 52

End point values	Alglucosidase alfa			
Subject group type	Reporting group			
Number of subjects analysed	37			
Units: Score on a scale				
least squares mean (confidence interval 95%)	5.6 (4.41 to 6.81)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in 12-Item Short-Form Health Survey Scores for Participants >=5-Year old at Week 52

End point title	Change From Baseline in 12-Item Short-Form Health Survey Scores for Participants >=5-Year old at Week 52

End point description:

The 12-Item Short Form Health Survey (SF-12) which was developed for the medical outcomes evaluation of participants with chronic conditions. The SF-12 has 12 questions covering 8 health domains commonly represented in health surveys: physical functioning, role functioning physical, bodily pain, general health, vitality, social functioning, role functioning emotional, and mental health. Results are expressed in terms of 2 meta-scores: the Physical Component Summary (PCS) and the Mental Component Summary (MCS). The score ranges from 0 to 100; higher scores indicated better outcomes. Baseline was defined as the last available value before the treatment. ITT population included all enrolled participants treated with alglucosidase alfa. Only those participants with data collected at Baseline and at Week 52 are reported.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and Week 52

End point values	Alglucosidase alfa			
Subject group type	Reporting group			
Number of subjects analysed	37			
Units: Score on a scale				
least squares mean (confidence interval 95%)				
PCS-12	3.762 (1.252 to 6.271)			
MCS-12	0.608 (-1.986 to 3.203)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events: From first dose of study treatment (Day 1) up to 30 days after last dose, approximately 14.4 months. All-cause mortality (death): From first dose of study treatment (Day 1) up to end of study, approximately 40.56 months.

Adverse event reporting additional description:

Analysis was performed on Safety population.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	27.0

Reporting groups

Reporting group title	Alglucosidase alfa

Reporting group description:

Participants received alglucosidase alfa at a dose of 20 mg/kg body weight every 2 weeks as an IV infusion for up to 52 weeks.

Serious adverse events	Alglucosidase alfa		
Total subjects affected by serious adverse events			
subjects affected / exposed	7 / 41 (17.07%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Injury, poisoning and procedural complications			
Fracture			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Lumbar Vertebral Fracture			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Cerebral Infarction			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			

Intestinal Obstruction			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Respiratory Failure			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Pneumonia			
subjects affected / exposed	2 / 41 (4.88%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Pneumonia Bacterial			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Alglucosidase alfa		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	24 / 41 (58.54%)		
Investigations			
Blood Creatine Phosphokinase Increased			
subjects affected / exposed	9 / 41 (21.95%)		
occurrences (all)	10		
Blood Lactate Dehydrogenase Increased			
subjects affected / exposed	7 / 41 (17.07%)		
occurrences (all)	7		
Carbon Dioxide Combining Power Increased			
subjects affected / exposed	3 / 41 (7.32%)		
occurrences (all)	5		

Creatinine Urine Decreased subjects affected / exposed occurrences (all)	3 / 41 (7.32%) 4		
Electrocardiogram T Wave Peaked subjects affected / exposed occurrences (all)	2 / 41 (4.88%) 2		
Gastrointestinal disorders Diarrhoea subjects affected / exposed occurrences (all)	3 / 41 (7.32%) 3		
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all)	3 / 41 (7.32%) 4		
Nasal Turbinate Hypertrophy subjects affected / exposed occurrences (all)	1 / 41 (2.44%) 1		
Oropharyngeal Pain subjects affected / exposed occurrences (all)	3 / 41 (7.32%) 3		
Pulmonary Hypertension subjects affected / exposed occurrences (all)	4 / 41 (9.76%) 4		
Respiratory Failure subjects affected / exposed occurrences (all)	1 / 41 (2.44%) 1		
Skin and subcutaneous tissue disorders Dermatitis subjects affected / exposed occurrences (all)	1 / 41 (2.44%) 2		
Infections and infestations Covid-19 subjects affected / exposed occurrences (all)	4 / 41 (9.76%) 4		
Nasopharyngitis			

subjects affected / exposed	2 / 41 (4.88%)		
occurrences (all)	2		
Upper Respiratory Tract Infection			
subjects affected / exposed	10 / 41 (24.39%)		
occurrences (all)	13		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
29 May 2020	Statistical considerations were modified. Updates were made in study flow chart, determination of sample size, compliance, and graphical study design. Analysis of primary and secondary efficacy endpoints were modified. Multiplicity considerations and other analyses were updated. Clarifications were provided in duration of study participation for each participant, selection of participants and visit schedule. Safety and other safety endpoints were updated.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported