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

Summary

EudraCT number	2021-004047-25
Trial protocol	Outside EU/EEA
Global end of trial date	30 December 2020

Results information

Result version number	v1 (current)
This version publication date	11 September 2021
First version publication date	11 September 2021

Trial information

Trial identification

Sponsor protocol code	ALGMYL08718

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03687333
WHO universal trial number (UTN)	U1111-1203-8484
Other trial identifiers	Study Name: APOLLO-IOPD

Notes:

Sponsors

Sponsor organisation name	Genzyme, a Sanofi Company
Sponsor organisation address	50 Binney Street, Cambridge, Massachusetts, United States, 02142
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	22 March 2021
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	30 December 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study was to evaluate effect of 52-week treatment with Alglucosidase Alfa in the extension of survival and improvement of cardiomyopathy measured by Left Ventricular Mass Index (LVMI) in Chinese subjects with infantile-onset Pompe Disease (IOPD).

Protection of trial subjects:

The study was conducted by investigators experienced in the treatment of paediatric patients. 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 might have been used to minimise distress and discomfort.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	04 December 2018
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: 10
Worldwide total number of subjects	10
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)	10
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	0

From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Study was conducted at 4 active study centres in China. A total of 12 subjects were screened between 04 Dec 2018 and 3 Dec 2019, of which 02 subjects failed screening mainly due to unmet inclusion criteria and/or met exclusion criteria and withdrawal of the informed consent by parents or legal guardians of subject, respectively.

Pre-assignment

Screening details:

A total of 10 subjects were treated 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	Alglucosidase Alfa

Arm description:

Subjects received Alglucosidase alfa, 20 milligrams per kilogram (mg/kg) body weight intravenous (IV) infusion every 2 weeks 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:

Alglucosidase alfa 20 mg/kg body weight IV infusion every 2 weeks for 52 Weeks. Dose was allowed to be increased up to 40 mg/kg for subjects who showed sub-optimal response to the treatment.

Number of subjects in period 1	Alglucosidase Alfa
Started	10
Completed	9
Not completed	1
Unspecified	1

Baseline characteristics

Reporting groups	
Reporting group title	Alglucosidase Alfa
Reporting group description:	
Subjects received Alglucosidase alfa, 20 milligrams per kilogram (mg/kg) body weight intravenous (IV) infusion every 2 weeks for up to 52 weeks.	

Reporting group values	Alglucosidase Alfa	Total	
Number of subjects	10	10	
Age categorical Units: Subjects			
Age continuous Units: months arithmetic mean standard deviation	 4.91 ± 1.607	 -	
Gender categorical Units: Subjects			
Female	6	6	
Male	4	4	

End points

End points reporting groups

Reporting group title	Alglucosidase Alfa

Reporting group description:

Subjects received Alglucosidase alfa, 20 milligrams per kilogram (mg/kg) body weight intravenous (IV) infusion every 2 weeks for up to 52 weeks.

Primary: Percentage of Subjects Who Survived at Week 52

End point title	Percentage of Subjects Who Survived at Week 52[1]

End point description:

Binomial proportion and its 95% confidence interval were used to analyse the percentage of survivals. Analysis was performed on intent-to-treat (ITT) population which included all subjects treated with Alglucosidase alfa.

End point type	Primary

End point timeframe:

At Week 52

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 inferential statistical analysis was provided.

End point values	Alglucosidase Alfa			
Subject group type	Reporting group			
Number of subjects analysed	10			
Units: percentage of subjects				
number (confidence interval 95%)	90.0 (55.5 to 99.7)			

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline in Left Ventricular Mass (LVM) Index at Week 52

End point title	Change From Baseline in Left Ventricular Mass (LVM) Index at Week 52[2]

End point description:

LVM were assessed by echocardiograms. LVM index was an index value derived by normalizing LVM by body surface area. LVM index provides evidence of cardiomyopathy. LVM index values less than (<) 65 gram per metre quare (g/m^2) were considered as normal and LVM index values greater than or equal to (>=) 65 g/m^2 were considered as abnormal. Analysis was performed on ITT population. Here, 'number of subjects analysed' signifies those subjects who were evaluable for this endpoint.

End point type	Primary

End point timeframe:

Baseline, Week 52

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 inferential statistical analysis was provided.

End point values	Alglucosidase Alfa			
Subject group type	Reporting group			
Number of subjects analysed	9			
Units: g/m^2				
arithmetic mean (standard deviation)	-227.60 (± 155.991)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Invasive Ventilator Use-Free Survival at Week 52

End point title	Percentage of Subjects With Invasive Ventilator Use-Free Survival at Week 52

End point description:

Invasive ventilator-free survival was defined as the time during which the subject was alive and not invasively ventilated. Binomial proportion and its 95% confidence interval were used to analyse the percentage of invasive ventilator use-free survival. Analysis was performed on ITT population. Here, 'number of subjects analysed' signifies those subjects who did not use any invasive ventilator and were evaluable for this endpoint.

End point type	Secondary

End point timeframe:

At Week 52

End point values	Alglucosidase Alfa			
Subject group type	Reporting group			
Number of subjects analysed	9			
Units: percentage of subjects				
number (confidence interval 95%)	100 (66.4 to 100)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Any Ventilator Use-Free Survival at Week 52

End point title	Percentage of Subjects With Any Ventilator Use-Free Survival at Week 52

End point description:

Ventilator-free survival was defined as the time during which the subject was alive and not ventilated. Binomial proportion and its 95% confidence interval were used to analyse the percentage of any ventilator use-free survival. Analysis was performed on ITT population. Here, 'number of subjects analysed' signifies those subjects who did not use any ventilator and were evaluable for this endpoint.

End point type	Secondary

End point timeframe:

At Week 52

End point values	Alglucosidase Alfa			
Subject group type	Reporting group			
Number of subjects analysed	8			
Units: percentage of subjects				
number (confidence interval 95%)	100 (63.1 to 100)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Physical Growth at Week 52: Length

End point title	Change From Baseline in Physical Growth at Week 52: Length

End point description:

Analysis was performed on ITT population. Here, 'number of subjects analysed' signifies those subjects who were evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Baseline, Week 52

End point values	Alglucosidase Alfa			
Subject group type	Reporting group			
Number of subjects analysed	9			
Units: centimetre				
arithmetic mean (standard deviation)	12.66 (± 4.676)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Physical Growth at Week 52: Weight

End point title	Change From Baseline in Physical Growth at Week 52: Weight

End point description:

Analysis was performed on ITT population. Here, 'number of subjects analysed' signifies those subjects who were evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Baseline, Week 52

End point values	Alglucosidase Alfa			
Subject group type	Reporting group			
Number of subjects analysed	9			
Units: kilogram				
arithmetic mean (standard deviation)	2.69 (± 0.752)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Motor Development Milestones Achieved at Week 52

End point title	Number of Motor Development Milestones Achieved at Week 52

End point description:

Motor development was assessed by a 11-point scale ranged from 0 (worst motor behavior) to 11 (better motor behavior). A higher score means better motor behavior. Analysis was performed on ITT population. Here, 'number of subjects analysed' signifies those subjects who were evaluable for this endpoint.

End point type	Secondary

End point timeframe:

At Week 52

End point values	Alglucosidase Alfa			
Subject group type	Reporting group			
Number of subjects analysed	9			
Units: score on a scale				
arithmetic mean (standard deviation)	4.8 (± 1.99)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Motor Development Status at Week 52

End point title	Change From Baseline in Motor Development Status at Week

	52

End point description:

Motor development was assessed by a 11-point scale ranged from 0 (worst motor behavior) to 11 (better motor behavior). A higher score means better motor status. Analysis was performed on ITT population. Here, 'number of subjects analysed' signifies those subjects who were evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Baseline, Week 52

End point values	Alglucosidase Alfa			
Subject group type	Reporting group			
Number of subjects analysed	9			
Units: score on a scale				
arithmetic mean (standard deviation)	3.9 (± 1.62)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in GESELL Developmental Scale at Week 52

End point title	Change From Baseline in GESELL Developmental Scale at Week 52

End point description:

GESELL developmental scale was used to assess motor development and functional independence of infants. The GESELL developmental scale measures: adaptive (cognitive) behavior, motor, language behavior, and personal-social behavior. Higher measured mature age represented higher developmental quotient, and higher developmental quotient represented better status. Analysis was performed on ITT population. Here, 'number of subjects analysed' signifies those subjects who were evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Baseline, Week 52

End point values	Alglucosidase Alfa			
Subject group type	Reporting group			
Number of subjects analysed	9			
Units: score on a scale				
arithmetic mean (standard deviation)				
Motor	5.87 (± 3.68)			
Adaptive (cognitive)	8.50 (± 3.26)			
Language	6.82 (± 3.05)			
Personal-social behavior	8.73 (± 3.11)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Signs and/or Symptoms of Cardiac Failure at Week 52

End point title	Percentage of Subjects With Signs and/or Symptoms of Cardiac Failure at Week 52

End point description:

Analysis was performed on ITT population. Here, 'number of subjects analysed' signifies those subjects who were evaluable for this endpoint.

End point type	Secondary

End point timeframe:

At Week 52

End point values	Alglucosidase Alfa			
Subject group type	Reporting group			
Number of subjects analysed	9			
Units: percentage of subjects				
number (not applicable)	0			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events (AEs) were collected from first dose of investigational medicinal product (IMP) up to 30 days after the last dose of IMP (Week 56).

Adverse event reporting additional description:

Reported AEs were treatment-emergent AEs (TEAEs), that developed/worsened or became serious during during TEAE period (from first dose of IMP up to 30 days after last dose of IMP [Week 56]). Analysis was performed on safety population which included subjects who received at least 1 dose or part of a dose of IMP.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	23.1

Reporting groups

Reporting group title	Alglucosidase Alfa

Reporting group description:

Subjects received Alglucosidase alfa, 20 mg/kg body weight IV infusion every 2 weeks for up to 52 weeks.

Serious adverse events	Alglucosidase Alfa		
Total subjects affected by serious adverse events			
subjects affected / exposed	9 / 10 (90.00%)		
number of deaths (all causes)	1		
number of deaths resulting from adverse events	1		
Respiratory, thoracic and mediastinal disorders			
Pnenumonitis			
subjects affected / exposed	6 / 10 (60.00%)		
occurrences causally related to treatment / all	0 / 6		
deaths causally related to treatment / all	0 / 0		
Pnenumonia aspiration			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Choking			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Asphyxia			

subjects affected / exposed	1 / 10 (10.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory tract infection			
subjects affected / exposed	2 / 10 (20.00%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Bronchitis			
subjects affected / exposed	2 / 10 (20.00%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Gastroenteritis rotavirus			
subjects affected / exposed	2 / 10 (20.00%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Pnenumonia			
subjects affected / exposed	3 / 10 (30.00%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Alglucosidase Alfa		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	10 / 10 (100.00%)		
Investigations			
Respiratory rate decreased			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Heart rate decreased			

subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1		
Injury, poisoning and procedural complications Device use error subjects affected / exposed occurrences (all)	 1 / 10 (10.00%) 1		
Surgical and medical procedures Central venous catheterisation subjects affected / exposed occurrences (all)	 1 / 10 (10.00%) 1		
Cardiac disorders Cardiac failure subjects affected / exposed occurrences (all)	 1 / 10 (10.00%) 1		
General disorders and administration site conditions Pyrexia subjects affected / exposed occurrences (all)	 1 / 10 (10.00%) 1		
Ear and labyrinth disorders Eustachian tube dysfunction subjects affected / exposed occurrences (all)	 1 / 10 (10.00%) 1		
Gastrointestinal disorders Vomiting subjects affected / exposed occurrences (all) Aphthous ulcer subjects affected / exposed occurrences (all) Diarrhoea subjects affected / exposed occurrences (all) Upper gastrointestinal haemorrhage subjects affected / exposed occurrences (all) Dyspepsia	 3 / 10 (30.00%) 3 1 / 10 (10.00%) 1 1 / 10 (10.00%) 1 1 / 10 (10.00%) 1		

subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Infantile spitting up			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Respiratory, thoracic and mediastinal disorders			
Pnenumonitis			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Pnenumonia aspiration			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Skin and subcutaneous tissue disorders			
Dermatitis allergic			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Eczema			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	3 / 10 (30.00%)		
occurrences (all)	3		
Respiratory tract infection			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Bronchitis			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Otitis media			
subjects affected / exposed	2 / 10 (20.00%)		
occurrences (all)	2		
Gastroenteritis			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Lower respiratory tract infection			

subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
08 October 2018	Following changes were made: Adjustment of instruction of use of MYOZYME® for those subjects whose cross-reacting immunologic material (CRIM) was negative, revised to "CRIM status was rapidly inferred by gene mutation analysis, using an established mutation database." Adjustment of assessment during treatment, revised to "blood sample was collected for CRIM status determination through genotyping at screening visit in each site, only if written results was not available." On May 2021, following changes were made: Due to adenosine deaminase (ADA) test was not done in China, according to global medical suggestions to of removing the ADA related content. The Kaplan-Meier methodology and modified relevant description was removed due to not enough sample size for Kaplan-Meier methodology.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported