



## Clinical trial results:

### An Open-label Study of the Safety, Pharmacokinetics, Pharmacodynamics, and Efficacy of 12 Month Treatment With Migalastat in Pediatric Subjects (Aged 12 to <18 Years) With Fabry Disease and Amenable GLA Variants

#### Summary

EudraCT number	2017-000146-21
Trial protocol	GB DE ES IT
Global end of trial date	02 February 2021

#### Results information

Result version number	v1 (current)
This version publication date	04 August 2021
First version publication date	04 August 2021

#### Trial information

##### Trial identification

Sponsor protocol code	AT1001-020
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##### Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03500094
WHO universal trial number (UTN)	-

Notes:

#### Sponsors

Sponsor organisation name	Amicus Therapeutics UK Limited
Sponsor organisation address	One Globeside, Fieldhouse Lane, Marlow, United Kingdom, SL7 1HZ
Public contact	Medical Affairs, Amicus Therapeutics, 001 609662-2000, clinicaltrials@amicusrx.com
Scientific contact	Medical Affairs, Amicus Therapeutics, 001 609662-2000, MedInfoUSA@amicusrx.com

Notes:

#### Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMA-001194-PIP01-11
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 May 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	02 February 2021
Global end of trial reached?	Yes
Global end of trial date	02 February 2021
Was the trial ended prematurely?	No

Notes:

## General information about the trial

Main objective of the trial:

Stage 1:

- to characterize the pharmacokinetics (PK) of migalastat in adolescents with Fabry disease and to validate extrapolation of migalastat plasma exposure in adults to adolescents weighing  $\geq 45$  kilograms (kg) for the 150 milligrams (mg) migalastat capsule administered every other day
- to evaluate the safety of migalastat treatment in pediatric participants diagnosed with Fabry disease and who have variants in the gene encoding  $\alpha$  galactosidase A ( $\alpha$  Gal A) (GLA) amenable to treatment with migalastat

Stage 2:

- to evaluate the safety of migalastat treatment in pediatric participants diagnosed with Fabry disease and who have GLA variants amenable to treatment with migalastat

Upon study completion, participants had the option to enroll in a long-term extension study conducted under a separate protocol (EudraCT number 2019-000222-21).

Protection of trial subjects:

This study was conducted in accordance with International Council on Harmonisation Good Clinical Practice guidelines, and the principles of the Declaration of Helsinki, in addition to following the laws and regulations of the country or countries in which the study was conducted.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	03 September 2018
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	5 Years
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

## Population of trial subjects

### Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 4
Country: Number of subjects enrolled	United States: 18
Worldwide total number of subjects	22
EEA total number of subjects	0

Notes:

### Subjects enrolled per age group

In utero	0
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Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	22
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

Participants must have been naïve to enzyme replacement therapy (ERT) or have stopped ERT at least 14 days at the time of screening.

### Period 1

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

### Arms

Arm title	Migalastat HCl 150 mg
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Arm description:

Migalastat was administered every other day for 12 months.

Arm type	Experimental
Investigational medicinal product name	Migalastat
Investigational medicinal product code	
Other name	AT1001, Galafold
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

One migalastat 123 milligrams (mg) capsule equivalent to 150 mg migalastat hydrochloride (HCl) (herein referred to as "migalastat") was administered every other day for 12 months.

<b>Number of subjects in period 1</b>	Migalastat HCl 150 mg
Started	22
Received at Least 1 Dose of Study Drug	21
Completed	19
Not completed	3
Consent withdrawn by subject	1
Lost to follow-up	1
Withdrawal by Parent or Legally-authorized Re	1

## Baseline characteristics

### Reporting groups

Reporting group title	Overall
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Reporting group description:

All participants who enrolled in the study.

Reporting group values	Overall	Total	
Number of subjects	22	22	
Age categorical			
Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	22	22	
Adults (18-64 years)	0	0	
From 65-84 years	0	0	
85 years and over	0	0	
Age continuous			
Units: years			
arithmetic mean	14.6		
standard deviation	± 1.62	-	
Gender categorical			
Units: Subjects			
Female	12	12	
Male	10	10	

## End points

### End points reporting groups

Reporting group title	Migalastat HCl 150 mg
Reporting group description: Migalastat was administered every other day for 12 months.	
Subject analysis set title	Migalastat HCl 150 mg
Subject analysis set type	Safety analysis
Subject analysis set description: Participants who received at least 1 dose of study drug.	
Subject analysis set title	Migalastat HCl 150 mg: ERT Naive
Subject analysis set type	Sub-group analysis
Subject analysis set description: Migalastat was administered every other day for 12 months to ERT Naive participants.	
Subject analysis set title	Migalastat HCl 150 mg: ERT Experienced
Subject analysis set type	Sub-group analysis
Subject analysis set description: Migalastat was administered every other day for 12 months to ERT experienced participants.	

### Primary: Number Of Participants Who Experienced Treatment-related Treatment-emergent Adverse Events (TEAEs)

End point title	Number Of Participants Who Experienced Treatment-related Treatment-emergent Adverse Events (TEAEs) <sup>[1]</sup>
End point description: TEAEs included adverse events that began after the first dose of study drug until 30 days after the last dose. Treatment-related TEAEs were defined as TEAEs that had an investigator-defined relationship to study drug of "Definite," "Probable," or "Possible." A summary of serious and all other non-serious adverse events, regardless of causality, is located in the Adverse Events section.	
End point type	Primary
End point timeframe: Day 1 (after dosing) through Month 12 and follow-up (30 days after last dose)	

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: Descriptive analysis was performed as per protocol.

End point values	Migalastat HCl 150 mg			
Subject group type	Subject analysis set			
Number of subjects analysed	21			
Units: participants				
number (not applicable)	5			

### Statistical analyses

No statistical analyses for this end point

### Primary: PK: Area Under The Plasma Concentration-time Curve Over The Dosing Interval (AUCtau) Of Migalastat

End point title	PK: Area Under The Plasma Concentration-time Curve Over The
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## End point description:

Four blood samples were collected during Stage 1 according to random 1:1:1 assignment to 1 of 3 PK sampling groups: Group 1: 1 hour (hr), 1.5 hr, 5 hr, 6.5 hr; Group 2: 1 hr, 2.75 hr, 5.25 hr, 10.75 hr; Group 3: 3.25 hr, 3.75 hr, 8.25 hr, 8.75 hr; and for all groups: one sample at Month 6 and at Month 12. Simulations were conducted to predict steady-state PK profiles and PK parameters for adolescent age subgroups 12 to <16 years, 16 to <18 years, and overall, 12 to <18 years. Population PK results are presented.

End point type	Primary
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End point timeframe:

Baseline to 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: Descriptive analysis was performed as per protocol.

End point values	Migalastat HCl 150 mg			
Subject group type	Subject analysis set			
Number of subjects analysed	120			
Units: h*ng/mL				
geometric mean (geometric coefficient of variation)				
12 to <16 years old (n=13)	8920 (± 47.2)			
16 to <18 years old (n=7)	8430 (± 41.7)			
12 to <18 years old (n=20)	8740 (± 44.2)			
Adults (n=100)	7980 (± 37.5)			

## Statistical analyses

No statistical analyses for this end point

## Primary: PK: Maximum Observed Plasma Concentration (Cmax) Of Migalastat

End point title	PK: Maximum Observed Plasma Concentration (Cmax) Of Migalastat <sup>[3]</sup>
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## End point description:

Four blood samples were collected during Stage 1 according to random 1:1:1 assignment to 1 of 3 PK sampling groups: Group 1: 1 hour (hr), 1.5 hr, 5 hr, 6.5 hr; Group 2: 1 hr, 2.75 hr, 5.25 hr, 10.75 hr; Group 3: 3.25 hr, 3.75 hr, 8.25 hr, 8.75 hr; and for all groups: one sample at Month 6 and at Month 12. Simulations were conducted to predict steady-state PK profiles and PK parameters for pediatric age groups. Results by age group are presented.

End point type	Primary
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End point timeframe:

Baseline to 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: Descriptive analysis was performed as per protocol.

<b>End point values</b>	Migalastat HCl 150 mg			
Subject group type	Subject analysis set			
Number of subjects analysed	120			
Units: ng/mL				
geometric mean (geometric coefficient of variation)				
12 to <16 years old (n=13)	1200 ( $\pm$ 60.9)			
16 to <18 years old (n=7)	1160 ( $\pm$ 39.2)			
12 to <18 years old (n=20)	1200 ( $\pm$ 52.7)			
Adults (n=100)	1140 ( $\pm$ 40.4)			

### Statistical analyses

No statistical analyses for this end point

### Secondary: Change In Estimated Glomerular Filtration Rate (eGFR) From Baseline To Month 12

End point title	Change In Estimated Glomerular Filtration Rate (eGFR) From Baseline To Month 12
End point description: Estimated GFR was calculated using the modified Schwartz formula for creatinine clearance.	
End point type	Secondary
End point timeframe: Baseline, Month 12 and last observation (up to Month 12)	

<b>End point values</b>	Migalastat HCl 150 mg			
Subject group type	Subject analysis set			
Number of subjects analysed	20			
Units: mL/min x 1.73 m <sup>2</sup>				
arithmetic mean (standard deviation)				
Month 12	-1.6 ( $\pm$ 15.40)			
Last observation (up to Month 12)	-1.6 ( $\pm$ 14.99)			

### Statistical analyses

No statistical analyses for this end point

### Secondary: Annualized Rate Of Change From Baseline

End point title	Annualized Rate Of Change From Baseline
End point description: Annualized rate of change from baseline of eGFR was defined as change from baseline to last visit divided by the duration from baseline to the last visit (Last assessment date – First dose date +1) and multiplied by 365.25. Baseline was defined as the last non-missing assessment prior to the first dose of study drug.	



End point type	Secondary
End point timeframe:	
Baseline up to Month 12	

<b>End point values</b>	Migalastat HCl 150 mg			
Subject group type	Subject analysis set			
Number of subjects analysed	20			
Units: mL/min x 1.73 m <sup>2</sup> /year				
arithmetic mean (standard deviation)	-1.5 (± 15.11)			

### Statistical analyses

No statistical analyses for this end point

### Secondary: Change From Baseline In Total Urine Protein And Urine Albumin Levels At Month 12

End point title	Change From Baseline In Total Urine Protein And Urine Albumin Levels At Month 12
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End point description:

End point type	Secondary
End point timeframe:	
Baseline, Month 12 and last observation (up to Month 12)	

<b>End point values</b>	Migalastat HCl 150 mg			
Subject group type	Subject analysis set			
Number of subjects analysed	20 <sup>[4]</sup>			
Units: mg/L				
arithmetic mean (standard deviation)				
Total Urine Protein: Month 12	36.0 (± 111.61)			
Total Urine Protein: Last observation	36.2 (± 108.64)			
Urine Albumin: Month 12	16.2 (± 28.27)			
Urine Albumin: Last observation	15.6 (± 27.67)			

Notes:

[4] - Month 12: n=19

### Statistical analyses

No statistical analyses for this end point

### Secondary: Change From Baseline In Left Ventricular Mass Index (LVMI)

End point title	Change From Baseline In Left Ventricular Mass Index (LVMI)
End point description:	
LVMI was assessed as a measure of cardiac impairment in the study participants. LVMI values for both M Mode and 2D views are presented.	
End point type	Secondary
End point timeframe:	
Baseline, Month 12 and last observation (up to Month 12)	

<b>End point values</b>	Migalastat HCl 150 mg			
Subject group type	Subject analysis set			
Number of subjects analysed	20			
Units: g/m <sup>2</sup>				
arithmetic mean (standard deviation)				
M Mode: Month 12 (n=18)	-3.9 (± 13.53)			
2D: Month 12 (n=19)	4.9 (± 9.12)			
M Mode: Last observation (up to Month 12) (n=19)	-4.4 (± 13.31)			
2D: Last observation (up to Month 12) (n=20)	4.3 (± 9.34)			

### Statistical analyses

No statistical analyses for this end point

### Secondary: Change In Plasma Levels Of Globotriaosylsphingosine (Lyso-Gb3)

End point title	Change In Plasma Levels Of Globotriaosylsphingosine (Lyso-Gb3)
End point description:	
End point type	Secondary
End point timeframe:	
Baseline, Month 12 and last observation (up to Month 12)	

<b>End point values</b>	Migalastat HCl 150 mg: ERT Naive	Migalastat HCl 150 mg: ERT Experienced		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	9	11 <sup>[5]</sup>		
Units: ng/mL				
arithmetic mean (standard deviation)				
Month 12	-14.0 (± 23.13)	12.5 (± 36.33)		
Last Observation (up to Month 12)	-14.0 (± 23.13)	11.3 (± 34.67)		

Notes:

[5] - Month 12: n=10

## Statistical analyses

No statistical analyses for this end point

### Secondary: FABPRO-GI And Pain Scores At Month 12

End point title	FABPRO-GI And Pain Scores At Month 12
End point description: The Fabry Disease Patient-Reported Outcome – Gastrointestinal Signs And Symptoms (FABPRO-GI) And Pain Questionnaire For Clinical Trials (24-hr Version) consists of questions regarding gastrointestinal signs and symptoms and pain relative to the past 24 hours. Participants rated the severity of their symptoms and pain from 0 (none) to 10 (worst possible). The monthly average score at Month 12 is presented. A higher score indicated higher levels of symptoms and pain.	
End point type	Secondary
End point timeframe: Month 12	

<b>End point values</b>	Migalastat HCl 150 mg			
Subject group type	Subject analysis set			
Number of subjects analysed	5			
Units: units on a scale				
arithmetic mean (standard deviation)				
Daily Ratings of Severity in Constipation	0.90 (± 1.91)			
Daily Ratings of Severity in Diarrhea	0.97 (± 1.65)			
Overall Pain	0.60 (± 0.71)			
Worst Tummy Pain	0.32 (± 0.38)			

## Statistical analyses

No statistical analyses for this end point

### Secondary: FABPRO-GI And Pain Scores At Last Observation

End point title	FABPRO-GI And Pain Scores At Last Observation
End point description: The Fabry Disease Patient-Reported Outcome – Gastrointestinal Signs And Symptoms (FABPRO-GI) And Pain Questionnaire For Clinical Trials (24-hr Version) consists of questions regarding gastrointestinal signs and symptoms and pain relative to the past 24 hours. Participants rated the severity of their symptoms and pain from 0 (none) to 10 (worst possible). The monthly average score at last observation is presented. A higher score indicated higher levels of symptoms and pain.	
End point type	Secondary
End point timeframe: Last observation (up to Month 12)	

<b>End point values</b>	Migalastat HCl 150 mg			
Subject group type	Subject analysis set			
Number of subjects analysed	18			
Units: units on a scale				
arithmetic mean (standard deviation)				
Daily Ratings of Severity in Constipation	0.4 (± 1.00)			
Daily Ratings of Severity in Diarrhea	0.4 (± 0.91)			
Overall Pain	1.2 (± 1.50)			
Worst Tummy Pain	0.9 (± 1.52)			

### Statistical analyses

No statistical analyses for this end point

### Secondary: Patient's Global Impression Of Change (PGI-C) Scores

End point title	Patient's Global Impression Of Change (PGI-C) Scores
End point description:	
The PGI-C consists of 4 questions regarding diarrhea, abdominal pain, overall pain, and daily living. Participants rated their status based on improvement, worsening, or the same. Improved status includes "Much better", "Better" and "A little better"; worsened status includes "A little worse", "Worse" and "Much worse".	
End point type	Secondary
End point timeframe:	
Month 12	

<b>End point values</b>	Migalastat HCl 150 mg			
Subject group type	Subject analysis set			
Number of subjects analysed	19			
Units: participants				
number (not applicable)				
Diarrhea: Status Improved	12			
Diarrhea: Status Same	7			
Diarrhea: Status Worse	0			
Abdominal pain: Status Improved	10			
Abdominal pain: Status Same	8			
Abdominal pain: Status Worse	1			
Overall pain: Status Improved	10			
Overall pain: Status Same	8			
Overall pain: Status Worse	1			
Daily living: Status Improved	10			
Daily living: Status Same	8			
Daily living: Status Worse	1			

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number Of Participants Who Experienced Sudden Onset Of Pain As Assessed Using The Fabry-Specific Pediatric Health And Pain Questionnaire (FPHPQ)

End point title	Number Of Participants Who Experienced Sudden Onset Of Pain As Assessed Using The Fabry-Specific Pediatric Health And Pain Questionnaire (FPHPQ)
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End point description:

The assessment of "In the last 3 months how many times did you experience sudden onset of pain?" using the FPHPQ for ages 13 to 18 is presented.

End point type	Secondary
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End point timeframe:

Month 12

<b>End point values</b>	Migalastat HCl 150 mg			
Subject group type	Subject analysis set			
Number of subjects analysed	19			
Units: participants				
number (not applicable)				
0 times	4			
1-3 times	5			
4-6 times	4			
> 6 times	3			

## Statistical analyses

No statistical analyses for this end point

### Secondary: Change From Baseline In FPHPQ Score For Pain Intensity

End point title	Change From Baseline In FPHPQ Score For Pain Intensity
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End point description:

The assessment of "How bad is your pain today?" using the FPHPQ for ages 13 to 18 is presented. Pain intensity was measured on a 10-point scale, 0 (no pain) to 10 (pain as bad as you can imagine). A decrease from baseline indicates an improvement in the condition.

End point type	Secondary
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End point timeframe:

Baseline, Month 12 and last observation (up to Month 12)

End point values	Migalastat HCl 150 mg			
Subject group type	Subject analysis set			
Number of subjects analysed	17 <sup>[6]</sup>			
Units: units on a scale				
arithmetic mean (standard deviation)				
Month 12	0.4 (± 1.82)			
Last observation (up to Month 12)	0.4 (± 1.77)			

Notes:

[6] - Month 12: n=16

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change From Baseline In Pediatric Quality Of Life (PedsQL) At Month 12

End point title	Change From Baseline In Pediatric Quality Of Life (PedsQL) At Month 12
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End point description:

The PedsQL is a modular approach to measuring health-related quality of life in healthy children and adolescents and those with acute and chronic health conditions. The psychosocial score for the PedsQL encompassed 15 questions relating to the participants' feelings, social interaction with others, and school. The physical score was derived from answers to 8 questions about the participants' ease of managing physical activity.

All components of the PedsQL were scored based on a scale of 0 (never) to 4 (almost always) and linearly transformed to a 0-100 scale as follows: 0 = 100, 1 = 75, 2 = 50, 3 = 25, 4 = 0. Both categories were combined for a total score. Total scores for the child report ages 13 to 18 years old and parent report are presented at Month 12.

End point type	Secondary
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End point timeframe:

Baseline, Month 12

End point values	Migalastat HCl 150 mg			
Subject group type	Subject analysis set			
Number of subjects analysed	15			
Units: units on a scale				
arithmetic mean (standard deviation)				
Child Report	2.2 (± 6.13)			
Parent Report	3.1 (± 10.29)			

## Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Day 1 (after dosing) through Month 12 and follow-up (30 days after last dose)

Assessment type	Systematic
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### Dictionary used

Dictionary name	MedDRA
Dictionary version	21.0

### Reporting groups

Reporting group title	Migalastat HCl 150 mg
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Reporting group description:

Migalastat was administered every other day for 12 months.

Serious adverse events	Migalastat HCl 150 mg		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 21 (4.76%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Psychiatric disorders			
Psychiatric disorders			
subjects affected / exposed	1 / 21 (4.76%)		
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	Migalastat HCl 150 mg		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	20 / 21 (95.24%)		
Nervous system disorders			
Back pain			
subjects affected / exposed	3 / 21 (14.29%)		
occurrences (all)	4		
Paraesthesia			

subjects affected / exposed occurrences (all)	2 / 21 (9.52%) 3		
General disorders and administration site conditions Complication associated with device subjects affected / exposed occurrences (all)	2 / 21 (9.52%) 2		
Gastrointestinal disorders Vomiting subjects affected / exposed occurrences (all)	2 / 21 (9.52%) 2		
Skin and subcutaneous tissue disorders Rash subjects affected / exposed occurrences (all)	2 / 21 (9.52%) 2		
Musculoskeletal and connective tissue disorders Headache subjects affected / exposed occurrences (all)	3 / 21 (14.29%) 4		
Infections and infestations Influenza subjects affected / exposed occurrences (all)  Nasopharyngitis subjects affected / exposed occurrences (all)  Pharyngitis streptococcal subjects affected / exposed occurrences (all)  Upper respiratory tract infection subjects affected / exposed occurrences (all)	3 / 21 (14.29%) 4  3 / 21 (14.29%) 4  2 / 21 (9.52%) 2  6 / 21 (28.57%) 8		



## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
10 September 2018	<ul style="list-style-type: none"><li>• A change in terminology of GLA mutation to GLA variant was implemented.</li><li>• The inclusion requirement for subjects to be off ERT treatment for 6 months was reduced to 14 days.</li><li>• The number of participants targeted for enrollment was increased from 7 to 10 participants to 20 participants</li><li>• Prior or anticipated use of gene therapy was added as an exclusion criterion.</li><li>• The safety criteria of change in body weight and height was revised from percentile to absolute change.</li><li>• The procedure for GLA genotyping conducted at screening was clarified.</li><li>• Visit windows for Months 6, 9, and 12 (or early termination) were increased from <math>\pm 3</math> days to <math>\pm 6</math> days and the follow-up visit window was increased to <math>+ 6</math> days.</li><li>• Microalbumin was added as an alternative to albumin for urinalyses/urine chemistry parameters.</li><li>• Procedure and timing of PK blood sampling was clarified.</li><li>• The modified Schwartz formula was specified as the method of calculating eGFR.</li><li>• An alternate method of reporting serious adverse events via email was added as a back-up in the event that notification via fax failed.</li></ul>
31 October 2018	<ul style="list-style-type: none"><li>• The design of the study was separated into 2 stages. Stage 1 was 1 month during which PK samples were collected and evaluated. Stage 2 was 11 months during which safety and efficacy were assessed. The total duration of the study (12 months) remained unchanged.</li><li>• A subpopulation of subjects aged 12 to <math>&lt; 16</math> years was planned for PK analysis since in some global markets 16 years of age is considered an adult.</li><li>• Duplicative exclusion criterion regarding prior ERT use was eliminated.</li><li>• Collection of PK samples was moved from between Days 1 to 15 to between Days 15 to 30 in order to capture steady-state data.</li><li>• Provision was made for 2 interim analyses in order to evaluate the subgroup of subjects aged 12 to <math>&lt; 16</math> years.</li><li>• The requirement for GLA genotype testing prior to migalastat administration was clarified.</li><li>• Plasma lyso-Gb3 was eliminated at screening, since it is also collected at baseline and does not impact inclusion criteria.</li><li>• Evaluation of PGI-C was moved from Month 2 to Month 3 and added to Month 9.</li><li>• Height measurement was added to every site visit in order to calculate eGFR.</li><li>• Questioning regarding the date of last menstrual period for menstruating females was added to all telephone contacts.</li><li>• Exploratory pharmacodynamic (PD) biomarkers were specified.</li><li>• A clarification was added to note that subjects enrolling in an extension study will not need to attend the follow-up visit.</li><li>• Procedures critical to collection of PK samples were specified and emphasized.</li></ul>

Notes:

### Interruptions (globally)

Were there any global interruptions to the trial? No

## Limitations and caveats

None reported