



Clinical trial results:

An Open-Label Extension Study to Evaluate the Long-Term Safety and Efficacy of Migalastat Hydrochloride Monotherapy in Subjects with Fabry Disease

Summary

EudraCT number	2014-002701-38
Trial protocol	AT BE GB ES DK
Global end of trial date	23 October 2019

Results information

Result version number	v1 (current)
This version publication date	06 November 2020
First version publication date	06 November 2020

Trial information

Trial identification

Sponsor protocol code	AT1001-042
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02194985
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Amicus Therapeutics, Inc.
Sponsor organisation address	1 Cedar Brook Drive, Cranbury, NJ, United States, 08512
Public contact	Medical Affairs, Amicus Therapeutics, medinfo@amicusrx.com
Scientific contact	Medical Affairs, Amicus Therapeutics, medinfo@amicusrx.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?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	26 August 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	23 October 2019
Global end of trial reached?	Yes
Global end of trial date	23 October 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess long-term safety of migalastat hydrochloride (HCl) in the treatment of participants with Fabry disease who have completed treatment in a previous study of migalastat HCl.

Protection of trial subjects:

This study was conducted in accordance with International Conference on Harmonisation (ICH) Good Clinical Practice, 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	14 March 2015
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Argentina: 1
Country: Number of subjects enrolled	Australia: 13
Country: Number of subjects enrolled	Brazil: 3
Country: Number of subjects enrolled	Egypt: 1
Country: Number of subjects enrolled	Japan: 5
Country: Number of subjects enrolled	Turkey: 3
Country: Number of subjects enrolled	United States: 25
Country: Number of subjects enrolled	Canada: 3
Country: Number of subjects enrolled	Spain: 1
Country: Number of subjects enrolled	United Kingdom: 7
Country: Number of subjects enrolled	Austria: 2
Country: Number of subjects enrolled	Belgium: 1
Country: Number of subjects enrolled	Denmark: 12
Country: Number of subjects enrolled	France: 4
Country: Number of subjects enrolled	Italy: 3
Worldwide total number of subjects	84
EEA total number of subjects	30

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)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	72
From 65 to 84 years	12
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Participants entered this extension study immediately upon completion of their final treatment visit in a previous migalastat HCl study.

Period 1

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

Arms

Arm title	Migalastat HCl 150 mg
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Arm description:

Migalastat HCl 150 milligram (mg) was administered orally once every other day for a median duration of 3.1 years (ranged from approximately 1 month to 4.3 years).

Arm type	Experimental
Investigational medicinal product name	Migalastat HCl 150 mg
Investigational medicinal product code	
Other name	AT1001
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Migalastat HCl 150 mg (equivalent to 123 mg migalastat) was provided as capsules in blister packs. One capsule was taken orally every other day.

Number of subjects in period 1	Migalastat HCl 150 mg
Started	84
Received at Least 1 Dose of Study Drug	84
Completed	73
Not completed	11
Consent withdrawn by subject	2
Physician decision	4
Adverse event, non-fatal	1
Met Protocol Defined Stopping Criteria	3
Lost to follow-up	1

Baseline characteristics

Reporting groups

Reporting group title	Overall
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Reporting group description:

All participants who took at least 1 dose of the study drug after they had enrolled into this study.

Reporting group values	Overall	Total	
Number of subjects	84	84	
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)	0	0	
Adults (18-64 years)	72	72	
From 65-84 years	12	12	
85 years and over	0	0	
Age continuous			
Units: years			
arithmetic mean	51.9		
standard deviation	± 12.27	-	
Gender categorical			
Units: Subjects			
Female	50	50	
Male	34	34	

End points

End points reporting groups

Reporting group title	Migalastat HCl 150 mg
Reporting group description: Migalastat HCl 150 milligram (mg) was administered orally once every other day for a median duration of 3.1 years (ranged from approximately 1 month to 4.3 years).	
Subject analysis set title	Safety Population
Subject analysis set type	Safety analysis
Subject analysis set description: All participants who received at least 1 dose of study drug after they enrolled into this open-label extension study.	
Subject analysis set title	Intent-to-Treat Population
Subject analysis set type	Intention-to-treat
Subject analysis set description: All participants who received at least 1 dose of study drug after they enrolled into this open-label extension study.	

Primary: Number Of Participants Experiencing Adverse Events (AEs)

End point title	Number Of Participants Experiencing Adverse Events (AEs) ^[1]
End point description: An AE was defined as any untoward medical occurrence in a participant administered migalastat that did not necessarily have a causal relationship with the treatment. Each AE was recorded at time of reporting; visits typically occurred every 6 months. Serious AEs were life threatening or resulted in death, resulted in disability/incapacity, hospitalization or prolonged hospitalization, or a congenital anomaly. The criteria for AE severity were: Mild: awareness of sign or symptom, does not interfere with normal everyday activities; Moderate: discomforting, interferes with normal everyday activities, but able to function; Severe: incapacitating, prevents normal everyday activities or significantly affects clinical status and requires medical intervention. A summary of serious and all other non-serious AEs regardless of causality is located in the Adverse Events section.	
End point type	Primary
End point timeframe: Day 1 (after dosing) to End of Study	

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: Quantitative statistical analysis was not performed for this end point; no treatment groups were compared in this single-group study.

End point values	Migalastat HCl 150 mg			
Subject group type	Reporting group			
Number of subjects analysed	84			
Units: participants				
number (not applicable)				
Participants with at least 1 AE	80			
Participants with at least 1 serious AE	26			
Participants discontinued due to AEs	1			
Participants with AEs leading to death	0			
Participants with AEs related to study drug	24			
Participants with AEs unrelated to study drug	56			
Participants with at least 1 mild AE	19			
Participants with at least 1 moderate AE	46			

Participants with at least 1 severe AE	15			
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Statistical analyses

No statistical analyses for this end point

Secondary: Annualized Rate Of Change In The Estimated Glomerular Filtration Rate (eGFR)

End point title	Annualized Rate Of Change In The Estimated Glomerular Filtration Rate (eGFR)
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End point description:

The annualized rate of change in the eGFR was assessed per participant by the slope of the simple linear regression between the observed values and the assessment times. It was calculated by using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation (eGFR [CKD-EPI]) and the Modification of Diet in Renal Disease (MDRD) equation (eGFR [MDRD]). The equations are as follows:

$$\text{eGFR [MDRD]} = 175 \times (1/\text{Serum Creatinine in mg/deciliter}^{1.154}) \times (1/\text{Age in years}^{0.203}) \times 0.742$$
[if female] $\times 1.212$ [if black] $\times 0.808$ [if Japanese];

$$\text{eGFR [CKD-EPI]} = 141 \times \min(\text{Serum creatinine [Scr]/k, 1})^a \times \max(\text{Scr/k, 1}) - 1.209 \times 0.993\text{Age} \times 1.018$$
[if female] $\times 1.159$ [if black],
where Scr is serum creatinine, k is 0.7 for females and 0.9 for males, a is -0.329 for females and -0.411 for males, min indicates the minimum of Scr/k or 1, and max indicates the maximum of Scr/k or 1.
Participants with at least a Baseline and a post-Baseline value are presented.

End point type	Secondary
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End point timeframe:

Baseline, End of Study

End point values	Migalastat HCl 150 mg			
Subject group type	Reporting group			
Number of subjects analysed	84 ^[2]			
Units: mL/min/1.73 m ²				
arithmetic mean (standard deviation)				
eGFR[MDRD]	-1.6107 (\pm 5.62761)			
eGFR[CKD-EPI]	-1.3528 (\pm 4.84795)			

Notes:

[2] - Intent-to-Treat (ITT) Population

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline In eGFR At End Of Study

End point title	Change From Baseline In eGFR At End Of Study
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End point description:

The change from baseline in eGFR was calculated using eGFR[CKD-EPI]) and eGFR[MDRD]) equations.

Baseline was defined as the data collected at Month 0, if not available, it was the last visit of the previous (feeder) study if done within 6 months. End of Study was the last recorded observation for each participant (approximately 30 days after last treatment). Only participants with both a Baseline value and an End of Study value were included in the change from baseline analysis.

End point type	Secondary
End point timeframe:	
Baseline, End of Study	

End point values	Migalastat HCl 150 mg			
Subject group type	Reporting group			
Number of subjects analysed	84 ^[3]			
Units: mL/min/1.73 m ²				
arithmetic mean (standard deviation)				
Baseline eGFR[MDRD] (n=82)	79.0 (± 22.56)			
End of Study eGFR[MDRD] (n=73)	75.8 (± 22.90)			
Change from Baseline eGFR[MDRD] (n=72)	-1.4 (± 10.62)			
Baseline eGFR[CKD-EPI] (n=82)	84.70 (± 23.092)			
End of Study eGFR[CKD-EPI] (n=73)	82.02 (± 23.890)			
Change from Baseline eGFR[CKD-EPI] (n=72)	-0.93 (± 9.828)			

Notes:

[3] - ITT population who had analysable data at the specified time points.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline In Plasma Globotriaosylsphingosine (Lyso-Gb3) To End Of Study

End point title	Change From Baseline In Plasma Globotriaosylsphingosine (Lyso-Gb3) To End Of Study
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End point description:

Concentrations of lyso-Gb3 were measured in plasma using a qualified assay. Baseline was defined as the data collected at Month 0, if not available, it was the last visit of the previous (feeder) study if done within 6 months. End of study was the last recorded observation for each participant (approximately 30 days after last treatment). Only participants with both a Baseline value and an End of Study value were included in the change from baseline analysis.

End point type	Secondary
End point timeframe:	
Baseline, End of Study	

End point values	Migalastat HCl 150 mg			
Subject group type	Reporting group			
Number of subjects analysed	84 ^[4]			
Units: nmol/L				
arithmetic mean (standard deviation)				
Baseline (n=83)	13.294 (± 17.5566)			
End of Study (n=74)	6.724 (± 7.5343)			
Change from Baseline (n=74)	-4.785 (± 9.0283)			

Notes:

[4] - ITT population who had analysable data at the specified time points.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline In White Blood Cell α-Gal A Activity To End Of Study

End point title	Change From Baseline In White Blood Cell α-Gal A Activity To End Of Study
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End point description:

The activity of the α-galactosidase A (α-Gal A) enzyme was measured in leukocyte lysate by a validated fluorometric assay method, using 4-methylumbelliferone as a reference. The activity values obtained were normalized to protein (measured using a colorimetric assay). Baseline was defined as the data collected at Month 0, if not available, it was the last visit of the previous (feeder) study if done within 6 months. End of Study was the last recorded observation for each participant (approximately 30 days after last treatment). Results for male participants are reported. Only participants with both a Baseline value and an End of Study value were included in the change from baseline analysis.

End point type	Secondary
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End point timeframe:

Baseline, End of Study

End point values	Migalastat HCl 150 mg			
Subject group type	Reporting group			
Number of subjects analysed	34 ^[5]			
Units: nmol/hr/mg				
arithmetic mean (standard deviation)				
Baseline (n=27)	6.882 (± 6.6857)			
End of Study (n=30)	5.290 (± 5.4054)			
Change from Baseline (n=24)	-1.375 (± 3.3432)			

Notes:

[5] - Male participants in ITT population who had analyzable data at the specified time points.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline In 24-hour Urine Protein To End Of Study

End point title	Change From Baseline In 24-hour Urine Protein To End Of Study
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End point description:

A 24-hour urine sample was collected to measure 24-hour urine protein. Baseline was defined as the data collected at Month 0, if not available, it was the last visit of the previous (feeder) study if done within 6 months. End of Study was the last recorded observation for each participant (approximately 30 days after last treatment). Only participants with both a Baseline value and an End of Study value were included in the change from baseline analysis.

End point type	Secondary
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End point timeframe:

Baseline, End of Study

End point values	Migalastat HCl 150 mg			
Subject group type	Reporting group			
Number of subjects analysed	84 ^[6]			
Units: mg/day				
arithmetic mean (standard deviation)				
Baseline (n=83)	478.9 (± 948.59)			
End of Study (n=66)	394.0 (± 547.77)			
Change from Baseline (n=66)	5.4 (± 233.49)			

Notes:

[6] - ITT population who had analysable data at the specified time points.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline In Left Ventricular Mass (LVM) To End Of Study

End point title	Change From Baseline In Left Ventricular Mass (LVM) To End Of Study
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End point description:

LVM was measured by echocardiography. Baseline was defined as the data collected at Month 0, if not available, it was the last visit of the previous (feeder) study if done within 6 months. End of Study was the last recorded observation for each participant (approximately 30 days after last treatment). Only participants with both a Baseline value and an End of Study value were included in the change from baseline analysis.

End point type	Secondary
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End point timeframe:

Baseline, End of Study

End point values	Migalastat HCl 150 mg			
Subject group type	Reporting group			
Number of subjects analysed	84 ^[7]			
Units: gram				
arithmetic mean (standard deviation)				
Baseline (n=70)	178.879 (± 78.6761)			
End of Study (n=25)	157.896 (± 47.9947)			
Change from Baseline (n=24)	-0.803 (± 18.8522)			

Notes:

[7] - ITT population who had analysable data at the specified time points.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline In Left Ventricular Mass Index (LVMI) To End Of Study

End point title	Change From Baseline In Left Ventricular Mass Index (LVMI) To End Of Study
End point description:	
LVMI was measured by echocardiography. Baseline was defined as the data collected at Month 0, if not available, it was the last visit of the previous (feeder) study if done within 6 months. End of Study was the last recorded observation for each participant (approximately 30 days after last treatment). Only participants with both a Baseline value and an End of Study value were included in the change from baseline analysis.	
End point type	Secondary
End point timeframe:	
Baseline, End of Study	

End point values	Migalastat HCl 150 mg			
Subject group type	Reporting group			
Number of subjects analysed	84 ^[8]			
Units: g/m ²				
arithmetic mean (standard deviation)				
Baseline (n=68)	96.513 (± 36.5691)			
End of Study (n=25)	83.912 (± 22.7633)			
Change from Baseline (n=68)	-0.809 (± 11.8056)			

Notes:

[8] - ITT population who had analysable data at the specified time points.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline In Patient Reported Quality Of Life To End Of Study, As Assessed By The Short Form-36 (SF-36) Questionnaire

End point title	Change From Baseline In Patient Reported Quality Of Life To End Of Study, As Assessed By The Short Form-36 (SF-36) Questionnaire
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End point description:

The SF-36 is a participant self-rated questionnaire that is a general measure of perceived health status comprising 36 questions, which yields an 8-scale health profile (Physical Functioning, Role Physical, Bodily Pain, General Health, Vitality, Social Functioning, Role Emotional, and Mental Health). Scores on each item are summed and averaged (range: 0=worst to 100=best). Scores were normed to the US population. Higher score indicates less disability. A positive change from baseline indicates improvement. Baseline was defined as the data collected in the last visit of the previous (feeder) study. Only participants with both a Baseline value and an End of Study value were included in the change from baseline analysis.

End point type	Secondary
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End point timeframe:

Baseline, End of Study

End point values	Migalastat HCl 150 mg			
Subject group type	Reporting group			
Number of subjects analysed	84 ^[9]			
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline Physical Functioning (n=84)	48.313 (± 9.2345)			
End of Study Physical Functioning (n=75)	46.415 (± 10.2466)			
Change from Baseline Physical Functioning (n=75)	-1.276 (± 7.1627)			
Baseline Role Physical (n=84)	46.197 (± 10.0761)			
End of Study Role Physical (n=75)	45.929 (± 10.5723)			
Change from Baseline Role Physical (n=75)	0.390 (± 7.3500)			
Baseline Bodily Pain (n=84)	46.889 (± 10.5983)			
End of Study Bodily Pain (n=75)	46.737 (± 10.3368)			
Change from Baseline Bodily Pain (n=75)	0.425 (± 8.1342)			
Baseline General Health (n=84)	44.016 (± 10.2497)			
End of Study General Health (n=75)	42.352 (± 10.1185)			
Change from Baseline General Health (n=75)	-0.811 (± 5.8672)			
Baseline Vitality (n=84)	46.375 (± 11.8451)			
End of Study Vitality (n=75)	45.429 (± 12.4340)			
Change from Baseline Vitality (n=75)	-0.674 (± 8.5076)			
Baseline Social Functioning (n=84)	47.433 (± 10.4985)			

End of Study Social Functioning (n=75)	47.648 (± 9.5165)			
Change from Baseline Social Functioning (n=75)	0.401 (± 8.4356)			
Baseline Role Emotional (n=84)	47.547 (± 10.3897)			
End of Study Role Emotional (n=75)	46.141 (± 10.9054)			
Change from Baseline Role Emotional (n=75)	-0.929 (± 10.6679)			
Baseline Mental Health (n=84)	48.501 (± 10.6878)			
End of Study Mental Health (n=75)	49.578 (± 10.5732)			
Change from Baseline Mental Health (n=75)	0.872 (± 6.2528)			
Baseline Physical Component (n=84)	46.184 (± 10.2268)			
End of Study Physical Component (n=75)	44.825 (± 10.4292)			
Change from Baseline Physical Component (n=75)	-0.508 (± 6.2494)			
Baseline Mental Component (n=84)	47.917 (± 11.5480)			
End of Study Mental Component (n=75)	48.175 (± 10.9497)			
Change from Baseline Mental Component (n=75)	0.187 (± 8.2714)			

Notes:

[9] - ITT population who had analysable data at the specified time points.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Baseline to up to 4.4 years (includes safety follow-up)

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	16.1
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Reporting groups

Reporting group title	Migalastat HCl 150 mg
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Reporting group description:

Migalastat HCl 150 mg was administered orally once every other day for a median duration of 3.1 years (ranged from approximately 1 month to 4.3 years).

Serious adverse events	Migalastat HCl 150 mg		
Total subjects affected by serious adverse events			
subjects affected / exposed	26 / 84 (30.95%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Breast cancer			
subjects affected / exposed	2 / 84 (2.38%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Invasive lobular breast carcinoma			
subjects affected / exposed	1 / 84 (1.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Air embolism			
subjects affected / exposed	1 / 84 (1.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hypertension			

subjects affected / exposed	1 / 84 (1.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hypotension			
subjects affected / exposed	1 / 84 (1.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Device malfunction			
subjects affected / exposed	1 / 84 (1.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Immune system disorders			
Drug hypersensitivity			
subjects affected / exposed	1 / 84 (1.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Reproductive system and breast disorders			
Uterine prolapse			
subjects affected / exposed	1 / 84 (1.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	2 / 84 (2.38%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
Pneumothorax			
subjects affected / exposed	1 / 84 (1.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Depression			

subjects affected / exposed	1 / 84 (1.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Suicidal ideation			
subjects affected / exposed	1 / 84 (1.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Investigations			
Heart rate increased			
subjects affected / exposed	1 / 84 (1.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Rib fracture			
subjects affected / exposed	1 / 84 (1.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	2 / 84 (2.38%)		
occurrences causally related to treatment / all	0 / 7		
deaths causally related to treatment / all	0 / 0		
Atrioventricular block complete			
subjects affected / exposed	1 / 84 (1.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Left ventricular hypertrophy			
subjects affected / exposed	1 / 84 (1.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Ventricular tachycardia			
subjects affected / exposed	1 / 84 (1.19%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		

Nervous system disorders			
Convulsion			
subjects affected / exposed	1 / 84 (1.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Embolic stroke			
subjects affected / exposed	1 / 84 (1.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Headache			
subjects affected / exposed	1 / 84 (1.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Neuralgia			
subjects affected / exposed	1 / 84 (1.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Syncope			
subjects affected / exposed	1 / 84 (1.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Transient ischaemic attack			
subjects affected / exposed	1 / 84 (1.19%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Eye disorders			
Visual impairment			
subjects affected / exposed	1 / 84 (1.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Abdominal pain			

subjects affected / exposed	1 / 84 (1.19%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Abdominal pain upper			
subjects affected / exposed	1 / 84 (1.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Abdominal wall haematoma			
subjects affected / exposed	1 / 84 (1.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Barrett's oesophagus			
subjects affected / exposed	1 / 84 (1.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Large intestine perforation			
subjects affected / exposed	1 / 84 (1.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Biliary dyskinesia			
subjects affected / exposed	1 / 84 (1.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Subcutaneous emphysema			
subjects affected / exposed	1 / 84 (1.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Renal failure			
subjects affected / exposed	1 / 84 (1.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Musculoskeletal and connective tissue disorders			
Arthritis			
subjects affected / exposed	1 / 84 (1.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Osteoarthritis			
subjects affected / exposed	1 / 84 (1.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Periarthritis			
subjects affected / exposed	1 / 84 (1.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Tendon calcification			
subjects affected / exposed	1 / 84 (1.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Appendicitis perforated			
subjects affected / exposed	1 / 84 (1.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Biliary sepsis			
subjects affected / exposed	1 / 84 (1.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Diverticulitis			
subjects affected / exposed	1 / 84 (1.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infective exacerbation of bronchiectasis			

subjects affected / exposed	1 / 84 (1.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumonia			
subjects affected / exposed	1 / 84 (1.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	2 / 84 (2.38%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Diabetes mellitus			
subjects affected / exposed	1 / 84 (1.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Lipomatosis			
subjects affected / exposed	1 / 84 (1.19%)		
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	Migalastat HCl 150 mg		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	74 / 84 (88.10%)		
Vascular disorders			
Hypotension			
subjects affected / exposed	5 / 84 (5.95%)		
occurrences (all)	5		
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	16 / 84 (19.05%)		
occurrences (all)	22		

Oedema peripheral subjects affected / exposed occurrences (all)	12 / 84 (14.29%) 18		
Pyrexia subjects affected / exposed occurrences (all)	9 / 84 (10.71%) 12		
Pain subjects affected / exposed occurrences (all)	5 / 84 (5.95%) 5		
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain subjects affected / exposed occurrences (all)	7 / 84 (8.33%) 11		
Asthma subjects affected / exposed occurrences (all)	6 / 84 (7.14%) 7		
Cough subjects affected / exposed occurrences (all)	6 / 84 (7.14%) 7		
Dyspnoea subjects affected / exposed occurrences (all)	6 / 84 (7.14%) 6		
Dyspnoea exertional subjects affected / exposed occurrences (all)	6 / 84 (7.14%) 7		
Psychiatric disorders			
Depression subjects affected / exposed occurrences (all)	8 / 84 (9.52%) 9		
Insomnia subjects affected / exposed occurrences (all)	6 / 84 (7.14%) 6		
Investigations			
Albumin urine present subjects affected / exposed occurrences (all)	6 / 84 (7.14%) 6		

Blood uric acid increased subjects affected / exposed occurrences (all)	6 / 84 (7.14%) 6		
Protein urine present subjects affected / exposed occurrences (all)	6 / 84 (7.14%) 7		
Blood creatinine increased subjects affected / exposed occurrences (all)	5 / 84 (5.95%) 5		
Glomerular filtration rate decreased subjects affected / exposed occurrences (all)	5 / 84 (5.95%) 5		
Injury, poisoning and procedural complications Overdose subjects affected / exposed occurrences (all)	12 / 84 (14.29%) 18		
Cardiac disorders Palpitations subjects affected / exposed occurrences (all)	6 / 84 (7.14%) 7		
Nervous system disorders Paraesthesia subjects affected / exposed occurrences (all)	13 / 84 (15.48%) 18		
Headache subjects affected / exposed occurrences (all)	12 / 84 (14.29%) 18		
Dizziness subjects affected / exposed occurrences (all)	10 / 84 (11.90%) 11		
Hypoaesthesia subjects affected / exposed occurrences (all)	10 / 84 (11.90%) 17		
Migraine subjects affected / exposed occurrences (all)	5 / 84 (5.95%) 5		

Neuralgia subjects affected / exposed occurrences (all)	5 / 84 (5.95%) 5		
Ear and labyrinth disorders Tinnitus subjects affected / exposed occurrences (all) Vertigo subjects affected / exposed occurrences (all)	7 / 84 (8.33%) 8 7 / 84 (8.33%) 7		
Gastrointestinal disorders Nausea subjects affected / exposed occurrences (all) Diarrhoea subjects affected / exposed occurrences (all) Abdominal pain subjects affected / exposed occurrences (all) Abdominal pain upper subjects affected / exposed occurrences (all) Constipation subjects affected / exposed occurrences (all) Dyspepsia subjects affected / exposed occurrences (all) Gastrooesophageal reflux disease subjects affected / exposed occurrences (all) Vomiting subjects affected / exposed occurrences (all)	10 / 84 (11.90%) 21 9 / 84 (10.71%) 15 7 / 84 (8.33%) 18 6 / 84 (7.14%) 8 6 / 84 (7.14%) 7 5 / 84 (5.95%) 5 5 / 84 (5.95%) 6 5 / 84 (5.95%) 5		
Renal and urinary disorders			

Proteinuria subjects affected / exposed occurrences (all)	12 / 84 (14.29%) 12		
Endocrine disorders Hypothyroidism subjects affected / exposed occurrences (all)	5 / 84 (5.95%) 5		
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all) Pain in extremity subjects affected / exposed occurrences (all) Musculoskeletal pain subjects affected / exposed occurrences (all) Back pain subjects affected / exposed occurrences (all) Muscle spasms subjects affected / exposed occurrences (all) Muscular weakness subjects affected / exposed occurrences (all) Tendonitis subjects affected / exposed occurrences (all)	16 / 84 (19.05%) 23 14 / 84 (16.67%) 21 10 / 84 (11.90%) 13 9 / 84 (10.71%) 18 7 / 84 (8.33%) 7 7 / 84 (8.33%) 11 7 / 84 (8.33%) 7		
Infections and infestations Nasopharyngitis subjects affected / exposed occurrences (all) Upper respiratory tract infection subjects affected / exposed occurrences (all)	17 / 84 (20.24%) 29 12 / 84 (14.29%) 20		

Urinary tract infection subjects affected / exposed occurrences (all)	12 / 84 (14.29%) 17		
Influenza subjects affected / exposed occurrences (all)	10 / 84 (11.90%) 14		
Sinusitis subjects affected / exposed occurrences (all)	9 / 84 (10.71%) 10		
Bronchitis subjects affected / exposed occurrences (all)	6 / 84 (7.14%) 9		
Metabolism and nutrition disorders Hypercholesterolaemia subjects affected / exposed occurrences (all)	5 / 84 (5.95%) 5		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
21 October 2015	<ul style="list-style-type: none">• Revised the lowest age limit for enrollment from 16 to 18 years of age. The participants under the age of 18 were allowed to enroll at sites with required relevant regulatory and ethics approvals.• Added a new stopping criterion: An eGFR value of $< 30 \text{ mL/min/1.73 m}^2$.• Removed a requirement to collect historical (up to 5-year) Fabry disease data from the participants.• Revised contraception requirements for both male and female participants, clarifying that contraception methods must be medically accepted, and abstinence was not allowed.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

None

Notes: