



## 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	2011-004800-40
Trial protocol	GB ES IT DK BE AT
Global end of trial date	17 February 2016

#### Results information

Result version number	v1 (current)
This version publication date	19 May 2017
First version publication date	19 May 2017

#### Trial information

##### Trial identification

Sponsor protocol code	AT1001-041
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##### Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01458119
WHO universal trial number (UTN)	-

Notes:

#### Sponsors

Sponsor organisation name	Amicus Therapeutics, Inc.
Sponsor organisation address	1 Cedarbrook Drive, Cranbury, United States, NJ 08512
Public contact	Medical Information, Amicus Therapeutics, Inc., MedInfo_Amicus@quintiles.com
Scientific contact	Medical Information, Amicus Therapeutics, Inc., MedInfo_Amicus@quintiles.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:

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**Results analysis stage**

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Analysis stage	Final
Date of interim/final analysis	17 February 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	17 February 2016
Global end of trial reached?	Yes
Global end of trial date	17 February 2016
Was the trial ended prematurely?	Yes

Notes:

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**General information about the trial**

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Main objective of the trial:

To assess the long-term safety of migalastat in the treatment of subjects with Fabry disease who completed treatment in a previous study of migalastat. The previous studies include AT1001-011, AT1001-012 and FAB-CL-205.

Protection of trial subjects:

The study was conducted in accordance with the principles of the Declaration of Helsinki including amendments in force up to and including the time the study was conducted. The study was conducted in compliance with the International Conference on Harmonisation E6 Guideline for Good Clinical Practice, and is compliant with the European Union Clinical Trial Directive 2001/20/EC. The study was also conducted in compliance with the United States Food and Drug Administration regulations in 21 Code of Federal Regulations.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	14 October 2011
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

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**Population of trial subjects**

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**Subjects enrolled per country**

Country: Number of subjects enrolled	Argentina: 1
Country: Number of subjects enrolled	Australia: 16
Country: Number of subjects enrolled	Belgium: 1
Country: Number of subjects enrolled	Brazil: 5
Country: Number of subjects enrolled	Canada: 3
Country: Number of subjects enrolled	Denmark: 12
Country: Number of subjects enrolled	Egypt: 1
Country: Number of subjects enrolled	France: 7
Country: Number of subjects enrolled	Italy: 1
Country: Number of subjects enrolled	Spain: 2
Country: Number of subjects enrolled	Turkey: 4
Country: Number of subjects enrolled	United Kingdom: 6
Country: Number of subjects enrolled	United States: 26
Worldwide total number of subjects	85
EEA total number of subjects	29

Notes:

<b>Subjects enrolled per age group</b>	
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)	76
From 65 to 84 years	9
85 years and over	0

## Subject disposition

### Recruitment

Recruitment details:

85 eligible subjects with Fabry disease who had completed migalastat monotherapy treatment in a previous study (AT1001-011, AT1001-012 or FAB-CL-205) were enrolled in this open-label extension study to enable collection of longer term safety and efficacy data. First subject enrolled: 14 October 2011. Last subject completed: 17 February 2016.

### Pre-assignment

Screening details:

Eligible subjects were enrolled if in the opinion of the investigator they could benefit from remaining on migalastat treatment. 85 subjects received at least 1 dose of study drug; of these 68 had amenable mutations in the gene encoding an alpha-galactosidase-A ( $\alpha$ -Gal-A)(GLA) genotype that responds to migalastat in the migalastat amenability assay.

### Period 1

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

### Arms

Arm title	Migalastat
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Arm description:

Subjects who completed migalastat monotherapy treatment in a previous study and who were eligible to participate were enrolled in this study to enable continued migalastat treatment on a dosing regimen of migalastat hydrochloride (migalastat HCl) 150 milligrams (mg) once every other day (QOD). Inactive reminder capsules were taken on alternate days. In order to ensure continuous treatment with migalastat during the transition from the previous study, subjects were given the first dose of either migalastat HCl or the inactive reminder capsule during the baseline visit to maintain the migalastat HCl 150 mg QOD dosing regimen.

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

Dosage and administration details:

150 mg of migalastat HCl was administered orally QOD at approximately the same time each day. Subjects were required to fast 2 hours before and 2 hours after taking each dose.

Number of subjects in period 1	Migalastat
Started	85
Completed	65
Not completed	20
Adverse event, serious fatal	2
Consent withdrawn by subject	8
Physician decision	4
Withdrawal due to nonamenable mutation	1

Adverse event, non-fatal	1
Pregnancy	1
Non-Compliance with study drug	3

## Baseline characteristics

### Reporting groups

Reporting group title	Migalastat
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Reporting group description:

Subjects who completed migalastat monotherapy treatment in a previous study and who were eligible to participate were enrolled in this study to enable continued migalastat treatment on a dosing regimen of migalastat hydrochloride (migalastat HCl) 150 milligrams (mg) once every other day (QOD). Inactive reminder capsules were taken on alternate days. In order to ensure continuous treatment with migalastat during the transition from the previous study, subjects were given the first dose of either migalastat HCl or the inactive reminder capsule during the baseline visit to maintain the migalastat HCl 150 mg QOD dosing regimen.

Reporting group values	Migalastat	Total	
Number of subjects	85	85	
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)	76	76	
From 65-84 years	9	9	
85 years and over	0	0	
Age Continuous			
Units: years			
arithmetic mean	48.8		
standard deviation	± 12.25	-	
Gender Categorical			
Units: Subjects			
Female	52	52	
Male	33	33	

## End points

### End points reporting groups

Reporting group title	Migalastat
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Reporting group description:

Subjects who completed migalastat monotherapy treatment in a previous study and who were eligible to participate were enrolled in this study to enable continued migalastat treatment on a dosing regimen of migalastat hydrochloride (migalastat HCl) 150 milligrams (mg) once every other day (QOD). Inactive reminder capsules were taken on alternate days. In order to ensure continuous treatment with migalastat during the transition from the previous study, subjects were given the first dose of either migalastat HCl or the inactive reminder capsule during the baseline visit to maintain the migalastat HCl 150 mg QOD dosing regimen.

### Primary: Number of subjects experiencing treatment emergent adverse events (TEAEs).

End point title	Number of subjects experiencing treatment emergent adverse events (TEAEs). <sup>[1]</sup>
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End point description:

The long term safety of migalastat was assessed in the treatment of subjects with Fabry disease who completed treatment in a previous study of migalastat. The number of subjects experiencing TEAEs is presented for subjects who received migalastat treatment in this open-label extension study. The duration of migalastat exposure was from less than 6 months up to approximately 42 months, over a period of approximately 4 years and 4 months (52 months).

End point type	Primary
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End point timeframe:

Up to 52 months

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: The study analyses were performed using descriptive statistics. No statistical inference testing was performed for this end point.

End point values	Migalastat			
Subject group type	Reporting group			
Number of subjects analysed	85			
Units: Participants				
Subjects with at least 1 TEAE	74			
Subjects with at least 1 serious TEAE	22			
Subjects discontinued due to TEAEs	1			
Subjects with adverse events leading to death	2			
Subjects with TEAEs related to study drug	14			
Subjects with TEAEs unrelated to study drug	60			
Subjects with at least 1 mild TEAE	22			
Subjects with at least 1 moderate TEAE	40			
Subjects with at least 1 severe TEAE	12			

## Statistical analyses

**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 was assessed per subject by the slope of the simple linear regression between the observed values and the assessment times. The annualized rate of change in the eGFR was assessed in the following ways:

- by the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation (eGFR[CKD-EPI])
- by the Modification of Diet in Renal Disease equation (eGFR[MDRD]).

The mean change in eGFR[CKD-EPI] and eGFR[MDRD] from baseline to End of Study is presented for the Intention-to-Treat [ITT]-Amenable Population. The ITT-Amenable Population included all subjects with mutations amenable to migalastat in the migalastat amenability assay who took at least 1 dose of study drug after they enrolled into this open-label extension study. The number of subjects with at least a baseline and a post-baseline value are presented. The mean duration of this period was 2.03+/-0.691 years.

End point type	Secondary
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## End point timeframe:

Baseline to End of Study (approximately 2 years mean duration)

End point values	Migalastat			
Subject group type	Reporting group			
Number of subjects analysed	47			
Units: milliliters/minute/1.73 square meters				
arithmetic mean (confidence interval 95%)				
Annualized Rate of Change in eGFR[CKD-EPI]	1.54 (-1.63 to 4.71)			
Annualized Rate of Change in eGFR[MDRD]	1.4 (-3.14 to 5.94)			

**Statistical analyses**

No statistical analyses for this end point

**Secondary: Change from Baseline in 24-Hour Urine Protein**

End point title	Change from Baseline in 24-Hour Urine Protein
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## End point description:

The change from baseline at each visit in the 24 hour urine protein are presented.

The ITT-Amenable Population included all subjects with mutations amenable to migalastat in the migalastat amenability assay who took at least 1 dose of study drug after they enrolled into this open-label extension study. The number of subjects (n) with values at each timepoint are presented.

End point type	Secondary
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## End point timeframe:

Baseline to Month 36 visit



End point values	Migalastat			
Subject group type	Reporting group			
Number of subjects analysed	68			
Units: grams/day				
arithmetic mean (confidence interval 95%)				
Month 6 (n=38)	0.043 (-0.034 to 0.121)			
Month 12 (n=39)	0.01 (-0.066 to 0.086)			
Month 18 (n=34)	0.018 (-0.132 to 0.167)			
Month 24 (n=27)	0.12 (-0.039 to 0.28)			
Month 30 (n=19)	0.049 (-0.043 to 0.141)			
Month 36 (n=7)	0.062 (-0.213 to 0.337)			

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change from Baseline in 24-Hour Urine Albumin:Creatinine Ratio

End point title	Change from Baseline in 24-Hour Urine Albumin:Creatinine Ratio
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End point description:

The change from baseline at each visit in the 24 hour urine Albumin:Creatinine Ratio are presented.

The ITT-Amenable Population included all subjects with mutations amenable to migalastat in the migalastat amenability assay who took at least 1 dose of study drug after they enrolled into this open-label extension study. The number of subjects (n) with values at each timepoint are presented.

End point type	Secondary
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End point timeframe:

Baseline to Month 36 visit

End point values	Migalastat			
Subject group type	Reporting group			
Number of subjects analysed	68			
Units: mg/millimole				
arithmetic mean (confidence interval 95%)				
Month 6 (n=33)	-1.324 (-6.924 to 4.277)			
Month 12 (n=32)	4.675 (-3.214 to 12.563)			

Month 18 (n=29)	1.567 (-7.493 to 10.627)			
Month 24 (n=23)	4.58 (-4.643 to 13.804)			
Month 30 (n=13)	5.455 (-1.262 to 12.172)			
Month 36 (n=4)	0.839 (-14.536 to 16.214)			

## 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)
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End point description:

The change from baseline at the Month 12, 24 and 36 visits in the LVMI as measured by echocardiogram (ECHO) are presented.

The following are the LVMI ranges:

Female:

Normal: 43-95 g/m<sup>2</sup>; mildly abnormal: 96-108 g/m<sup>2</sup>; moderately abnormal: 109-121 g/m<sup>2</sup>; severely abnormal:  $\geq$ 122 g/m<sup>2</sup>.

Male:

Normal: 49-115 g/m<sup>2</sup>; mildly abnormal: 116-131 g/m<sup>2</sup>; moderately abnormal: 132-148 g/m<sup>2</sup>; severely abnormal:  $\geq$ 149 g/m<sup>2</sup>.

The ITT-Amenable Population included all subjects with mutations amenable to migalastat in the migalastat amenability assay who took at least 1 dose of study drug after they enrolled into this open-label extension study. The number of subjects (n) with values at each timepoint are presented.

End point type	Secondary
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End point timeframe:

Baseline to Month 36 visit

End point values	Migalastat			
Subject group type	Reporting group			
Number of subjects analysed	68			
Units: grams/square meter (g/m <sup>2</sup> )				
arithmetic mean (confidence interval 95%)				
Month 12 (n=36)	-0.758 (-5.306 to 3.79)			
Month 24 (n=28)	-0.465 (-4.991 to 4.061)			
Month 36 (n=4)	-4.823 (-10.512 to 0.867)			

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change from Baseline in the White Blood Cell (WBC) $\alpha$ -Gal-A activity for male subjects

End point title	Change from Baseline in the White Blood Cell (WBC) $\alpha$ -Gal-A activity for male subjects
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End point description:

The change from baseline at each visit in the  $\alpha$ -Gal-A activity in WBCs is presented for male subjects in the ITT-Amenable Population. Higher values indicate less disability. As females are mosaic and express both mutant and wild-type  $\alpha$ -Gal-A, the assessment of  $\alpha$ -Gal-A activity is not relevant in female patients.

The ITT-Amenable Population included all subjects with mutations amenable to migalastat in the migalastat amenability assay who took at least 1 dose of study drug after they enrolled into this open-label extension study. The number of subjects (n) with values at each timepoint are presented.

End point type	Secondary
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End point timeframe:

Baseline to Month 36 visit

End point values	Migalastat			
Subject group type	Reporting group			
Number of subjects analysed	29			
Units: nanomole/mg				
arithmetic mean (confidence interval 95%)				
Month 6 (n=20)	-0.64 (-1.47 to 0.19)			
Month 12 (n=17)	-0.03 (-1.42 to 1.36)			
Month 18 (n=17)	-1.36 (-4.1 to 1.39)			
Month 24 (n=14)	0.29 (-0.83 to 1.41)			
Month 30 (n=11)	0.48 (-4.74 to 5.71)			
Month 36 (n=3)	-0.85 (-10.45 to 8.76)			

## Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

AEs were collected from the baseline visit to End of Study at each 6 monthly clinic visit. Treatment duration varied among subjects, ranging from under 6 months to approximately 42 months, over a period of approximately 4 years and 4 months (52 months).

Adverse event reporting additional description:

The Safety Population included all subjects who took at least 1 dose of study drug after they enrolled into this open-label extension study.

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
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Reporting group description:

Subjects who completed migalastat monotherapy treatment in a previous study and who were eligible to participate were enrolled in this study to enable continued migalastat treatment on a dosing regimen of migalastat hydrochloride (migalastat HCl) 150 milligrams (mg) once every other day (QOD). Inactive reminder capsules were taken on alternate days. In order to ensure continuous treatment with migalastat during the transition from the previous study, subjects were given the first dose of either migalastat HCl or the inactive reminder capsule during the baseline visit to maintain the migalastat HCl 150 mg QOD dosing regimen.

Serious adverse events	Migalastat		
Total subjects affected by serious adverse events			
subjects affected / exposed	22 / 85 (25.88%)		
number of deaths (all causes)	2		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Breast cancer metastatic			
subjects affected / exposed	1 / 85 (1.18%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Metastatic squamous cell carcinoma			
subjects affected / exposed	1 / 85 (1.18%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Papillary thyroid cancer			

subjects affected / exposed	1 / 85 (1.18%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Surgical and medical procedures			
Implantable defibrillator insertion			
subjects affected / exposed	2 / 85 (2.35%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Death			
subjects affected / exposed	1 / 85 (1.18%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Device malfunction			
subjects affected / exposed	1 / 85 (1.18%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Reproductive system and breast disorders			
Priapism			
subjects affected / exposed	1 / 85 (1.18%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Uterine polyp			
subjects affected / exposed	1 / 85 (1.18%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Conversion disorder			
subjects affected / exposed	1 / 85 (1.18%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Foot fracture			

subjects affected / exposed	1 / 85 (1.18%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	1 / 85 (1.18%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Atrial fibrillation			
subjects affected / exposed	2 / 85 (2.35%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Brain stem ischaemia			
subjects affected / exposed	1 / 85 (1.18%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hemiplegic migraine			
subjects affected / exposed	1 / 85 (1.18%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Presyncope			
subjects affected / exposed	1 / 85 (1.18%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	1 / 85 (1.18%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hiatus hernia			
subjects affected / exposed	1 / 85 (1.18%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Pancreatitis			
subjects affected / exposed	1 / 85 (1.18%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Hepatic infarction			
subjects affected / exposed	1 / 85 (1.18%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Angioedema			
subjects affected / exposed	1 / 85 (1.18%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Skin lesion			
subjects affected / exposed	1 / 85 (1.18%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Calculus urinary			
subjects affected / exposed	1 / 85 (1.18%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Endocrine disorders			
Thyroid mass			
subjects affected / exposed	1 / 85 (1.18%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Muscle spasms			
subjects affected / exposed	1 / 85 (1.18%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal chest pain			

subjects affected / exposed	1 / 85 (1.18%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Infections and infestations</b>			
Pneumonia			
subjects affected / exposed	2 / 85 (2.35%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		

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

<b>Non-serious adverse events</b>	Migalastat		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	57 / 85 (67.06%)		
<b>Injury, poisoning and procedural complications</b>			
Contusion			
subjects affected / exposed	5 / 85 (5.88%)		
occurrences (all)	6		
<b>Vascular disorders</b>			
Hypertension			
subjects affected / exposed	6 / 85 (7.06%)		
occurrences (all)	7		
<b>Cardiac disorders</b>			
Atrial fibrillation			
subjects affected / exposed	7 / 85 (8.24%)		
occurrences (all)	8		
Palpitations			
subjects affected / exposed	5 / 85 (5.88%)		
occurrences (all)	5		
<b>Nervous system disorders</b>			
Dizziness			
subjects affected / exposed	9 / 85 (10.59%)		
occurrences (all)	10		
Headache			
subjects affected / exposed	11 / 85 (12.94%)		
occurrences (all)	14		



Paraesthesia subjects affected / exposed occurrences (all)	5 / 85 (5.88%) 6		
General disorders and administration site conditions			
Fatigue subjects affected / exposed occurrences (all)	9 / 85 (10.59%) 9		
Oedema peripheral subjects affected / exposed occurrences (all)	6 / 85 (7.06%) 6		
Pain subjects affected / exposed occurrences (all)	5 / 85 (5.88%) 6		
Pyrexia subjects affected / exposed occurrences (all)	7 / 85 (8.24%) 8		
Ear and labyrinth disorders			
Vertigo subjects affected / exposed occurrences (all)	5 / 85 (5.88%) 5		
Gastrointestinal disorders			
Abdominal distension subjects affected / exposed occurrences (all)	5 / 85 (5.88%) 5		
Abdominal pain upper subjects affected / exposed occurrences (all)	5 / 85 (5.88%) 6		
Constipation subjects affected / exposed occurrences (all)	6 / 85 (7.06%) 6		
Diarrhoea subjects affected / exposed occurrences (all)	13 / 85 (15.29%) 14		
Nausea subjects affected / exposed occurrences (all)	10 / 85 (11.76%) 18		

Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all)	6 / 85 (7.06%) 6		
Psychiatric disorders Anxiety subjects affected / exposed occurrences (all)	5 / 85 (5.88%) 7		
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all)  Back pain subjects affected / exposed occurrences (all)  Pain in extremity subjects affected / exposed occurrences (all)	11 / 85 (12.94%) 13  6 / 85 (7.06%) 7  11 / 85 (12.94%) 12		
Infections and infestations Influenza subjects affected / exposed occurrences (all)  Nasopharyngitis subjects affected / exposed occurrences (all)  Upper respiratory tract infection subjects affected / exposed occurrences (all)  Urinary Tract Infection subjects affected / exposed occurrences (all)	9 / 85 (10.59%) 11  9 / 85 (10.59%) 12  6 / 85 (7.06%) 9  8 / 85 (9.41%) 11		

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
06 February 2012	<ol style="list-style-type: none"><li>1. Review of informed consent and inclusion/exclusion criteria at baseline added; clarified that labs, except for eGFR and pregnancy tests would be performed at the Follow-up visit, regardless of subject's withdrawal status, and removed the urine globotriaosylceramide (GL-3) assessment.</li><li>2. Clarified that subjects who met any withdrawal criteria and withdrew from the study were asked to return for a Follow-up visit within 30 days of the last treatment dose for assessments.</li><li>3. Footnote added to Table 1 (Time and Events) to clarify that an ECHO was to be performed for withdrawn subjects who did not have an ECHO performed in the previous 6 months.</li><li>4. Follow-Up visit defined as approximately 30 days after last treatment.</li><li>5. Clarified avoidance of certain drugs with potential for interaction with migalastat.</li><li>6. Removed urobilinogen for the urinalysis parameters.</li></ol>
31 July 2012	<ol style="list-style-type: none"><li>1. Clarified the window time for collection of baseline visit assessments.</li><li>2. Clarified the assessments performed for Early Withdrawal.</li></ol>
26 November 2012	<ol style="list-style-type: none"><li>1. Optional GLA genotyping added.</li><li>2. Etonogestrel implants included as a contraceptive method with a failure rate of &lt;1% per year.</li><li>3. Language in Retained Urine and Serum Samples section altered to offer the option to decline.</li></ol>
27 January 2014	<ol style="list-style-type: none"><li>1. Amicus added as sponsor and relevant updates made.</li><li>2. Urine GL-3 was removed as an assessment.</li><li>3. Data Safety Monitoring Board added to review safety data and stopping criteria.</li><li>4. Addition of cardiac measures to match previous studies.</li><li>5. Requirement to review inclusion/exclusion criteria every 6 months added.</li><li>6. Information about how long the protocol remained open added.</li><li>7. Reference to French subjects inclusion criteria removed.</li><li>8. Exclusion criteria updated to match previous studies.</li><li>9. Investigational Product text removed.</li><li>10. Prohibited medications and nondrug therapies updated and sites requested to avoid certain drugs that resulted in accumulation of phospholipids in lysosomes.</li><li>11. Critical baseline assessments updated to discuss conditions that had potential to impact subjects' condition on trial.</li><li>12. Safety assessments updated to include stopping criteria.</li><li>13. Addition of optional blood draw for testing of Fabry biomarkers for future exploratory analyses.</li><li>14. ITT efficacy Population removed.</li></ol>
09 July 2014	<ol style="list-style-type: none"><li>1. New text added about study discontinuation for logistical reasons and not due to either safety concerns or lack of efficacy. Text on reasons for study conclusion deleted.</li><li>2. End of Study visit added.</li><li>3. Text on Early Withdrawal, End of Study and Follow-Up Visit added.</li></ol>

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.

The study was discontinued for logistical reasons and not due to either safety concerns or lack of efficacy. The investigators discussed participation in a similar long-term migalastat treatment study for subjects ongoing at time of discontinuation.

Notes: