Clinical trial results:
An Open-label, Multicenter, Multinational Extension Study of the Long-term Safety, Pharmacodynamics, and Exploratory Efficacy of GZ/SAR402671 in Adult Male Patients Diagnosed With Fabry Disease

Summary

EudraCT number	2014-004995-49
Trial protocol	GB PL FR
Global end of trial date	20 November 2018

Results information

Result version number	v2 (current)
This version publication date	18 March 2021
First version publication date	18 December 2019
Version creation reason	• New data added to full data set • Correction of full data set Add endpoint presenting plasma chitotriosidase results, make corrections to data for gastrointestinal symptoms endpoints

Trial information

Trial identification

Sponsor protocol code	LTS14116

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02489344
WHO universal trial number (UTN)	U1111-1165-9049

Notes:

Sponsors

Sponsor organisation name	Genzyme Corporation
Sponsor organisation address	500 Kendall Street, Cambridge, MA, United States, 02142
Public contact	Trial Transparency Team, Genzyme Corporation, Contact-US@sanofi.com
Scientific contact	Trial Transparency Team, Genzyme Corporation, Contact-US@sanofi.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	18 January 2019
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	20 November 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the long-term safety of GZ/SAR402671 in adult male subjects with Fabry disease who previously completed study ACT13739 (NCT02228460). In this LTS14116 results record, all presentations and summaries include all subjects who received at least 1 dose of investigational medicinal product (IMP) during the ACT13739 study, and all data collected during ACT13739 and LTS14116 studies were included in analyses. As such, overall enrolment for the trial (enrolled per country and per age group) is presented for the previously completed study ACT13739 (refer to below tabular summary). Actual enrolment in LTS14116 study only was 8 subjects (France 1, Poland 1, Russian Federation 1, United Kingdom 1, and United States 4).

Protection of trial subjects:

Subjects were fully informed of all pertinent aspects of the clinical trial as well as the possibility to discontinue at any time in language and terms appropriate for the subject and considering the local culture. During the course of the trial, subjects were provided with individual subject cards indicating the nature of the trial the subject is participating, contact details and any information needed in the event of a medical emergency. Collected personal data and human biological samples were processed in compliance with the Sanofi-Aventis Group Personal Data Protection Charter ensuring that the Group abides by the laws governing personal data protection in force in all countries in which it operates.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	07 July 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	Poland: 1
Country: Number of subjects enrolled	United Kingdom: 4
Country: Number of subjects enrolled	France: 1
Country: Number of subjects enrolled	Russian Federation: 1
Country: Number of subjects enrolled	United States: 4
Worldwide total number of subjects	11
EEA total number of subjects	6

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)	11
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Subjects who successfully completed 26 weeks of treatment in prior ACT13739 study (NCT02228460) were eligible to continue their treatment for up to 30 additional months in this extension study LTS14116. Eleven subjects had enrolled and were treated in ACT13739 study, and 9 completed study. Of these 9 subjects, 8 entered extension study.

Pre-assignment

Screening details:

In extension study, subjects continued on same dose regimen they had received in initial study. Two subjects in LTS14116 study completed treatment and did not discontinue early, but were counted as not completed study due to no record of completion.

Period 1

Period 1 title	ACT13739 (Initial Study): 26 Weeks
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	GZ/SAR402671

Arm description:

Subjects with Fabry disease received GZ/SAR402671 15 milligrams (mg) once daily orally for 36 months during combined ACT13739/LTS14116 treatment period.

Arm type	Experimental
Investigational medicinal product name	GZ/SAR402671
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

15 mg hard gelatin capsules once daily orally.

Number of subjects in period 1	GZ/SAR402671
Started	11
Completed	9
Not completed	2
Adverse Event	1
Lost to follow-up	1

Period 2

Period 2 title	LTS14116 (Extension Study): 31 Months
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	GZ/SAR402671

Arm description:

Subjects received GZ/SAR402671 15 mg once daily orally for 36 months during combined ACT13739/LTS14116 treatment period.

Arm type	Experimental
Investigational medicinal product name	GZ/SAR402671
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

15 mg hard gelatin capsules once daily orally.

Number of subjects in period 2[1]	GZ/SAR402671
Started	8
Completed	5
Not completed	3
Adverse Event	1
Treatment completed/Study not completed	2

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.
Justification: Eleven subjects were enrolled and treated in ACT13739 study. Of which 9 subjects completed the study. Out of which, 8 entered the extension study.

Baseline characteristics

Reporting groups	
Reporting group title	GZ/SAR402671
Reporting group description:	
Subjects with Fabry disease received GZ/SAR402671 15 milligrams (mg) once daily orally for 36 months during combined ACT13739/LTS14116 treatment period.	

Reporting group values	GZ/SAR402671	Total	
Number of subjects	11	11	
Age categorical Units: Subjects			
Age continuous Units: years arithmetic mean standard deviation	 26.5 ± 7.6	 -	
Gender categorical Units: Subjects			
Female	0	0	
Male	11	11	
Race Units: Subjects			
Caucasian/White	8	8	
Other	3	3	

End points

End points reporting groups

Reporting group title	GZ/SAR402671
Reporting group description:	
Subjects with Fabry disease received GZ/SAR402671 15 milligrams (mg) once daily orally for 36 months during combined ACT13739/LTS14116 treatment period.	
Reporting group title	GZ/SAR402671
Reporting group description:	
Subjects received GZ/SAR402671 15 mg once daily orally for 36 months during combined ACT13739/LTS14116 treatment period.	

Primary: Number of Subjects With Treatment Emergent Adverse Events (TEAEs)

End point title	Number of Subjects With Treatment Emergent Adverse Events (TEAEs)[1]
End point description:	
Any untoward medical occurrence in a subject who received study drug was considered an adverse event (AE) without regard to possibility of causal relationship with this treatment. TEAEs were defined as AEs that developed or worsened during TEAE period (period from the first administration of study drug in ACT13739 through the last administration of the study drug in the combined ACT13739/LTS14116 treatment period plus 1 month or end of study participation for subject, whichever occurred first). For this analysis, baseline was defined as initial ACT13739 study baseline. Analysis was performed on safety population: all subjects who received at least 1 dose of IMP during the ACT13739 study. All data collected during ACT13739 and LTS14116 studies were included in analysis.	
End point type	Primary
End point timeframe:	
From baseline of ACT13739 study up to 37 months post-ACT13739 baseline	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: As the endpoint is descriptive in nature, no statistical analysis is provided.

End point values	GZ/SAR402671			
Subject group type	Reporting group			
Number of subjects analysed	11			
Units: subjects				
number (not applicable)	9			

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Potentially Clinically Significant Laboratory Abnormalities: Haematological Parameters

End point title	Number of Subjects With Potentially Clinically Significant Laboratory Abnormalities: Haematological Parameters[2]
End point description:	
Criteria for potentially clinically significant abnormalities: •Haemoglobin: less than or equal to (<=) 115 grams per litre (g/L); greater than or equal to (>=)185	

g/L; decreased from baseline (DFB) >=20 g/L
•Haematocrit: <=0.37 volume/volume (v/v); >=0.55 v/v
•Erythrocytes: >=6 Tera/L
•Platelets: lesser than (<) 100 Giga/L; >=700 Giga/L
•Leukocytes: <3.0 Giga/L (Non-Black [NB]) or <2.0 Giga/L (Black [B]); >=16.0 Giga/L
•Neutrophils: <1.5 Giga/L (NB) or <1.0 Giga/L (B);
•Lymphocytes: greater than (>) 4.0 Giga/L
•Monocytes: >0.7 Giga/L
•Basophils: >0.1 Giga/L
•Eosinophils: >0.5 Giga/L or >upper limit of normal (ULN) (if ULN >=0.5 Giga/L).
For the analysis, baseline was defined as initial ACT13739 study baseline. Analysis was performed on safety population: all subjects who received at least 1 dose of IMP during ACT13739 study. All data collected during ACT13739 and LTS14116 studies were included in analysis.

End point type	Primary

End point timeframe:

From baseline of ACT13739 study up to 37 months post-ACT13739 baseline

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: As the endpoint is descriptive in nature, no statistical analysis is provided.

End point values	GZ/SAR402671			
Subject group type	Reporting group			
Number of subjects analysed	11			
Units: subjects				
number (not applicable)				
Haemoglobin <=115 g/L	1			
Haemoglobin >=185 g/L	0			
Haemoglobin DFB >=20 g/L	0			
Haematocrit <=0.37 v/v	6			
Haematocrit >0.55 v/v	0			
Erythrocytes: >=6 Tera/L	0			
Platelets <100 Giga/L	0			
Platelets >=700 Giga/L	0			
Leukocytes <3.0 Giga/L (NB) or <2.0 Giga/L (B)	0			
Leukocytes >=16.0 Giga/L	0			
Neutrophils <1.5 Giga/L (NB) or <1.0 Giga/L (B)	0			
Lymphocytes >4.0 Giga/L	0			
Monocytes >0.7 Giga/L	2			
Basophils >0.1 Giga/L	1			
Eosinophils >0.5 Giga/L or >ULN (ULN >=0.5 Giga/L)	0			

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Potentially Clinically Significant Laboratory Abnormalities: Electrolytes

End point title	Number of Subjects With Potentially Clinically Significant Laboratory Abnormalities: Electrolytes[3]

End point description:

Criteria for potentially clinically significant abnormalities:
•Sodium: <=129 millimoles (mmol)/L; >=160 mmol/L
•Potassium: <3 mmol/L; >=5.5 mmol/L
•Chloride: <80 mmol/L; >115 mmol/L.
Analysis was performed on safety population: all subjects who received at least 1 dose of IMP during the ACT13739 study. All data collected during ACT13739 and LTS14116 studies were included in analysis.

End point type	Primary

End point timeframe:

From baseline of ACT13739 study up to 37 months post-ACT13739 baseline

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: As the endpoint is descriptive in nature, no statistical analysis is provided.

End point values	GZ/SAR402671			
Subject group type	Reporting group			
Number of subjects analysed	11			
Units: subjects				
number (not applicable)				
Sodium <=129 mmol/L	0			
Sodium >=160 mmol/L	0			
Potassium <3 mmol/L	0			
Potassium >=5.5 mmol/L	0			
Chloride <80 mmol/L	0			
Chloride >115 mmol/L	0			

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Potentially Clinically Significant Laboratory Abnormalities: Liver Function Parameters

End point title	Number of Subjects With Potentially Clinically Significant Laboratory Abnormalities: Liver Function Parameters[4]

End point description:

Criteria for potentially clinically significant abnormalities:
•Alanine Aminotransferase (ALT): >3 ULN; >5 ULN; >10 ULN and >20 ULN
•Aspartate aminotransferase (AST): >3 ULN; >5 ULN; >10 ULN and >20 ULN
•Alkaline phosphatase: >1.5 ULN
•Bilirubin: >1.5 ULN; >2 ULN
Analysis was performed on safety population: all subjects who received at least 1 dose of IMP during the ACT13739 study. All data collected during ACT13739 and LTS14116 studies were included in analysis.

End point type	Primary

End point timeframe:

From baseline of ACT13739 study up to 37 months post-ACT13739 baseline

Notes:

[4] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: As the endpoint is descriptive in nature, no statistical analysis is provided.

End point values	GZ/SAR402671			
Subject group type	Reporting group			
Number of subjects analysed	11			
Units: subjects				
number (not applicable)				
ALT >3 ULN	0			
ALT >5 ULN	0			
ALT >10 ULN	0			
ALT >20 ULN	0			
AST >3 ULN	0			
AST >5 ULN	0			
AST >10 ULN	0			
AST >20 ULN	0			
Alkaline Phosphatase >1.5 ULN	0			
Bilirubin >1.5 ULN	0			
Bilirubin >2 ULN	0			

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Potentially Clinically Significant Laboratory Abnormalities: Metabolic Parameters

End point title	Number of Subjects With Potentially Clinically Significant Laboratory Abnormalities: Metabolic Parameters[5]

End point description:

Criteria for potentially clinically significant abnormalities:
•Glucose: <=3.9 mmol/L and < lower limits of normal (LLN); >=11.1 mmol/L (unfasted [unfas]) or >=7 mmol/L (fasted [fas])
•Lipase: >= 3 ULN
•C Reactive Protein (CRP): > 2 ULN or > 10 mg/L (if ULN not provided)
Analysis was performed on safety population: all subjects who received at least 1 dose of IMP during the ACT13739 study. All data collected during ACT13739 and LTS14116 studies were included in analysis.

End point type	Primary

End point timeframe:

From baseline of ACT13739 study up to 37 months post-ACT13739 baseline

Notes:

[5] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: As the endpoint is descriptive in nature, no statistical analysis is provided.

End point values	GZ/SAR402671			
Subject group type	Reporting group			
Number of subjects analysed	11			
Units: subjects				
number (not applicable)				
Glucose <=3.9 mmol/L and <LLN	3			
Glucose >=11.1 mmol/L (unfas) or >=7 mmol/L (fas)	1			
Albumin <=25 g/L	0			
Lipase >=3 ULN	0			

CRP >2 ULN or >10 mg/L (if ULN not provided)	2			

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Potentially Clinically Significant Laboratory Abnormalities: Renal Function Parameters

End point title	Number of Subjects With Potentially Clinically Significant Laboratory Abnormalities: Renal Function Parameters[6]

End point description:

Criteria for potentially clinically significant abnormalities:
• Creatinine: >=150 micromoles per litre (mcmol/L) (Adults); >=30 percent (%) change from baseline; >= 100% change from baseline
• Blood urea nitrogen: >=17 mmol/L
• Urate: <120 mcmol/L; >408 mcmol/L.
For this analysis, baseline was defined as initial ACT13739 study baseline.
Analysis was performed on safety population: all subjects who received at least 1 dose of IMP during the ACT13739 study. All data collected during ACT13739 and LTS14116 studies were included in analysis.

End point type	Primary

End point timeframe:

From baseline of ACT13739 study up to 37 months post-ACT13739 baseline

Notes:

[6] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: As the endpoint is descriptive in nature, no statistical analysis is provided.

End point values	GZ/SAR402671			
Subject group type	Reporting group			
Number of subjects analysed	11			
Units: subjects				
number (not applicable)				
Creatinine >=150 mcmol/L	0			
Creatinine >=30% change from baseline	2			
Creatinine >=100% change from baseline	0			
Blood Urea Nitrogen >=17 mmol/L	0			
Urate <120 mcmol/L	0			
Urate >408 mcmol/L	5			

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Potentially Clinically Significant Laboratory Abnormalities: Urinalysis

End point title	Number of Subjects With Potentially Clinically Significant

	Laboratory Abnormalities: Urinalysis[7]

End point description:

Criteria with potentially clinically significant urine abnormalities:
pH: <=4.6; pH: >=8.0.
Analysis was performed on safety population: all subjects who received at least 1 dose of IMP during the ACT13739 study. All data collected during ACT13739 and LTS14116 studies were included in analysis.

End point type	Primary

End point timeframe:

From baseline of ACT13739 study up to 37 months post-ACT13739 baseline

Notes:

[7] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: As the endpoint is descriptive in nature, no statistical analysis is provided.

End point values	GZ/SAR402671			
Subject group type	Reporting group			
Number of subjects analysed	11			
Units: subjects				
number (not applicable)				
pH <=4.6	0			
pH >=8.0	0			

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Potentially Clinically Significant Abnormalities: Vital Signs

End point title	Number of Subjects With Potentially Clinically Significant Abnormalities: Vital Signs[8]

End point description:

Criteria for potentially clinically significant vital sign abnormalities:
• Systolic blood pressure (SBP) supine: <=95 millimetres of mercury (mmHg) and DFB >=20 mmHg; >=160 mmHg and increase from baseline (IFB) >=20 mmHg
• Diastolic blood pressure (DBP) supine: <=45 mmHg and DFB >=10 mmHg; >=110 mmHg and IFB >=10 mmHg
• Heart rate (HR) supine: <=50 beats per minute (bpm) and DFB >=20 bpm; >=120 bpm and IFB >=20 bpm
• Weight: >=5% DFB; >=5% IFB.
For this analysis, baseline was defined as initial ACT13739 study baseline.
Analysis was performed on safety population: all subjects who received at least 1 dose of IMP during the ACT13739 study. All data collected during ACT13739 and LTS14116 studies were included in analysis.

End point type	Primary

End point timeframe:

From baseline of ACT13739 study up to 37 months post-ACT13739 baseline

Notes:

[8] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: As the endpoint is descriptive in nature, no statistical analysis is provided.

End point values	GZ/SAR402671			
Subject group type	Reporting group			
Number of subjects analysed	11			
Units: subjects				
number (not applicable)				
SBP (supine) <=95 mmHg and DFB >=20 mmHg	0			
SBP (supine) >=160 mmHg and IFB >=20 mmHg	0			
DBP (supine) <=45 mmHg and DFB >=10 mmHg	0			
DBP (supine) >=110 mmHg and IFB >=10 mmHg	0			
HR (supine) <=50 bpm and DFB >= 20 bpm	1			
HR (supine) >=120 bpm and IFB >=20 bpm	0			
Weight >=5% DFB	3			
Weight >=5% IFB	2			

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Potentially Clinically Significant Abnormalities: Electrocardiogram (ECG)

End point title	Number of Subjects With Potentially Clinically Significant Abnormalities: Electrocardiogram (ECG)[9]

End point description:

Criteria for potentially clinically significant ECG abnormalities:
• ECG mean HR: <30 bpm; <30 bpm and DFB >=20 bpm; <40 bpm; <40 bpm and DFB >=20 bpm; <50 bpm; <50 bpm and DFB >=20 bpm; >90 bpm; <90 bpm and DFB >=20 bpm; >100 bpm; <100 bpm and DFB >=20 bpm; >120 bpm; <120 bpm and DFB >=20 bpm
• PR Interval: >200 milliseconds (ms); >200 ms and IFB >=25%; >220 ms; >220 ms and IFB >=25%; >240 ms; >240 ms and IFB >=25%
• QRS duration: >110 ms; >110 ms and IFB >=25%; >120 ms; >120 ms and IFB >=25%
• QTc Bazett (QTcB) interval: >450 ms; >480 ms; >500 ms; IFB >30 and <=60 ms, IFB >60 ms
• QTc Fridericia (QTc F): >450 ms; >480 ms; >500 ms; IFB >30 and <=60 ms; IFB >60 ms
• QT Interval: >500 ms.
For this analysis, baseline was defined as initial ACT13739 study baseline.
Analysis was performed on safety population: all subjects who received at least 1 dose of IMP during the ACT13739 study. All data collected during ACT13739 and LTS14116 studies were included in analysis.

End point type	Primary

End point timeframe:

From baseline of ACT13739 study up to 37 months post-ACT13739 baseline

Notes:

[9] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: As the endpoint is descriptive in nature, no statistical analysis is provided.

End point values	GZ/SAR402671			
Subject group type	Reporting group			
Number of subjects analysed	11			
Units: subjects				
number (not applicable)				
ECG Mean HR <30 bpm	0			
ECG Mean HR <30 bpm and DFB >=20 bpm	0			
ECG Mean HR <40 bpm	0			
ECG Mean HR <40 bpm and DFB >=20 bpm	0			
ECG Mean HR <50 bpm	1			
ECG Mean HR <50 bpm and DFB >=20 bpm	0			
ECG Mean HR >90 bpm	1			
ECG Mean HR <90 bpm and DFB >=20 bpm	0			
ECG Mean HR >100 bpm	0			
ECG Mean HR <100 bpm and DFB >=20 bpm	0			
ECG Mean HR >120 bpm	0			
ECG Mean HR <120 bpm and DFB >=20 bpm	0			
PR interval >200 ms	2			
PR interval >200 ms and IFB >=25%	0			
PR interval >220 ms	0			
PR interval >220 ms and IFB >=25%	0			
PR >240 ms	0			
PR interval >240 ms and IFB >=25%	0			
QRS duration >110 ms	1			
QRS duration >110 ms and IFB >=25%	0			
QRS duration >120 ms	0			
QRS duration >120 ms and IFB >=25%	0			
QTcB interval >450 ms	0			
QTcB interval >480 ms	0			
QTc B interval >500 ms	0			
QTcB interval IFB >30 and <=60 ms	1			
QTcB interval IFB >60 ms	0			
QTcF interval >450 ms	0			
QTc F interval >480 ms	0			
QTcF interval >500 ms	0			
QTcF interval IFB >30 and <=60 ms	0			
QTcF interval IFB >60 ms	0			
QT interval >500 ms	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Plasma Globotriaosylceramide (GL-3) Concentration at Weeks 26, 52, 104 and 156

End point title	Change From Baseline in Plasma Globotriaosylceramide (GL-3) Concentration at Weeks 26, 52, 104 and 156

End point description:

Change from baseline in plasma GL-3 was obtained by subtracting baseline value from post-baseline value at Weeks 26, 52, 104 and 156. Concentration of GL-3 in plasma was determined using a validated liquid chromatography tandem mass spectrometry (LC-MS/MS) method. For this analysis, baseline was defined as initial ACT13739 study baseline. Analysis was performed on full analysis set: all subjects who received at least 1 dose of IMP during the ACT13739 study. All data collected during ACT13739 and LTS14116 studies were included in analysis. Here, 'n' signifies subjects with available data for specified category.

End point type	Secondary

End point timeframe:

Baseline of ACT13739 study and Weeks 26, 52, 104 and 156 post-ACT13739 baseline

End point values	GZ/SAR402671			
Subject group type	Reporting group			
Number of subjects analysed	11			
Units: micrograms per millilitre (mcg/mL)				
arithmetic mean (standard deviation)				
Week 26 (n = 9)	-3.62 (± 1.07)			
Week 52 (n = 7)	-5.06 (± 1.04)			
Week 104 (n = 7)	-6.32 (± 2.53)			
Week 156 (n = 7)	-6.97 (± 2.27)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Plasma Lyso Globotriaosylceramide (Lyso GL-3) Concentration at Weeks 26, 52, 104 and 156

End point title	Change From Baseline in Plasma Lyso Globotriaosylceramide (Lyso GL-3) Concentration at Weeks 26, 52, 104 and 156

End point description:

Change from baseline in plasma GL-3 was obtained by subtracting baseline value from post-baseline value at Weeks 26, 52, 104 and 156. Concentration of lyso-GL-3 in plasma was determined using a validated LC-MS/MS method. For this analysis, baseline was defined as initial ACT13739 study baseline. Analysis was performed on full analysis set: all subjects who received at least 1 dose of IMP during the ACT13739 study. All data collected during ACT13739 and LTS14116 studies were included in analysis. Here, 'n' signifies subjects with available data for specified category.

End point type	Secondary

End point timeframe:

Baseline of ACT13739 study and Weeks 26, 52, 104 and 156 post-ACT13739 baseline

End point values	GZ/SAR402671			
Subject group type	Reporting group			
Number of subjects analysed	11			
Units: nanograms per mL (ng/mL)				
arithmetic mean (standard deviation)				
Week 26 (n = 9)	-30.99 (± 22.83)			
Week 52 (n = 7)	-37.10 (± 20.69)			
Week 104 (n = 7)	-39.84 (± 18.12)			
Week 156 (n = 7)	-48.13 (± 15.65)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Plasma Glucosylceramide (GL-1) Concentration at Weeks 26, 52, 104 and 156

End point title	Change From Baseline in Plasma Glucosylceramide (GL-1) Concentration at Weeks 26, 52, 104 and 156

End point description:

Change from baseline in plasma GL-1 was obtained by subtracting baseline value from post-baseline value at Weeks 26, 52, 104 and 156. Concentration of GL-1 in plasma was determined using a validated LC-MS/MS method. For this analysis, baseline was defined as initial ACT13739 study baseline. Analysis was performed on full analysis set: all subjects who received at least 1 dose of IMP during the ACT13739 study. All data collected during ACT13739 and LTS14116 studies were included in analysis. Here, 'n' signifies subjects with available data for specified category.

End point type	Secondary

End point timeframe:

Baseline of ACT13739 study and Weeks 26, 52, 104 and 156 post-ACT13739 baseline

End point values	GZ/SAR402671			
Subject group type	Reporting group			
Number of subjects analysed	11			
Units: mcg/mL				
arithmetic mean (standard deviation)				
Week 26 (n = 9)	-3.26 (± 1.43)			
Week 52 (n = 7)	-3.58 (± 0.85)			
Week 104 (n = 7)	-3.70 (± 0.85)			
Week 156 (n = 7)	-3.23 (± 1.11)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Plasma Monosialodihexosylganglioside (GM3) Concentration at Weeks 26, 52, 104 and 156

End point title	Change From Baseline in Plasma Monosialodihexosylganglioside (GM3) Concentration at Weeks 26, 52, 104 and 156

End point description:

Change from baseline in plasma GM3 was obtained by subtracting baseline value from post-baseline value at Weeks 26, 52, 104 and 156. Concentration of GM3 in plasma was determined using a validated LC-MS/MS method. For this analysis, baseline was defined as initial ACT13739 study baseline. Analysis was performed on full analysis set: all subjects who received at least 1 dose of IMP during the ACT13739 study. All data collected during ACT13739 and LTS14116 studies were included in analysis. Here, 'n' signifies subjects with available data for specified category.

End point type	Secondary

End point timeframe:

Baseline of ACT13739 study and Weeks 26, 52, 104 and 156 post-ACT13739 baseline

End point values	GZ/SAR402671			
Subject group type	Reporting group			
Number of subjects analysed	11			
Units: mcg/mL				
arithmetic mean (standard deviation)				
Week 26 (n = 9)	-10.77 (± 6.02)			
Week 52 (n = 7)	-8.84 (± 4.55)			
Week 104 (n = 7)	-9.92 (± 3.26)			
Week 156 (n = 7)	-8.12 (± 5.37)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Urine GL-3 Concentration At Weeks 26, 52, 104 and 156

End point title	Change From Baseline in Urine GL-3 Concentration At Weeks 26, 52, 104 and 156

End point description:

Change from baseline in urine GL-3 was obtained by subtracting baseline value from post-baseline value at Weeks 26, 52, 104 and 156. Concentration of GL-3 in urine was determined using a validated LC-MS/MS method. For this analysis, baseline was defined as initial ACT13739 study baseline. Analysis was performed on full analysis set: all subjects who received at least 1 dose of IMP during the ACT13739 study. All data collected during ACT13739 and LTS14116 studies were included in analysis. Here, 'n' signifies subjects with available data for specified category.

End point type	Secondary

End point timeframe:

Baseline of ACT13739 study and Weeks 26, 52, 104 and 156 post-ACT13739 baseline

End point values	GZ/SAR402671			
Subject group type	Reporting group			
Number of subjects analysed	11			
Units: mg/mmol creatinine (Cr)				
arithmetic mean (standard deviation)				
Week 26 (n = 8)	-0.25 (± 0.19)			
Week 52 (n = 6)	-0.20 (± 0.22)			
Week 104 (n = 7)	-0.18 (± 0.22)			
Week 156 (n = 7)	-0.18 (± 0.27)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in High Sensitivity Cardiac Troponin T At Weeks 26, 52, 104 and 156

End point title	Change From Baseline in High Sensitivity Cardiac Troponin T At Weeks 26, 52, 104 and 156

End point description:

Change from baseline in high sensitivity cardiac troponin T was obtained by subtracting baseline value from postbaseline value at Weeks 26, 52, 104 and 156. For this analysis, baseline was defined as initial ACT13739 study baseline. Analysis was performed on full analysis set: all subjects who received at least 1 dose of IMP during the ACT13739 study. All data collected during ACT13739 and LTS14116 studies were included in analysis. Here, 'n' signifies subjects with available data for specified category.

End point type	Secondary

End point timeframe:

Baseline of ACT13739 study and Weeks 26, 52, 104 and 156 post-ACT13739 baseline

End point values	GZ/SAR402671			
Subject group type	Reporting group			
Number of subjects analysed	11			
Units: mcg/L				
arithmetic mean (standard deviation)				
Week 26 (n = 9)	0.0000 (± 0.0000)			
Week 52 (n = 5)	0.0105 (± 0.0241)			
Week 104 (n = 7)	-0.0015 (± 0.0000)			
Week 156 (n = 7)	0.0006 (± 0.0027)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Podocyturia Counts (Per Milligram of Creatinine) At Weeks 12, 26 and 156

End point title	Change From Baseline in Podocyturia Counts (Per Milligram of Creatinine) At Weeks 12, 26 and 156

End point description:

Change from baseline in podocyturia was obtained by subtracting baseline value from post-baseline value at Weeks 12, 26 and 156. Urine samples were processed to identify podocyte (podocalyxin, PCX) and parietal cell (claudin 1, CL1) markers. PCX +/CL1 negative cells were identified as podocytes and PCX +/CL1 positive cells as parietal cells with podocyte phenotype. All counts were corrected for urine Cr. For this analysis, baseline was defined as initial ACT13739 study baseline. Analysis was performed on full analysis set: all subjects who received at least 1 dose of IMP during the ACT13739 study. All data collected during ACT13739 and LTS14116 studies were included in analysis. Here, 'n' signifies subjects with available data for specified category.

End point type	Secondary

End point timeframe:

Baseline of ACT13739 study and Weeks 12, 26 and 156 post-ACT13739 baseline

End point values	GZ/SAR402671			
Subject group type	Reporting group			
Number of subjects analysed	11			
Units: Count of podocytes/mg Cr				
arithmetic mean (standard deviation)				
Week 12 (n = 9)	-1.40 (± 2.69)			
Week 26 (n = 7)	-1.65 (± 2.97)			
Week 156 (n = 4)	-2.73 (± 3.97)			

Statistical analyses

No statistical analyses for this end point

Secondary: Summary of Shifts From Baseline in Skin GL-3 Score in Superficial Capillary Endothelial Cells Over Time: Number of Subjects in Categories of Shift in GL-3 Score

End point title	Summary of Shifts From Baseline in Skin GL-3 Score in Superficial Capillary Endothelial Cells Over Time: Number of Subjects in Categories of Shift in GL-3 Score

End point description:

Skin biopsies were done to score GL-3 accumulation/inclusions by light microscopy. Three independent pathologists scored GL-3 clearance by using an inclusion severity score of 0 (none/trace), 1 (mild), 2 (moderate), and 3 (severe), where higher score indicated more severe condition. A single score per subject per time point was derived by taking score rated by a majority of pathologists; if a majority score could not be derived, median score was used. Data were summarised and reported in terms of number of subjects with shift from baseline GL-3 score to Weeks 12, 26, 52 and 156 GL-3 score. Shift to lower score from baseline indicated less severe condition at that respective time point. Baseline was defined as initial ACT13739 study baseline. Analysed on full analysis set: all subject who received at least 1 dose of IMP during ACT13739 study. All data collected during ACT13739 and LTS14116 studies were analysed. Here, 'n' signifies subjects with available data for specified category.

End point type	Secondary

End point timeframe:

Baseline of ACT13739 study and Weeks 12, 26, 52 and 156 post-ACT13739 baseline

End point values	GZ/SAR402671			
Subject group type	Reporting group			
Number of subjects analysed	11			
Units: subjects				
number (not applicable)				
Baseline Score:1/Week 12 Score:1 (n=9)	4			
Baseline Score:1/Week 12 Score:2 (n=9)	1			
Baseline Score:2/Week 12 Score:1 (n=9)	3			
Baseline Score:2/Week 12 Score:2 (n=9)	1			
Baseline Score:1/Week 26 Score:1 (n=9)	4			
Baseline Score:1/Week 26 Score:2 (n=9)	1			
Baseline Score:2/Week 26 Score:1 (n=9)	3			
Baseline Score:2/Week 26 Score:2 (n=9)	1			
Baseline Score:1/Week 52 Score:1 (n=6)	3			
Baseline Score:2/Week 52 Score:1 (n=6)	2			
Baseline Score:2/Week 52 Score:2 (n=6)	1			
Baseline Score:1/Week 156 Score:0 (n=6)	2			
Baseline Sore:1/Week 156 Score:1 (n=6)	1			
Baseline Score:2/Week 156 Score:1 (n=6)	3			

Statistical analyses

No statistical analyses for this end point

Secondary: Summary of Shifts From Baseline in Skin GL-3 Score in Deep Vessels Endothelial Cells Over Time: Number of Subjects in Categories of Shift in GL-3 Score

End point title	Summary of Shifts From Baseline in Skin GL-3 Score in Deep Vessels Endothelial Cells Over Time: Number of Subjects in Categories of Shift in GL-3 Score

End point description:

Skin biopsies were done to score GL-3 accumulation/inclusions by light microscopy. Three independent pathologists scored GL-3 clearance by using an inclusion severity score of 0 (none/trace), 1 (mild), 2 (moderate), and 3 (severe), where higher score indicated more severe condition. A single score per subject per time point was derived by taking score rated by a majority of pathologists; if a majority score could not be derived, median score was used. Data were summarised and reported in terms of number of subjects with shift from baseline GL-3 score to Week 12, 26, 52 and 156 GL-3 score. Shift to lower score from baseline indicated less severe condition at that respective time point. Baseline was defined as initial ACT13739 study baseline. Analysed on full analysis set: all subject who received at least 1 dose of IMP during ACT13739 study. All data collected during ACT13739 and LTS14116 studies

were analysed. Here, 'n' signifies subjects with available data for specified category.

End point type	Secondary

End point timeframe:

Baseline of ACT13739 study and Weeks 12, 26, 52 and 156 post-ACT13739 baseline

End point values	GZ/SAR402671			
Subject group type	Reporting group			
Number of subjects analysed	11			
Units: subjects				
number (not applicable)				
Baseline Score:1/Week 12 Score:2 (n=9)	1			
Baseline Score:2/Week 12 Score:1 (n=9)	2			
Baseline Score:2/Week 12 Score:2 (n=9)	6			
Baseline Score:1/Week 26 Score:1 (n=9)	1			
Baseline Score:2/Week 26 Score:1 (n=9)	2			
Baseline Score:2/Week 26 Score:2 (n=9)	6			
Baseline Score:2/Week 52 Score:1 (n=6)	3			
Baseline Score:2/Week 52 Score:1.5 (n=6)	1			
Baseline Sore:2/Week 52 Score:2 (n=6)	2			
Baseline Score:1/Week 156 Score:1 (n=6)	1			
Baseline Score:2/Week 156 Score:0.5 (n=6)	1			
Baseline Score:2/Week 156 Score:1 (n=6)	3			
Baseline Score:2/Week 156 Score:2 (n=6)	1			

Statistical analyses

No statistical analyses for this end point

Secondary: Summary of Shifts From Baseline in Skin GL-3 Score in Deep Vessels Smooth Muscle Cells Over Time: Number of Subjects in Categories of Shift in GL-3 Score

End point title	Summary of Shifts From Baseline in Skin GL-3 Score in Deep Vessels Smooth Muscle Cells Over Time: Number of Subjects in Categories of Shift in GL-3 Score

End point description:

Skin biopsies were done to score GL-3 accumulation/inclusions by light microscopy. Three independent pathologists scored GL-3 clearance by using an inclusion severity score of 0 (none/trace), 1 (mild), 2 (moderate), and 3 (severe), where higher score indicated more severe condition. A single score per subject per time point was derived by taking score rated by a majority of pathologists; if a majority score could not be derived, median score was used. Data were summarised and reported in terms of

number of subjects with shift from baseline GL-3 score to Weeks 12, 26, 52 and 156 GL-3 score. Shift to lower score from baseline indicated less severe condition at that respective time point. Baseline was defined as initial ACT13739 study baseline. Analysed on full analysis set: all subject who received at least 1 dose of IMP during ACT13739 study. All data collected during ACT13739 and LTS14116 studies were analysed. Here, 'n' signifies subjects with available data for specified category.

End point type	Secondary

End point timeframe:

Baseline of ACT13739 study and Weeks 12, 26, 52 and 156 post-ACT13739 baseline

End point values	GZ/SAR402671			
Subject group type	Reporting group			
Number of subjects analysed	11			
Units: subjects				
number (not applicable)				
Baseline Score:1.5/Week 12 Score:2 (n=9)	2			
Baseline Score:2/Week 12 Score:2 (n=9)	7			
Baseline Score:1.5/Week 26 Score:1.5 (n=9)	2			
Baseline Score:2/Week 26 Score:2 (n=9)	7			
Baseline Score:1.5/Week 52 Score:2 (n=5)	1			
Baseline Score:2/Week 52 Score:2 (n=5)	4			
Baseline Score:1.5/Week 156 Score:2 (n=6)	1			
Baseline Score:2/Week 156 Score:1 (n=6)	1			
Baseline Score:2/Week 156 Score:1.5 (n=6)	1			
Baseline Score:2/Week 156 Score:2 (n=6)	3			

Statistical analyses

No statistical analyses for this end point

Secondary: Summary of Shifts From Baseline in Skin GL-3 Score in Perineurium Cells Over Time: Number of Subjects in Categories of Shift in GL-3 Score

End point title	Summary of Shifts From Baseline in Skin GL-3 Score in Perineurium Cells Over Time: Number of Subjects in Categories of Shift in GL-3 Score

End point description:

Skin biopsies were done to score GL-3 accumulation/inclusions by light microscopy. Three independent pathologists scored GL-3 clearance by using an inclusion severity score of 0 (none/trace), 1 (mild), 2 (moderate), and 3 (severe), where higher score indicated more severe condition. A single score per subject per time point was derived by taking score rated by a majority of pathologists; if a majority score could not be derived, median score was used. Data were summarised and reported in terms of number of subjects with shift from baseline GL-3 score to Week 12, 26, 52 and 156 GL-3 score. Shift to lower score from baseline indicated less severe condition at that respective time point. Baseline was defined as initial ACT13739 study baseline. Analysed on full analysis set: all subject who received at

least 1 dose of IMP during ACT13739 study. All data collected during ACT13739 and LTS14116 studies were analysed. Here, 'n' signifies subjects with available data for specified category.

End point type	Secondary

End point timeframe:

Baseline of ACT13739 study and Weeks 12, 26, 52 and 156 post-ACT13739 baseline

End point values	GZ/SAR402671			
Subject group type	Reporting group			
Number of subjects analysed	11			
Units: subjects				
number (not applicable)				
Baseline Score:1/Week 12 Score:2 (n=9)	1			
Baseline Score:2/Week 12 Score:2 (n=9)	8			
Baseline Score:1/Week 26 Score:2 (n=9)	1			
Baseline Score:2/Week 26 Score:2 (n=9)	8			
Baseline Score:1/Week 52 Score:2 (n=6)	1			
Baseline Score:2/Week 52 Score:1 (n=6)	1			
Baseline Score:2/Week 52 Score:1.5 (n=6)	1			
Baseline Score:2/Week 52 Score:2 (n=6)	3			
Baseline Score:1/Week 156 Score:1 (n=6)	1			
Baseline Score:2/Week 156 Score:1.5 (n=6)	1			
Baseline Score:2/Week 156 Score:2 (n=6)	4			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Mental Component Summary and Physical Component Summary of the Short Form-36 (SF-36) Health Survey at Weeks 26, 52, 104 and 156

End point title	Change From Baseline in Mental Component Summary and Physical Component Summary of the Short Form-36 (SF-36) Health Survey at Weeks 26, 52, 104 and 156

End point description:

SF-36, a subject-reported health survey, has 36-item questionnaire to assess 8 various health aspects (vitality, physical functioning, bodily pain, general health perceptions, physical role functioning, emotional role functioning, social role functioning, mental health). Score range of each of 8 aspects was from 0 (maximum disability) to 100 (no disability), higher scores indicating good health. SF-36 responses were used to calculate 2 summary scores: Physical component score (PCS) and mental component score (MCS). Score range for each of these 2 summary scores was from 0 (maximum disability) to 100 (no disability), where higher score indicated less disability/good health. Baseline was defined as initial ACT13739 study baseline. Analysed on full analysis set: all subjects who received at

least 1 dose of IMP during ACT13739 study. All data collected during ACT13739 and LTS14116 studies were included in analysis. Here, 'n' signifies subjects with available data for specified category.

End point type	Secondary

End point timeframe:

Baseline of ACT13739 study and Weeks 26, 52, 104 and 156 post-ACT13739 baseline

End point values	GZ/SAR402671			
Subject group type	Reporting group			
Number of subjects analysed	11			
Units: units on a scale				
arithmetic mean (standard deviation)				
Physical Component Summary: Week 26 (n=9)	8.39 (± 6.88)			
Physical Component Summary: Week 52 (n=7)	7.70 (± 7.76)			
Physical Component Summary: Week 104 (n=6)	9.72 (± 9.02)			
Physical Component Summary: Week 156 (n=6)	5.30 (± 11.83)			
Mental Component Summary: Week 26 (n=9)	-3.31 (± 20.34)			
Mental Component Summary: Week 52 (n=7)	1.69 (± 8.27)			
Mental Component Summary: Week 104 (n=6)	6.48 (± 8.14)			
Mental Component Summary: Week 156 (n=6)	2.87 (± 14.17)			

Statistical analyses

No statistical analyses for this end point

Secondary: Gastrointestinal (GI) Symptoms: Abdominal Pain at Baseline and Weeks 2, 4, 8, 12, 18, 26, 52, 104 and 156

End point title	Gastrointestinal (GI) Symptoms: Abdominal Pain at Baseline and Weeks 2, 4, 8, 12, 18, 26, 52, 104 and 156

End point description:

Subjects assessed their GI symptoms (abdominal pain, abdominal distention, bowel movements) by completing a questionnaire (modified version of the inflammatory bowel severity scoring system). Subjects were asked to report the presence of abdominal pain in past 10 days (before each of the specified time points). Subjects answered the question: "Do you currently suffer from abdominal (tummy) pain? [Yes/No]". For this analysis, baseline was defined as initial ACT13739 study. Analysis was performed on full analysis set: all subjects who received at least 1 dose of IMP during the ACT13739 study. All data collected during ACT13739 and LTS14116 studies were included in analysis. Here, 'n' signifies subjects with available data for specified category.

End point type	Secondary

End point timeframe:

Baseline of ACT13739 study and Weeks 2, 4, 8, 12, 18, 26, 52, 104 and 156 post-ACT13739 baseline

End point values	GZ/SAR402671			
Subject group type	Reporting group			
Number of subjects analysed	11			
Units: subjects				
number (not applicable)				
Baseline: No (n = 11)	5			
Baseline: Yes (n = 11)	6			
Week 2: No (n = 11)	6			
Week 2: Yes (n = 11)	5			
Week 4: No (n = 11)	7			
Week 4: Yes (n = 11)	4			
Week 8: No (n = 11)	8			
Week 8: Yes (n = 11)	3			
Week 12: No (n = 10)	8			
Week 12: Yes (n = 10)	2			
Week 18: No (n = 9)	7			
Week 18: Yes (n = 9)	2			
Week 26: No (n = 9)	6			
Week 26: Yes (n = 9)	3			
Week 52: No (n = 7)	5			
Week 52: Yes (n = 7)	2			
Week 104: No (n = 7)	5			
Week 104: Yes (n = 7)	2			
Week 156: No (n = 7)	5			
Week 156: Yes (n = 7)	2			

Statistical analyses

No statistical analyses for this end point

Secondary: Gastrointestinal Symptoms: Abdominal Pain Severity Score at Baseline and Weeks 2, 4, 8, 12, 18, 26, 52, 104 and 156

End point title	Gastrointestinal Symptoms: Abdominal Pain Severity Score at Baseline and Weeks 2, 4, 8, 12, 18, 26, 52, 104 and 156

End point description:

Subjects assessed their GI symptoms (abdominal pain, abdominal distention, bowel movements) by completing a questionnaire (modified version of the inflammatory bowel severity scoring system). Subjects were asked to mark the severity of the abdominal pain in past 10 days (before each of the specified time points) on a visual analogue scale (VAS). The scale ranged from 0% (no pain) to 100% (very severe), where higher score indicated more severity. For this analysis, baseline was defined as initial ACT13739 study baseline. Analysis was performed on full analysis set: all subjects who received at least 1 dose of IMP during the ACT13739 study. All data collected during ACT13739 and LTS14116 studies were included in analysis. Here, 'n' signifies subjects with available data for specified category. Standard deviation (SD) can only be calculated when there are more than 1 subject with data available, and "99999" is entered when SD cannot be calculated.

End point type	Secondary

End point timeframe:

Baseline of ACT13739 study and Weeks 2, 4, 8, 12, 18, 26, 52, 104 and 156 post-ACT13739 baseline

End point values	GZ/SAR402671			
Subject group type	Reporting group			
Number of subjects analysed	11			
Units: score on a 0-100 percent scale				
arithmetic mean (standard deviation)				
Baseline (n = 6)	52.50 (± 20.50)			
Week 2 (n = 5)	35.60 (± 18.47)			
Week 4 (n = 4)	29.75 (± 20.07)			
Week 8 (n = 3)	29.00 (± 21.28)			
Week 12 (n = 2)	40.00 (± 21.21)			
Week 18 (n = 2)	43.00 (± 29.70)			
Week 26 (n = 3)	31.33 (± 32.81)			
Week 52 (n = 1)	21.00 (± 99999)			
Week 104 (n = 1)	21.00 (± 99999)			
Week 156 (n = 2)	15.00 (± 7.07)			

Statistical analyses

No statistical analyses for this end point

Secondary: Gastrointestinal Symptoms: Number of Days With Abdominal Pain Score at Baseline and Weeks 2, 4, 8, 12, 18, 26, 52, 104 and 156

End point title	Gastrointestinal Symptoms: Number of Days With Abdominal Pain Score at Baseline and Weeks 2, 4, 8, 12, 18, 26, 52, 104 and 156

End point description:

Subjects assessed their GI symptoms (abdominal pain, abdominal distention, bowel movements) by completing a questionnaire (modified version of the inflammatory bowel severity scoring system). Subjects were asked to report the number of days they had abdominal pain in past 10 days (before each of the specified time points). Number of days with abdominal pain score was achieved by multiplying number of days with pain * 10. The score ranges from 10 to 100, where higher score signifies more number of days with pain. For this analysis, baseline was defined as initial ACT13739 study baseline. Analysis was performed on full analysis set: all subjects who received at least 1 dose of IMP during the ACT13739 study. All data collected during ACT13739 and LTS14116 studies were included in analysis. Here, 'n' signifies subjects with available data for specified category.

End point type	Secondary

End point timeframe:

Baseline of ACT13739 study and Weeks 2, 4, 8, 12, 18, 26, 52, 104 and 156 post-ACT13739 baseline

End point values	GZ/SAR402671			
Subject group type	Reporting group			
Number of subjects analysed	11			
Units: score on a scale				
arithmetic mean (standard deviation)				
Baseline (n = 6)	38.33 (± 31.89)			
Week 2 (n = 5)	26.00 (± 20.74)			
Week 4 (n = 4)	25.00 (± 20.82)			
Week 8 (n = 4)	25.00 (± 23.80)			
Week 12 (n = 2)	35.00 (± 7.07)			
Week 18 (n = 2)	35.00 (± 21.21)			
Week 26 (n = 3)	30.00 (± 34.64)			
Week 52 (n = 3)	7.00 (± 12.12)			
Week 104 (n = 2)	5.00 (± 7.07)			
Week 156 (n = 2)	20.00 (± 0.00)			

Statistical analyses

No statistical analyses for this end point

Secondary: Gastrointestinal Symptoms: Number of Subjects With Abdominal Distension at Baseline and Weeks 2, 4, 8, 12, 18, 26, 52, 104 and 156

End point title	Gastrointestinal Symptoms: Number of Subjects With Abdominal Distension at Baseline and Weeks 2, 4, 8, 12, 18, 26, 52, 104 and 156

End point description:

Subjects assessed their GI symptoms (abdominal pain, abdominal distention, bowel movements) by completing a questionnaire (modified version of the inflammatory bowel severity scoring system). Subjects were asked to report the presence of abdominal distention in past 10 days (before each of the specified time points). Subjects answered the question: "Do you currently suffer from abdominal distension (bloating, swelling or tight tummy)? [Yes/No]". For this analysis, baseline was defined as initial ACT13739 study baseline. Analysis was performed on full analysis set: all subjects who received at least 1 dose of IMP during the ACT13739 study. All data collected during ACT13739 and LTS14116 studies were included in analysis. Here, 'n' signifies subjects with available data for specified category.

End point type	Secondary

End point timeframe:

Baseline of ACT13739 study and Weeks 2, 4, 8, 12, 18, 26, 52, 104 and 156 post-ACT13739 baseline

End point values	GZ/SAR402671			
Subject group type	Reporting group			
Number of subjects analysed	11			
Units: subjects				
number (not applicable)				
Baseline: No (n = 11)	9			

Baseline: Yes (n = 11)	2			
Week 2: No (n = 11)	8			
Week 2: Yes (n = 11)	3			
Week 4: No (n = 11)	7			
Week 4: Yes (n = 11)	4			
Week 8: No (n = 11)	9			
Week 8: Yes (n = 11)	2			
Week 12: No (n = 10)	9			
Week 12: Yes (n = 10)	1			
Week 18: No (n = 9)	8			
Week 18: Yes (n = 9)	1			
Week 26: No (n = 9)	8			
Week 26: Yes (n = 9)	1			
Week 52: No (n = 7)	7			
Week 52: Yes (n = 7)	0			
Week 104: No (n = 7)	7			
Week 104: Yes (n = 7)	0			
Week 156: No (n = 7)	6			
Week 156: Yes (n = 7)	1			

Statistical analyses

No statistical analyses for this end point

Secondary: Gastrointestinal Symptoms: Abdominal Distension Severity Score at Baseline and Weeks 2, 4, 8, 12, 18, 26 and 156

End point title	Gastrointestinal Symptoms: Abdominal Distension Severity Score at Baseline and Weeks 2, 4, 8, 12, 18, 26 and 156

End point description:

Subjects assessed their GI symptoms (abdominal pain, abdominal distention, bowel movements) by completing a questionnaire (modified version of the inflammatory bowel severity scoring system). Subjects were asked to mark the severity of the abdominal distension in past 10 days (before each of the specified time points) on a VAS. The scale ranged from 0% (no distention) to 100% (very severe), where higher score indicated more severity. For this analysis, baseline was defined as initial ACT13739 study baseline. Analysis was performed on full analysis set: all subjects who received at least 1 dose of IMP during the ACT13739 study. All data collected during ACT13739 and LTS14116 studies were included in analysis. Here, 'n' signifies subjects with available data for specified category. The SD can only be calculated when there are more than 1 subject with data available, and "99999" is entered when SD cannot be calculated.

End point type	Secondary

End point timeframe:

Baseline of ACT13739 study and Weeks 2, 4, 8, 12, 18, 26 and 156 post-ACT13739 baseline

End point values	GZ/SAR402671			
Subject group type	Reporting group			
Number of subjects analysed	11			
Units: score on a 0-100 percent scale				
arithmetic mean (standard deviation)				

Baseline (n = 3)	45.33 (± 24.01)			
Week 2 (n = 3)	38.67 (± 38.42)			
Week 4 (n = 4)	21.00 (± 26.15)			
Week 8 (n = 2)	35.00 (± 48.08)			
Week 12 (n = 1)	72.00 (± 99999)			
Week 18 (n = 1)	69.00 (± 99999)			
Week 26 (n = 1)	80.00 (± 99999)			
Week 156 (n = 1)	5.00 (± 99999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Gastrointestinal Symptoms: Number of Subjects in Categories of Response Regarding Eating Less Due to Abdominal Pain/Bloating at Baseline and Weeks 2, 4, 8, 12, 18, 26, 52, 104 and 156

End point title	Gastrointestinal Symptoms: Number of Subjects in Categories of Response Regarding Eating Less Due to Abdominal Pain/Bloating at Baseline and Weeks 2, 4, 8, 12, 18, 26, 52, 104 and 156

End point description:

Subjects assessed their GI symptoms (abdominal pain, abdominal distention, bowel movements) by completing a questionnaire (modified version of the inflammatory bowel severity scoring system). Subjects responded to question "How often do you eat less during meals due to abdominal pain and/or bloating?" in past 10 days (before each of the specified time points) in the categories as 'never', 'occasionally' or 'often'. For this analysis, baseline was defined as initial ACT13739 study baseline. Analysis was performed on full analysis set: all subjects who received at least 1 dose of IMP during the ACT13739 study. All data collected during ACT13739 and LTS14116 studies were included in analysis. Here, 'n' signifies subjects with available data for specified category.

End point type	Secondary

End point timeframe:

Baseline of ACT13739 study and Weeks 2, 4, 8, 12, 18, 26, 52, 104 and 156 post-ACT13739 baseline

End point values	GZ/SAR402671			
Subject group type	Reporting group			
Number of subjects analysed	11			
Units: subjects				
number (not applicable)				
Baseline: Never (n = 11)	4			
Baseline: Occasionally (n = 11)	5			
Baseline: Often (n = 11)	2			
Week 2: Never (n = 11)	6			
Week 2: Occasionally (n = 11)	3			
Week 2: Often (n = 11)	2			

Week 4: Never (n = 11)	6			
Week 4: Occasionally (n = 11)	3			
Week 4: Often (n = 11)	2			
Week 8: Never (n = 11)	7			
Week 8: Occasionally (n = 11)	3			
Week 8: Often (n = 11)	1			
Week 12: Never (n = 10)	5			
Week 12: Occasionally (n= 10)	3			
Week 12: Often (n =10)	2			
Week 18: Never (n = 9)	4			
Week 18: Occasionally (n = 9)	3			
Week 18: Often (n = 9)	2			
Week 26:Never (n = 9)	4			
Week 26: Occasionally (n = 9)	3			
Week 26: Often (n = 9)	2			
Week 52: Never (n = 7)	3			
Week 52: Occasionally (n = 7)	3			
Week 52: Often (n = 7)	1			
Week 104: Never (n = 7)	4			
Week 104: Occasionally (n = 7)	3			
Week 104: Often (n = 7)	0			
Week 156: Never (n = 7)	4			
Week 156: Occasionally (n = 7)	3			
Week 156: Often (n = 7)	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Gastrointestinal Symptoms: Satisfaction Over Bowel Habits at Baseline and Weeks 2, 4, 8, 12, 18, 26, 52, 104 and 156

End point title	Gastrointestinal Symptoms: Satisfaction Over Bowel Habits at Baseline and Weeks 2, 4, 8, 12, 18, 26, 52, 104 and 156

End point description:

Subjects assessed their GI symptoms (abdominal pain, abdominal distention, bowel movements) by completing a questionnaire (modified version of the inflammatory bowel severity scoring system). Subjects were asked to mark their satisfaction over bowel habits in past 10 days (before each of the specified time points) on a VAS. The scale ranged from 0% (very happy) to 100% (very unhappy), where higher percentage indicated less satisfaction. For this analysis, baseline was defined as initial ACT13739 study baseline. Analysis was performed on full analysis set: all subjects who received at least 1 dose of IMP during the ACT13739 study. All data collected during ACT13739 and LTS14116 studies were included in analysis. Here, 'n' signifies subjects with available data for specified category.

End point type	Secondary

End point timeframe:

Baseline of ACT13739 study and Weeks 2, 4, 8, 12, 18, 26, 52, 104 and 156 post-ACT13739 baseline

End point values	GZ/SAR402671			
Subject group type	Reporting group			
Number of subjects analysed	11			
Units: score on a 0-100 percent scale				
arithmetic mean (standard deviation)				
Baseline (n = 11)	26.55 (± 19.09)			
Week 2 (n = 11)	30.82 (± 21.17)			
Week 4 (n = 11)	36.09 (± 28.68)			
Week 8 (n = 11)	34.27 (± 27.02)			
Week 12 (n =10)	21.50 (± 17.83)			
Week 18 (n = 9)	23.89 (± 21.29)			
Week 26 (n = 9)	35.56 (± 29.37)			
Week 52 (n = 6)	19.00 (± 17.05)			
Week 104 (n = 5)	18.00 (± 15.18)			
Week 156 (n = 6)	34.02 (± 36.67)			

Statistical analyses

No statistical analyses for this end point

Secondary: Gastrointestinal Symptoms: Frequency of Bowel Movements - Most Number of Times Bowel Movement Per Day at Baseline and Weeks 2, 4, 8, 12, 18, 26, 52, 104 and 156

End point title	Gastrointestinal Symptoms: Frequency of Bowel Movements - Most Number of Times Bowel Movement Per Day at Baseline and Weeks 2, 4, 8, 12, 18, 26, 52, 104 and 156

End point description:

Subjects assessed their GI symptoms (abdominal pain, abdominal distention, bowel movements) by completing a questionnaire (modified version of the inflammatory bowel severity scoring system). Subjects were asked to report the frequency of their bowel movement (per day or per week or per month) in past 10 days (before each of the specified time points) by answering the question "What is the most number of times you move your bowels per day/week/month?". Subjects selected their preferred time unit (e.g., per day). Response provided by subjects was converted to number of times per day for reporting the results. For this analysis, baseline was defined as initial ACT13739 study baseline. Analysis was performed on full analysis set: all subjects who received at least 1 dose of IMP during the ACT13739 study. All data collected during ACT13739 and LTS14116 studies were included in analysis. Here, 'n' signifies subjects with available data for specified category.

End point type	Secondary

End point timeframe:

Baseline of ACT13739 study and Weeks 2, 4, 8, 12, 18, 26, 52, 104 and 156 post-ACT13739 baseline

End point values	GZ/SAR402671			
Subject group type	Reporting group			
Number of subjects analysed	11			
Units: number of bowel movements per day				
arithmetic mean (standard deviation)				
Baseline (n = 11)	2.36 (± 1.03)			
Week 2 (n = 11)	2.00 (± 0.63)			
Week 4 (n = 11)	2.00 (± 1.00)			
Week 8 (n = 11)	1.74 (± 1.07)			
Week 12 (n = 10)	2.04 (± 1.08)			
Week 18 (n = 9)	2.17 (± 1.05)			
Week 26 (n = 9)	2.16 (± 1.07)			
Week 52 (n = 7)	2.08 (± 1.00)			
Week 104 (n = 7)	1.96 (± 1.05)			
Week 156 (n = 7)	1.65 (± 0.61)			

Statistical analyses

No statistical analyses for this end point

Secondary: Gastrointestinal Symptoms: Frequency of Bowel Movements - Least Number of Times Bowel Movement Per Day at Baseline and Weeks 2, 4, 8, 12, 18, 26, 52, 104 and 156

End point title	Gastrointestinal Symptoms: Frequency of Bowel Movements - Least Number of Times Bowel Movement Per Day at Baseline and Weeks 2, 4, 8, 12, 18, 26, 52, 104 and 156

End point description:

Subjects assessed their GI symptoms (abdominal pain, abdominal distention, bowel movements) by completing a questionnaire (modified version of the inflammatory bowel severity scoring system). Subjects were asked to report frequency of bowel movement (per day/per week or per month) in past 10 days (before each of specified time points). Subjects answered question "What is the least number of times you move your bowels per day/week/month?". Subjects selected their preferred time unit (e.g., per day). Response provided by subjects was converted to number of times per day for reporting results. For this analysis, baseline was defined as initial ACT13739 study baseline. Analysis was performed on full analysis set: all subjects who received at least 1 dose of IMP during the ACT13739 study. All data collected during ACT13739 and LTS14116 studies were included in analysis. Here, 'n' signifies subjects with available data for specified category.

End point type	Secondary

End point timeframe:

Baseline of ACT13739 study and Weeks 2, 4, 8, 12, 18, 26, 52, 104 and 156 post-ACT13739 baseline

End point values	GZ/SAR402671			
Subject group type	Reporting group			
Number of subjects analysed	11			
Units: number of bowel movements per day				
arithmetic mean (standard deviation)				
Baseline (n = 11)	0.78 (± 0.56)			
Week 2 (n = 11)	0.66 (± 0.43)			

Week 4 (n = 11)	0.65 (± 0.62)			
Week 8 (n = 11)	0.62 (± 0.64)			
Week 12 (n = 10)	0.67 (± 0.65)			
Week 18 (n = 9)	0.73 (± 0.65)			
Week 26 (n = 9)	0.75 (± 0.40)			
Week 52 (n = 7)	0.76 (± 0.72)			
Week 104 (n = 7)	0.61 (± 0.49)			
Week 156 (n = 7)	0.92 (± 0.62)			

Statistical analyses

No statistical analyses for this end point

Secondary: Gastrointestinal Symptoms: Influence of GI Symptoms of Fabry Disease on Life at Baseline and Weeks 2, 4, 8, 12, 18, 26, 52, 104 and 156

End point title	Gastrointestinal Symptoms: Influence of GI Symptoms of Fabry Disease on Life at Baseline and Weeks 2, 4, 8, 12, 18, 26, 52, 104 and 156

End point description:

Subjects assessed their GI symptoms (abdominal pain, abdominal distention, bowel movements) by completing a questionnaire (modified version of the inflammatory bowel severity scoring system). Subjects were asked to mark the influence of their GI symptoms of Fabry disease on life in past 10 days (before each of the specified time points) on a VAS. The scale ranged from 0% (no at all) to 100% (completely), where higher percentage indicated more influence of the GI symptoms of the disease on life. For this analysis, baseline was defined as initial ACT13739 study baseline. Analysis was performed on Full analysis set: all subjects who received at least 1 dose of IMP during the ACT13739 study. All data collected during ACT13739 and LTS14116 studies were included in analysis. Here, 'n' signifies subjects with available data for specified category.

End point type	Secondary

End point timeframe:

Baseline of ACT13739 study and Weeks 2, 4, 8, 12, 18, 26, 52, 104 and 156 post-ACT13739 baseline

End point values	GZ/SAR402671			
Subject group type	Reporting group			
Number of subjects analysed	11			
Units: score on a 0-100 percent scale				
arithmetic mean (standard deviation)				
Baseline (n = 11)	34.36 (± 26.47)			
Week 2 (n = 11)	26.73 (± 25.22)			
Week 4 (n = 11)	21.27 (± 19.88)			
Week 8 (n = 11)	22.09 (± 19.77)			
Week 12 (n = 10)	17.50 (± 19.92)			
Week 18 (n = 9)	24.89 (± 23.34)			
Week 26 (n = 9)	36.44 (± 30.18)			

Week 52 (n = 6)	20.33 (± 22.04)			
Week 104 (n = 5)	26.50 (± 23.31)			
Week 156 (n = 6)	19.82 (± 21.14)			

Statistical analyses

No statistical analyses for this end point

Secondary: Gastrointestinal Symptoms: Number of Subjects With Stool Consistency Assessment by Bristol Stool Scale Scoring at Baseline and Weeks 26, 52, 104 and 156

End point title	Gastrointestinal Symptoms: Number of Subjects With Stool Consistency Assessment by Bristol Stool Scale Scoring at Baseline and Weeks 26, 52, 104 and 156

End point description:

Subjects were asked to rate their stool consistency in past 10 days (before each specified time points) on a 7-point Bristol stool scale as types: 1=separate hard lumps, 2=sausage shaped but lumpy, 3=sausage-like with cracks on surface, 4=sausage-like but smooth and soft, 5=soft blobs with clear cut edges, 6=fluffy pieces with ragged edges, and 7=watery with no solid pieces. Types 1 and 2 indicate constipation, 3 and 4 indicate "ideal stools", and 5-7 indicate diarrhea. Type frequency was categorised as 'never', occasionally' or 'often'. Baseline was defined as initial ACT13739 study baseline. Analysed on Full analysis set: all subjects who received at least 1 dose of IMP during ACT13739. All data collected during ACT13739 and LTS14116 were included in analysis. Here, 'n' signifies subjects with available data for specified category.

End point type	Secondary

End point timeframe:

Baseline of ACT13739 study and Weeks 26, 52, 104 and 156 post-ACT13739 baseline

End point values	GZ/SAR402671			
Subject group type	Reporting group			
Number of subjects analysed	11			
Units: subjects				
number (not applicable)				
Stool Type 1: Baseline - Never (n = 11)	11			
Stool Type 1: Baseline - Occasionally (n = 11)	0			
Stool Type 1: Baseline - Often (n = 11)	0			
Stool Type 1: Week 26 - Never (n = 9)	8			
Stool Type 1: Week 26 - Occasionally (n = 9)	1			
Stool Type 1: Week 26 - Often (n = 9)	0			
Stool Type 1: Week 52 - Never (n = 7)	6			
Stool Type 1: Week 52 - Occasionally (n = 7)	0			
Stool Type 1: Week 52 - Often (n = 7)	1			
Stool Type 1: Week 104 - Never (n = 7)	6			
Stool Type 1: Week 104 - Occasionally (n = 7)	0			

Stool Type 1: Week 104 - Often (n = 7)	1			
Stool Type 1: Week 156 - Never (n = 7)	5			
Stool Type 1: Week 156 - Occasionally (n = 7)	1			
Stool Type 1: Week 156 - Often (n = 7)	1			
Stool Type 2: Baseline - Never (n = 11)	6			
Stool Type 2: Baseline - Occasionally (n = 11)	5			
Stool Type 2: Baseline - Often (n = 11)	0			
Stool Type 2: Week 26 - Never (n = 9)	6			
Stool Type 2: Week 26 - Occasionally (n = 9)	0			
Stool Type 2: Week 26 - Often (n = 9)	3			
Stool Type 2: Week 52 - Never (n = 7)	3			
Stool Type 2: Week 52 - Occasionally (n = 7)	4			
Stool Type 2: Week 52 - Often (n = 7)	0			
Stool Type 2: Week 104 - Never (n = 7)	4			
Stool Type 2: Week 104 - Occasionally (n = 7)	2			
Stool Type 2: Week 104 - Often (n = 7)	1			
Stool Type 2: Week 156 - Never (n = 7)	2			
Stool Type 2: Week 156 - Occasionally (n = 7)	3			
Stool Type 2: Week 156 - Often (n = 7)	2			
Stool Type 3: Baseline - Never (n = 11)	1			
Stool Type 3: Baseline - Occasionally (n = 11)	4			
Stool Type 3: Baseline - Often (n = 11)	6			
Stool Type 3: Week 26 - Never (n = 9)	1			
Stool Type 3: Week 26 - Occasionally (n = 9)	3			
Stool Type 3: Week 26 - Often (n = 9)	5			
Stool Type 3: Week 52 - Never (n = 7)	0			
Stool Type 3: Week 52 - Occasionally (n = 7)	3			
Stool Type 3: Week 52 - Often (n = 7)	4			
Stool Type 3: Week 104 - Never (n = 7)	0			
Stool Type 3: Week 104 - Occasionally (n = 7)	6			
Stool Type 3: Week 104 - Often (n = 7)	1			
Stool Type 3: Week 156 - Never (n = 7)	0			
Stool Type 3: Week 156 - Occasionally (n = 7)	4			
Stool Type 3: Week 156 - Often (n = 7)	3			
Stool Type 4: Baseline - Never (n = 11)	1			
Stool Type 4: Baseline - Occasionally (n = 11)	8			
Stool Type 4: Baseline - Often (n = 11)	2			
Stool Type 4: Week 26 - Never (n = 9)	2			
Stool Type 4: Week 26 - Occasionally (n = 9)	4			
Stool Type 4: Week 26 - Often (n = 9)	3			
Stool Type 4: Week 52 - Never (n = 7)	3			
Stool Type 4: Week 52 - Occasionally (n = 7)	1			

Stool Type 4: Week 52 - Often (n = 7)	3			
Stool Type 4: Week 104 - Never (n = 7)	2			
Stool Type 4: Week 104 - Occasionally (n = 7)	3			
Stool Type 4: Week 104 - Often (n = 7)	2			
Stool Type 4: Week 156 - Never (n = 7)	3			
Stool Type 4: Week 156 - Occasionally (n = 7)	2			
Stool Type 4: Week 156 - Often (n = 7)	2			
Stool type 5: Baseline - Never (n = 11)	1			
Stool type 5: Baseline - Occasionally (n = 11)	9			
Stool type 5: Baseline - Often (n = 11)	1			
Stool type 5: Week 26 - Never (n = 9)	4			
Stool type 5: Week 26 - Occasionally (n = 9)	4			
Stool type 5: Week 26 - Often (n = 9)	1			
Stool type 5: Week 52 - Never (n = 7)	5			
Stool type 5: Week 52 - Occasionally (n = 7)	2			
Stool type 5: Week 52 - Often (n = 7)	0			
Stool type 5: Week 104 - Never (n = 7)	4			
Stool type 5: Week 104 - Occasionally (n = 7)	1			
Stool type 5: Week 104 - Often (n = 7)	2			
Stool type 5: Week 156 - Never (n = 7)	3			
Stool type 5: Week 156 - Occasionally (n = 7)	3			
Stool type 5: Week 156 - Often (n = 7)	1			
Stool Type 6: Baseline - Never (n = 11)	5			
Stool Type 6: Baseline - Occasionally (n = 11)	5			
Stool Type 6: Baseline - Often (n = 11)	1			
Stool Type 6: Week 26 - Never (n = 9)	4			
Stool Type 6: Week 26 - Occasionally (n = 9)	4			
Stool Type 6: Week 26 - Often (n = 9)	1			
Stool Type 6: Week 52 - Never (n = 7)	4			
Stool Type 6: Week 52 - Occasionally (n = 7)	2			
Stool Type 6: Week 52 - Often (n = 7)	1			
Stool Type 6: Week 104 - Never (n = 7)	3			
Stool Type 6: Week 104 - Occasionally (n = 7)	3			
Stool Type 6: Week 104 - Often (n = 7)	1			
Stool Type 6: Week 156 - Never (n = 7)	4			
Stool Type 6: Week 156 - Occasionally (n = 7)	3			
Stool Type 6: Week 156 - Often (n = 7)	0			
Stool Type 7: Baseline - Never (n = 11)	5			
Stool Type 7: Baseline - Occasionally (n = 11)	5			
Stool Type 7: Baseline - Often (n = 11)	1			
Stool Type 7: Week 26 - Never (n = 9)	5			
Stool Type 7: Week 26 - Occasionally (n = 9)	4			

Stool Type 7: Week 26 - Often (n = 9)	0			
Stool Type 7: Week 52 - Never (n = 7)	5			
Stool Type 7: Week 52 - Occasionally (n = 7)	2			
Stool Type 7: Week 52 - Often (n = 7)	0			
Stool Type 7: Week 104 - Never (n = 7)	4			
Stool Type 7: Week 104 - Occasionally (n = 7)	3			
Stool Type 7: Week 104 - Often (n = 7)	0			
Stool Type 7: Week 156 - Never (n = 7)	3			
Stool Type 7: Week 156 - Occasionally (n = 7)	3			
Stool Type 7: Week 156 - Often (n = 7)	1			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Beck Depression Inventory (BDI) Total Score at Weeks 26, 104 and 156

End point title	Change From Baseline in Beck Depression Inventory (BDI) Total Score at Weeks 26, 104 and 156

End point description:

The BDI-II Scale was a 21-item scoring tool which measures the existence and severity of symptoms of depression. Each of the 21 items on BDI-II tool represent a depressive symptom. Each symptoms were scored on a 4-point scale of 0 to 3 (0=symptom not present); (3=symptom very intense). Scores for each symptom were added up to obtain the total scores for all 21 items, which were interpreted as follows: Scores of 0-13: minimal depression; 14-19: mild depression; 20-28: moderate depression and 29-63: severe depression, where higher scores indicated more depression. For this analysis, baseline was defined as initial ACT13739 study baseline. Analysis was performed on full analysis set: all subjects who received at least 1 dose of IMP during the ACT13739 study. All data collected during ACT13739 and LTS14116 studies were included in analysis. Here, 'n' signifies subjects with available data for specified category.

End point type	Secondary

End point timeframe:

Baseline of ACT13739 study and Weeks 26, 104 and 156 post-ACT13739 baseline

End point values	GZ/SAR402671			
Subject group type	Reporting group			
Number of subjects analysed	11			
Units: score on a scale				
arithmetic mean (standard deviation)				
Week 26 (n = 9)	-0.89 (± 8.13)			
Week 104 (n = 4)	2.00 (± 3.37)			
Week 156 (n = 7)	-3.43 (± 7.09)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Albumin/Creatinine Ratio (ACR) and Protein/Creatinine Ratio (PCR) at Weeks 26, 52, 104 and 156

End point title	Change From Baseline in Albumin/Creatinine Ratio (ACR) and Protein/Creatinine Ratio (PCR) at Weeks 26, 52, 104 and 156

End point description:

For each scheduled visit for this assessment, 3 timed overnight urine samples were collected between 4 to 7 days of each other. All urine samples were collected within a 16-day period. ACR and PCR were determined for each collection. The median of the values determined for the 3 collections/visit was used for analysis. Baseline was defined as initial ACT13739 study baseline. Analysis was performed on full analysis set: all subjects who received at least 1 dose of IMP during the ACT13739 study. All data collected during ACT13739 and LTS14116 studies were included in analysis. Here, 'n' signifies subjects with available data for specified category.

End point type	Secondary

End point timeframe:

Baseline of ACT13739 study and Weeks 26, 52, 104 and 156 post-ACT13739 baseline

End point values	GZ/SAR402671			
Subject group type	Reporting group			
Number of subjects analysed	11			
Units: mg/g				
arithmetic mean (standard deviation)				
ACR: Week 26 (n = 9)	-26.22 (± 26.75)			
ACR: Week 52 (n = 7)	1.00 (± 57.23)			
ACR: Week 104 (n = 7)	12.21 (± 71.82)			
ACR: Week 156 (n = 7)	-1.14 (± 54.80)			
PCR: Week 26 (n = 9)	-38.33 (± 24.40)			
PCR: Week 52 (n = 7)	0.33 (± 62.11)			
PCR: Week 104 (n = 7)	-12.88 (± 76.97)			
PCR: Week 156 (n = 7)	-34.38 (± 71.40)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects in Categories of Echocardiogram (ECHO) Results at Baseline and at Weeks 26, 52, 104 and 156

End point title	Number of Subjects in Categories of Echocardiogram (ECHO) Results at Baseline and at Weeks 26, 52, 104 and 156

End point description:

The summary statistics of all continuous echocardiogram variables were calculated for each visit. The overall interpretation of the readings were summarised in 3 categories: normal, abnormal but not clinically significant (NCS), and abnormal but clinically significant (CS) categories. For this analysis, baseline was defined as initial ACT13739 study baseline. Analysis was performed on full analysis set: all

subjects who received at least 1 dose of IMP during the ACT13739 study. All data collected during ACT13739 and LTS14116 studies were included in analysis. Here, 'n' signifies subjects with available data for specified category.

End point type	Secondary

End point timeframe:

Baseline of ACT13739 study and Weeks 26, 52, 104 and 156 post-ACT13739 baseline

End point values	GZ/SAR402671			
Subject group type	Reporting group			
Number of subjects analysed	11			
Units: subjects				
number (not applicable)				
Baseline: Normal (n = 8)	6			
Baseline: Abnormal NCS (n = 8)	2			
Baseline: Abnormal CS (n = 8)	0			
Week 26: Normal (n = 9)	6			
Week 26: Abnormal NCS (n = 9)	3			
Week 26: Abnormal CS (n = 9)	0			
Week 52: Normal (n = 7)	5			
Week 52: Abnormal NCS (n = 7)	2			
Week 52: Abnormal CS (n = 7)	0			
Week 104: Normal (n = 7)	4			
Week 104: Abnormal NCS (n = 7)	3			
Week 104: Abnormal CS (n = 7)	0			
Week 156: Normal (n = 7)	5			
Week 156: Abnormal NCS (n = 7)	2			
Week 156: Abnormal CS (n = 7)	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects in Categories of Brain Magnetic Resonance Imaging (MRI) Results at Baseline and Weeks 26 and 156

End point title	Number of Subjects in Categories of Brain Magnetic Resonance Imaging (MRI) Results at Baseline and Weeks 26 and 156

End point description:

All continuous MRI variables were summarised using descriptive statistics for each visit. The overall interpretation of the readings were summarised in 2 categories as: normal and abnormal. For this analysis, baseline was defined as initial ACT13739 study baseline. Analysis was performed on full analysis set: all subjects who received at least 1 dose of IMP during the ACT13739 study. All data collected during ACT13739 and LTS14116 studies were included in analysis. Here, 'n' signifies subjects with available data for specified category.

End point type	Secondary

End point timeframe:

Baseline of ACT13739 study and Weeks 26, and 156 post-ACT13739 baseline

End point values	GZ/SAR402671			
Subject group type	Reporting group			
Number of subjects analysed	11			
Units: subjects				
number (not applicable)				
Baseline: Normal (n = 10)	6			
Baseline: Abnormal (n = 10)	4			
Week 26: Normal (n = 9)	7			
Week 26: Abnormal (n = 9)	2			
Week 156: Normal (n = 7)	4			
Week 156: Abnormal (n = 7)	3			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Estimated Glomerular Filtration Rate (eGFR) at Weeks 26, 52, 104 and 156

End point title	Change From Baseline in Estimated Glomerular Filtration Rate (eGFR) at Weeks 26, 52, 104 and 156

End point description:

Estimated glomerular filtration rate was used to measure level of kidney function and determine the stage of kidney disease. Change from baseline in eGFR was obtained by subtracting baseline value from post-baseline value at Weeks 26, 52, 104 and 156. For this analysis, baseline was defined as initial ACT13739 study baseline. Analysis was performed on full analysis set: all subjects who received at least 1 dose of IMP during the ACT13739 study. All data collected during ACT13739 and LTS14116 studies were included in analysis. Here, 'n' signifies subjects with available data for specified category.

End point type	Secondary

End point timeframe:

Baseline of ACT13739 study and Weeks 26, 52, 104 and 156 post-ACT13739 baseline

End point values	GZ/SAR402671			
Subject group type	Reporting group			
Number of subjects analysed	11			
Units: mL/min/1.73m^2				
arithmetic mean (standard deviation)				
Week 26 (n = 7)	-3.43 (± 8.64)			
Week 52 (n = 7)	-5.57 (± 11.07)			
Week 104 (n = 7)	-5.71 (± 10.23)			
Week 156 (n = 6)	-4.83 (± 17.54)			

Statistical analyses

No statistical analyses for this end point

Secondary: Chitotriosidase (Chit1) Plasma Concentration Levels at Weeks 52, 104,156 and 160 (End of Treatment Follow-up)

End point title	Chitotriosidase (Chit1) Plasma Concentration Levels at Weeks 52, 104,156 and 160 (End of Treatment Follow-up)

End point description:

Plasma concentrations of Chit1 over time were determined using mass spectrometry (MS)-based assay. For the analysis, 52 ng/mL was considered as the lower limit of quantification. Although identified in protocol as a secondary endpoint, plasma Chit1 is also an exploratory measure. Only LTS14116 timepoints were analysed and are presented. Data summarised are the measured values at each time point (not change from baseline). Here, measured value '0.000' denotes no chitotriosidase detected in plasma for the 5 subjects at Week 156 reported by laboratory for all evaluable subjects. Analysis population included subjects in LTS14116 study with evaluable plasma Chit1 data. Only data collected during LTS14116 study were included in analysis. Here, 'number of subjects analysed' = subjects evaluable for this endpoint and 'n' = subjects with available data for each specified category.

End point type	Secondary

End point timeframe:

Weeks 52, 104, 156 and 160 (End of Treatment Follow-up) post-ACT13739 baseline

End point values	GZ/SAR402671			
Subject group type	Reporting group			
Number of subjects analysed	7			
Units: ng/mL				
arithmetic mean (standard deviation)				
Week 52 (n=7)	35.965 (± 46.520)			
Week 104 (n=7)	12.785 (± 20.993)			
Week 156 (n=5)	0.000 (± 0.000)			
Week 160 ((End of Treatment Follow-up) (n=4)	6.483 (± 6.309)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From baseline of ACT13739 study up to 37 months post-ACT13739 baseline

Adverse event reporting additional description:

Reported AEs were TEAEs, defined as AEs that developed/worsened during TEAE period (period from 1st administration of study drug in ACT13739 through last administration of study drug in the combined ACT13739/LTS14116 treatment period plus 1 month or end of study participation for subject, whichever occurs first). Analysed on safety population.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	21.1

Reporting groups

Reporting group title	GZ/SAR402671

Reporting group description:

Subjects received GZ/SAR402671 15 mg once daily orally for 36 months during combined ACT13739/LTS14116 treatment period.

Serious adverse events	GZ/SAR402671		
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 11 (27.27%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Nervous system disorders			
Ischaemic Stroke			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Haemolysis			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Ear and labyrinth disorders			
Deafness Unilateral			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vertigo			

subjects affected / exposed	1 / 11 (9.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Intentional Self-Injury			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Depressed Mood			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Floppy Infant			
subjects affected / exposed	1 / 11 (9.09%)		
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	GZ/SAR402671		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	9 / 11 (81.82%)		
General disorders and administration site conditions			
Influenza Like Illness			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Fatigue			
subjects affected / exposed	2 / 11 (18.18%)		
occurrences (all)	2		
Non-Cardiac Chest Pain			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Oedema Peripheral			

subjects affected / exposed	1 / 11 (9.09%)			
occurrences (all)	1			
Feeling Hot				
subjects affected / exposed	2 / 11 (18.18%)			
occurrences (all)	2			
Oedema				
subjects affected / exposed	1 / 11 (9.09%)			
occurrences (all)	1			
Pain				
subjects affected / exposed	2 / 11 (18.18%)			
occurrences (all)	2			
Temperature Intolerance				
subjects affected / exposed	1 / 11 (9.09%)			
occurrences (all)	1			
Pyrexia				
subjects affected / exposed	2 / 11 (18.18%)			
occurrences (all)	2			
Respiratory, thoracic and mediastinal disorders				
Hiccups				
subjects affected / exposed	1 / 11 (9.09%)			
occurrences (all)	1			
Dry Throat				
subjects affected / exposed	1 / 11 (9.09%)			
occurrences (all)	1			
Nasal Discomfort				
subjects affected / exposed	1 / 11 (9.09%)			
occurrences (all)	1			
Cough				
subjects affected / exposed	2 / 11 (18.18%)			
occurrences (all)	2			
Oropharyngeal Pain				
subjects affected / exposed	1 / 11 (9.09%)			
occurrences (all)	1			
Dyspnoea				

subjects affected / exposed	2 / 11 (18.18%)		
occurrences (all)	2		
Sinus Pain			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Psychiatric disorders			
Anxiety			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	2		
Depressed Mood			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Depression			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Nervousness			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Investigations			
Electrocardiogram T Wave Abnormal			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Glomerular Filtration Rate Decreased			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Nuclear Magnetic Resonance Imaging Brain Abnormal			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Electrocardiogram Abnormal			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Vibration Test Abnormal			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Injury, poisoning and procedural complications			

Arthropod Bite			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	2		
Contusion			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Joint Injury			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Limb Injury			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Meniscus Injury			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Muscle Strain			
subjects affected / exposed	2 / 11 (18.18%)		
occurrences (all)	4		
Tooth Fracture			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Wound			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Cardiac disorders			
Atrial Fibrillation			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Atrioventricular Block First Degree			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Cardiomyopathy			
subjects affected / exposed	2 / 11 (18.18%)		
occurrences (all)	2		
Sinus Bradycardia			

subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Nervous system disorders			
Amnesia			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	2		
Burning Sensation			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	2		
Balance Disorder			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Cerebral Ischaemia			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Carpal Tunnel Syndrome			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Hemiparesis			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Dizziness			
subjects affected / exposed	2 / 11 (18.18%)		
occurrences (all)	6		
Headache			
subjects affected / exposed	4 / 11 (36.36%)		
occurrences (all)	5		
Hypoaesthesia			
subjects affected / exposed	2 / 11 (18.18%)		
occurrences (all)	4		
Paraesthesia			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Migraine			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	2		

Memory Impairment subjects affected / exposed occurrences (all)	1 / 11 (9.09%) 1		
Monoparesis subjects affected / exposed occurrences (all)	1 / 11 (9.09%) 1		
White Matter Lesion subjects affected / exposed occurrences (all)	1 / 11 (9.09%) 1		
Presyncope subjects affected / exposed occurrences (all)	1 / 11 (9.09%) 1		
Neuralgia subjects affected / exposed occurrences (all)	1 / 11 (9.09%) 1		
Tremor subjects affected / exposed occurrences (all)	2 / 11 (18.18%) 3		
Ear and labyrinth disorders			
Deafness Unilateral subjects affected / exposed occurrences (all)	1 / 11 (9.09%) 1		
Ear Pain subjects affected / exposed occurrences (all)	1 / 11 (9.09%) 1		
Tinnitus subjects affected / exposed occurrences (all)	3 / 11 (27.27%) 3		
Middle Ear Effusion subjects affected / exposed occurrences (all)	1 / 11 (9.09%) 1		
Vertigo subjects affected / exposed occurrences (all)	1 / 11 (9.09%) 1		
Eye disorders			

Chalazion			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Blepharitis			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	2		
Diplopia			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Lacrimation Increased			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Eye Pain			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Lenticular Opacities			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	2		
Vision Blurred			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Retinal Vascular Disorder			
subjects affected / exposed	2 / 11 (18.18%)		
occurrences (all)	2		
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	2		
Diarrhoea			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Abdominal Pain Upper			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Gastrooesophageal Reflux Disease			

subjects affected / exposed occurrences (all) Dry Mouth subjects affected / exposed occurrences (all) Oesophageal Discomfort subjects affected / exposed occurrences (all) Nausea subjects affected / exposed occurrences (all) Toothache subjects affected / exposed occurrences (all) Vomiting subjects affected / exposed occurrences (all)	2 / 11 (18.18%) 2 1 / 11 (9.09%) 1 1 / 11 (9.09%) 1 2 / 11 (18.18%) 6 1 / 11 (9.09%) 1 2 / 11 (18.18%) 2		
Skin and subcutaneous tissue disorders Acne subjects affected / exposed occurrences (all) Dermatitis Contact subjects affected / exposed occurrences (all) Angiokeratoma subjects affected / exposed occurrences (all) Hyperhidrosis subjects affected / exposed occurrences (all)	 1 / 11 (9.09%) 1 1 / 11 (9.09%) 1 3 / 11 (27.27%) 4 1 / 11 (9.09%) 1		
Renal and urinary disorders Micturition Frequency Decreased subjects affected / exposed occurrences (all)	 1 / 11 (9.09%) 1		
Musculoskeletal and connective tissue disorders			

Arthralgia			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Musculoskeletal Chest Pain			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Muscle Twitching			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	3		
Back Pain			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Myalgia			
subjects affected / exposed	2 / 11 (18.18%)		
occurrences (all)	2		
Neck Pain			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Pain In Extremity			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Rotator Cuff Syndrome			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Infections and infestations			
Conjunctivitis			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Ear Infection			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Influenza			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Herpes Simplex			

subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Nasopharyngitis			
subjects affected / exposed	4 / 11 (36.36%)		
occurrences (all)	5		
Periodontitis			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Pharyngitis			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Pharyngitis Streptococcal			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Rhinitis			
subjects affected / exposed	2 / 11 (18.18%)		
occurrences (all)	2		
Upper Respiratory Tract Infection			
subjects affected / exposed	3 / 11 (27.27%)		
occurrences (all)	5		
Upper Respiratory Tract Infection Bacterial			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	3		
Metabolism and nutrition disorders			
Decreased Appetite			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
12 May 2015	•Expansion of contraception requirements following the end of treatment period included 15 days after the subject's last treatment with IMP •Photographs at Month 30 ophthalmology exam were included for all subjects •Removal of Beck Depression Inventory- II (BDI-II assessment was not available and removed) •Update to the bioanalytical standard operating procedure (SOP) for the analysis of plasma GZ/SAR402671 concentrations •The Pharmacodynamics (PD) was measured in secondary endpoints included additional language to endpoint: exploratory blood and urine biomarkers including, but not limited to high sensitivity cardiac troponin T and podocyturia; addition to the study flow chart to include this information was also added •Addition to exploratory efficacy endpoint included urinary albumin and protein measurements •Changes to the Graphical Study Design Chart included "OR" for the ACT13739 dose levels •Grammatical errors were also corrected •Change in the language on pregnancy reporting as an adverse event (AE) to be consistent with SOP to keep consistency between protocol sections regarding pregnancy reporting as an AEs of special interest by changing the language as to report pregnancy of participating subject's female partner as an AE reported on electronic case report form AE form in addition to the additional pregnancy form.
14 January 2016	•Addition of optional examination of globotriaosylceramide in skin biopsies at month 6 for all subjects to the one already planned at Month 30 or at early withdrawal which were not limited to superficial capillary endothelium •Addition of language regarding future use of samples •Addition of language regarding the "external genitalia" examination to the Physical Exam section of the amended protocol •Addition of language regarding subject withdrawal •Expansion of contraception requirement following the end of the treatment period •Change to text describing measures to evaluate the exploratory efficacy of the IMP. The study further evaluated changes in the GL-3 scores by light microscopy in skin biopsy, patient reported outcome (PRO) questionnaires, and urinary albumin and protein (ACR and PCR) •Addition to text regarding study treatments adding that the as an alternative to between clinical visit, the study drug might be supplied from the site to the subject via a sponsor-approved courier company where allowed by local regulations and approved by ethics committee, sponsor, and the subject.
19 September 2016	•BDI-II questionnaire to PRO to monitor the mood status for subjects and appropriate reference was added •Addition of chitotriosidase plasma activity and genotyping as an exploratory biomarker in the secondary endpoints and in specific parameters of PD •Expansion of contraception requirements following the end of treatment period from 6 weeks to 90 days after the subject's last treatment with IMP •Minor changes to replace phrase tense from "currently participating" to "that participated" in the Investigator/Trial Location information •Grammatical errors were also corrected •Footnote text on the study flow chart was changed to include the following: BDI-II is part of protocol amendment #3 and were conducted starting at the first subject visit after amendment approval and thereafter in subsequent visits.

10 November 2017	•Changed the subject's post treatment follow up phone call to a site visit in order to collect disease biomarkers in the urine and blood, and pharmacokinetic (PK) data •Addition of PKs assessment in early withdrawal visit and revision to footnote to correct a previous omission •Addition of in other endpoints PKs text for sampling time: "PK sample during the early withdrawal (if applicable)and post treatment follow up visit were collected at any time during the visit" •Correction of text within the secondary endpoint: "monosialodihexosylganglioside" to replace "GM3 ganglioside (GM3)" and correction to footnote on the study flow chart, removal of reference to GM3 ganglioside (GM3) were made throughout the protocol •Changes to the Graphical Study Design Chart included End of treatment Follow up Visit •Additions to the duration of study participations for each subject included the following: "Post-treatment follow up: 1 month (±7 days). Subjects who started commercial enzyme replacement therapy, investigational or any other Fabry disease treatment within the 1-month (± 7 days) follow up period were not contacted considered for follow up assessments" •Grammatical errors were also corrected •Addition of "Renin-Angiotensin-Aldosterone System" to abbreviation (RAAS) listed in heading text •Correction to Estimated sample blood volumes including the sample number and volume per study.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported