Clinical trial results:
A Phase 3, Randomized, Multi-Center, Multi-National, Double-Blind Study to Evaluate the Efficacy, Safety and Pharmacokinetics of Once Daily Versus Twice Daily Dosing of Genz-112638 in Patients With Gaucher Disease Type 1 Who Have Demonstrated Clinical Stability on a Twice Daily Dose of Genz-112638

Summary

EudraCT number	2009-015811-42
Trial protocol	SE PT AT GR
Global end of trial date	06 October 2015

Results information

Result version number	v1 (current)
This version publication date	04 November 2016
First version publication date	04 November 2016

Trial information

Trial identification

Sponsor protocol code	GZGD03109

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01074944
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Genzyme, a Sanofi Company
Sponsor organisation address	500 Kendall Street, Cambridge MA, United States, 02142
Public contact	Trial Transparency Team, Sanofi aventis recherche & développement, Contact-
Scientific contact	Trial Transparency Team, Sanofi aventis recherche & développement, Contact-

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	10 September 2016
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	06 October 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the efficacy and safety of once daily (QD) versus twice daily (BID) dosing of eliglustat in subjects with Gaucher disease type 1 (GD1) who had previously demonstrated clinical stability on BID dosing of eliglustat.

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	01 June 2010
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	Australia: 5
Country: Number of subjects enrolled	Austria: 4
Country: Number of subjects enrolled	Brazil: 40
Country: Number of subjects enrolled	Canada: 5
Country: Number of subjects enrolled	China: 25
Country: Number of subjects enrolled	France: 5
Country: Number of subjects enrolled	Greece: 3
Country: Number of subjects enrolled	Croatia: 5
Country: Number of subjects enrolled	India: 4
Country: Number of subjects enrolled	Japan: 10
Country: Number of subjects enrolled	Netherlands: 6
Country: Number of subjects enrolled	Portugal: 6
Country: Number of subjects enrolled	Romania: 2
Country: Number of subjects enrolled	Russian Federation: 12
Country: Number of subjects enrolled	Serbia: 7
Country: Number of subjects enrolled	Sweden: 3
Country: Number of subjects enrolled	United States: 28

Worldwide total number of subjects	170
EEA total number of subjects	34

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)	162
From 65 to 84 years	8
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted at 45 centers in 17 countries between 1 June 2010 and 6 October 2015. A total of 219 subjects were screened, out of which 170 entered into the lead in period. Remaining 48 subjects were screen failures and 1 subject withdrew before entering into the lead in period.

Pre-assignment

Screening details:

Subject disposition divided in 4 periods. Lead in Period (LIP):to assess randomization criteria.Primary analysis period(PAP):assess therapeutic efficacy at 2 dosing regimen in randomized subjects. Long-term treatment period (LTTP):assess long term efficacy. Extended treatment period(ETP):who were non-randomized after LIP continued in this period

Period 1

Period 1 title	LIP (up to 78 weeks)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	LIP, Eliglustat

Arm description:

All subjects (except in Japan) received eliglustat 50 mg, BID on Day 1 titrated up to 100 mg BID (50 or 100 mg capsules) based on their individual pharmacokinetics data for up to 78 weeks. All subjects in Japan received eliglustat 50 mg once only on Day 1 and then eliglustat 50 mg BID from Day 2 titrated up to 100 mg BID (50 or 100 mg capsules) based on their individual pharmacokinetics data for up to 78 weeks.

Arm type	Experimental
Investigational medicinal product name	Eliglustat
Investigational medicinal product code	Genz--112638
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

All subjects (except in Japan) received eliglustat 50 mg BID on Day 1 titrated up to 100 mg BID (50 or 100 mg capsules) based on their individual pharmacokinetics data for up to 78 weeks. All subjects in Japan received eliglustat 50 mg once only on Day 1 and then eliglustat 50 mg BID from Day 2 titrated up to 100 mg BID (50 or 100 mg capsules) based on their individual pharmacokinetics data for up to 78 weeks.

Number of subjects in period 1	LIP, Eliglustat
Started	170
Completed	131
Not completed	39
Consent withdrawn by subject	7
Failed to Meet Randomization Criteria	25
Adverse event, non-fatal	2
Pregnancy	4

Non-Compliance With Protocol	1

Period 2

Period 2 title	PAP (up to 52 weeks)
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	PAP, Eliglustat: QD

Arm description:

All subjects who were randomized after meeting all randomization criteria (defined as: no more than 1 bone crisis and was free of other clinically symptomatic bone disease [such as bone pain attributable to osteonecrosis and/or pathological fractures) during the first 6 months of the LIP; mean hemoglobin level of ≥11 g/ dL [if female] and ≥12 g/dL [if male]; mean platelet count ≥100,000/mm^3; spleen volume ≤10 times of normal; liver volume ≤1.5 times of normal; had a dose of 50 mg BID or 100 mg BID of eliglustat for at least 4 months and a peak (2-hour) Genz-99067 plasma concentration of <50 ng/mL) after either 26, 52 or 78 weeks of LIP received eliglustat capsules at the total daily dose (TDD) of 100 mg or 200 mg (the TDD they were on before randomization) QD from Day 1 up to Week 52 in PAP (50 or 100 mg capsules).

Arm type	Experimental
Investigational medicinal product name	Eliglustat
Investigational medicinal product code	Genz--112638
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

Eliglustat at the TDD of 100 mg or 200 mg QD from Day 1 up to Week 52 in PAP (50 or 100 mg capsules).

Arm title	PAP, Eliglustat: BID

Arm description:

All subjects who were randomized after meeting all randomization criteria (defined as: no more than 1 bone crisis and was free of other clinically symptomatic bone disease [such as bone pain attributable to osteonecrosis and/or pathological fractures) during the first 6 months of the LIP; mean hemoglobin level of ≥11 g/ dL [if female] and ≥12 g/dL [if male]; mean platelet count ≥100,000/mm^3; spleen volume ≤10 times of normal; liver volume ≤1.5 times of normal; had a dose of 50 mg BID or 100 mg BID of eliglustat for at least 4 months and a peak (2-hour) Genz-99067 plasma concentration of <50 ng/mL) after either 26, 52 or 78 weeks of LIP, received eliglustat at the TDD of 100 or 200 mg (the TDD they were on before randomization) given BID from Day 1 up to Week 52 in PAP (50 or 100 mg capsules).

Arm type	Experimental
Investigational medicinal product name	Eliglustat
Investigational medicinal product code	Genz--112638
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

Eliglustat at the TDD of 100 mg or 200 mg administered as 50 mg or 100 mg capsule BID from Day 1 up to Week 52 in PAP.

Number of subjects in period 2	PAP, Eliglustat: QD	PAP, Eliglustat: BID
Started	65	66
Completed Successfully the PAP	54 [1]	60 [2]
Completed	60	61
Not completed	5	5
Consent withdrawn by subject	1	1
Pregnancy	1	-
Adverse event	2	3
Non-Compliant to Protocol	1	1

Notes:

[1] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: Six subjects in the QD arm completed the PAP, but failed (did not maintain their therapeutic goals; see Period 3, LTTP arm description) below.
[2] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: One subject in the BID arm completed the PAP, but failed (did not maintain their therapeutic goals; see Period 3, LTTP, arm description) below.

Period 3

Period 3 title	LTTP
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	LTTP, Eliglustat

Arm description:

All subjects who entered PAP continued their blinded randomized treatment for first 4 weeks. subjects who at Week 52 of PAP maintained their therapeutic goals (defined as: no more than 2 bone crisis during PAP [with no more than 1 bone crisis during either first 6 months or later 6 months of PAP] and is free of other clinically symptomatic bone disease during PAP; hemoglobin level not decreased by >1.5 g/dL from Baseline for PAP [defined as last available assessment prior to randomization]; platelet count not decreased by >25% from Baseline for PAP; spleen volume not increased by 25% from Baseline for PAP; liver volume not increased by >20% from Baseline for PAP), continued into the LTTP and received their TDD of eliglustat (100 mg or 200 mg) QD till the end of the study. The subjects who did not maintain all their therapeutic goals continued into the LTTP and received their TDD of eliglustat (100 mg or 200 mg) BID till the end of the study.

Arm type	Experimental

Investigational medicinal product name	Eliglustat
Investigational medicinal product code	Genz--112638
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

Eliglustat at the TDD of 100 mg or 200 mg QD till the end of study. Subjects who did not maintain their therapeutic goals continued into the LTTP and received their TDD of eliglustat (100 mg or 200 mg) BID till the end of the study.

Number of subjects in period 3	LTTP, Eliglustat
Started	121
Completed	95
Not completed	26
Consent withdrawn by subject	2
Transitioned to Commercial Eliglustat	18
Entered in Period, But Not Treated	1
Adverse event	3
Lost to follow-up	2

Period 4

Period 4 title	ETP
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Extended Treatment Period (ETP), Eliglustat

Arm description:

All subjects who did not meet all the randomization criteria at Week 78 of the LIP continued in the ETP and received eliglustat capsules at the same dose as they were receiving at the end of LIP till the end of the study.

Arm type	Experimental
Investigational medicinal product name	Eliglustat
Investigational medicinal product code	Genz--112638
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

Eliglustat at the dose the subjects received at the end of LIP (50 mg QD, 50 mg BID or 100 mg BID).

Number of subjects in period 4[3]	Extended Treatment Period (ETP), Eliglustat
Started	25
Completed	20
Not completed	5
Transitioned to Commercial Eliglustat	3
Pregnancy	2

Notes:

[3] - 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:
Started number includes only those subjects who failed to meet the randomization criteria during the lea d in period.

Baseline characteristics

Reporting groups	
Reporting group title	LIP, Eliglustat

Reporting group description:

All subjects (except in Japan) received eliglustat 50 mg, BID on Day 1 titrated up to 100 mg BID (50 or 100 mg capsules) based on their individual pharmacokinetics data for up to 78 weeks. All subjects in Japan received eliglustat 50 mg once only on Day 1 and then eliglustat 50 mg BID from Day 2 titrated up to 100 mg BID (50 or 100 mg capsules) based on their individual pharmacokinetics data for up to 78 weeks.

Reporting group values	LIP, Eliglustat	Total	
Number of subjects	170	170	
Age categorical Units: Subjects			

Age Continuous Units: years			
arithmetic mean	37.7		
standard deviation	± 15.1	-	
Gender, Male/Female Units: subjects			
Female	81	81	
Male	89	89	

End points

End points reporting groups

Reporting group title	LIP, Eliglustat

Reporting group description:

All subjects (except in Japan) received eliglustat 50 mg, BID on Day 1 titrated up to 100 mg BID (50 or 100 mg capsules) based on their individual pharmacokinetics data for up to 78 weeks. All subjects in Japan received eliglustat 50 mg once only on Day 1 and then eliglustat 50 mg BID from Day 2 titrated up to 100 mg BID (50 or 100 mg capsules) based on their individual pharmacokinetics data for up to 78 weeks.

Reporting group title	PAP, Eliglustat: QD

Reporting group description:

All subjects who were randomized after meeting all randomization criteria (defined as: no more than 1 bone crisis and was free of other clinically symptomatic bone disease [such as bone pain attributable to osteonecrosis and/or pathological fractures) during the first 6 months of the LIP; mean hemoglobin level of ≥11 g/ dL [if female] and ≥12 g/dL [if male]; mean platelet count ≥100,000/mm^3; spleen volume ≤10 times of normal; liver volume ≤1.5 times of normal; had a dose of 50 mg BID or 100 mg BID of eliglustat for at least 4 months and a peak (2-hour) Genz-99067 plasma concentration of <50 ng/mL) after either 26, 52 or 78 weeks of LIP received eliglustat capsules at the total daily dose (TDD) of 100 mg or 200 mg (the TDD they were on before randomization) QD from Day 1 up to Week 52 in PAP (50 or 100 mg capsules).

Reporting group title	PAP, Eliglustat: BID

Reporting group description:

All subjects who were randomized after meeting all randomization criteria (defined as: no more than 1 bone crisis and was free of other clinically symptomatic bone disease [such as bone pain attributable to osteonecrosis and/or pathological fractures) during the first 6 months of the LIP; mean hemoglobin level of ≥11 g/ dL [if female] and ≥12 g/dL [if male]; mean platelet count ≥100,000/mm^3; spleen volume ≤10 times of normal; liver volume ≤1.5 times of normal; had a dose of 50 mg BID or 100 mg BID of eliglustat for at least 4 months and a peak (2-hour) Genz-99067 plasma concentration of <50 ng/mL) after either 26, 52 or 78 weeks of LIP, received eliglustat at the TDD of 100 or 200 mg (the TDD they were on before randomization) given BID from Day 1 up to Week 52 in PAP (50 or 100 mg capsules).

Reporting group title	LTTP, Eliglustat

Reporting group description:

All subjects who entered PAP continued their blinded randomized treatment for first 4 weeks. subjects who at Week 52 of PAP maintained their therapeutic goals (defined as: no more than 2 bone crisis during PAP [with no more than 1 bone crisis during either first 6 months or later 6 months of PAP] and is free of other clinically symptomatic bone disease during PAP; hemoglobin level not decreased by >1.5 g/dL from Baseline for PAP [defined as last available assessment prior to randomization]; platelet count not decreased by >25% from Baseline for PAP; spleen volume not increased by 25% from Baseline for PAP; liver volume not increased by >20% from Baseline for PAP), continued into the LTTP and received their TDD of eliglustat (100 mg or 200 mg) QD till the end of the study. The subjects who did not maintain all their therapeutic goals continued into the LTTP and received their TDD of eliglustat (100 mg or 200 mg) BID till the end of the study.

Reporting group title	Extended Treatment Period (ETP), Eliglustat

Reporting group description:

All subjects who did not meet all the randomization criteria at Week 78 of the LIP continued in the ETP and received eliglustat capsules at the same dose as they were receiving at the end of LIP till the end of the study.

Primary: PAP: Percentage of Subjects Who Remained Stable for 52 Weeks During the PAP

End point title	PAP: Percentage of Subjects Who Remained Stable for 52 Weeks During the PAP

End point description:

Subject were considered as stable if they met the following criteria: hemoglobin level did not decrease >1.5 g/dL from baseline for PAP, platelet count does not decrease >25% below Baseline for PAP, liver volume does not increase >20% above Baseline for PAP, spleen volume does not increase >25% above Baseline for PAP. Baseline for PAP was defined as last available assessment prior to randomization.

Analysis was performed on per protocol (PP) population which included all subjects who were at least 80% compliant with investigational medicinal product (IMP) dosing during PAP, had all of the necessary Baseline and Week 52 assessments to evaluate the primary endpoint, and did not have major protocol deviations.

End point type	Primary

End point timeframe:

PAP Baseline up to the end of PAP (Week 52)

End point values	PAP, Eliglustat: QD	PAP, Eliglustat: BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	56	59		
Units: percentage of subjects				
number (confidence interval 95%)	80.4 (67.6 to 89.8)	83.1 (71 to 91.6)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	PAP, Eliglustat: QD v PAP, Eliglustat: BID
Number of subjects included in analysis	115
Analysis specification	Pre-specified
Analysis type	non-inferiority[1]
Parameter estimate	Difference in Percentage Stable
Point estimate	-2.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-17.7
upper limit	11.9

Notes:

[1] - Eliglustat QD treatment was declared non-inferior to BID treatment if the lower bound of the 95% confidence interval (CI) for the difference was within the non-inferiority margin of -0.15 (or -15%).

Secondary: PAP: Mean Hemoglobin (Hb) Level at Baseline, Weeks 26, 52

End point title	PAP: Mean Hemoglobin (Hb) Level at Baseline, Weeks 26, 52

End point description:

PP population included all subjects who were at least 80% compliant with dosing during PAP, had all of the necessary Baseline and Week 52 assessments to evaluate the primary endpoint, and did not have major protocol deviations. Here 'n' signifies number of subjects with available data at specified time points for each arm respectively.

End point type	Secondary

End point timeframe:

Baseline, Week 26 and Week 52

End point values	PAP, Eliglustat: QD	PAP, Eliglustat: BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	56	59		
Units: g/dL				
arithmetic mean (standard deviation)				
Baseline (n=56, 59)	13.641 (± 1.214)	13.691 (± 1.273)		
Week 26 (n=56, 57)	13.677 (± 1.377)	13.946 (± 1.509)		
Week 52 (n=56, 59)	13.605 (± 1.432)	13.824 (± 1.442)		

Statistical analyses

No statistical analyses for this end point

Secondary: PAP: Mean Platelet Count at Baseline, Weeks 26, 52

End point title	PAP: Mean Platelet Count at Baseline, Weeks 26, 52

End point description:

PP population included all subjects who were at least 80% compliant with dosing during PAP, had all of the necessary Baseline and Week 52
assessments to evaluate the primary endpoint, and did not have major protocol deviations. Here 'n' signifies number of subjects with available data at specified time points for each arm respectively.

End point type	Secondary

End point timeframe:

Baseline, Week 26 and Week 52

End point values	PAP, Eliglustat: QD	PAP, Eliglustat: BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	56	59		
Units: platelets*10^9 /L				
arithmetic mean (standard deviation)				
Baseline (n=56, 59)	204.01 (± 81.49)	171.09 (± 63.5)		
Week 26 (n=56, 57)	195.75 (± 66.65)	173.94 (± 65.61)		
Week 52 (n=56, 59)	207.2 (± 80.62)	176.1 (± 62.01)		

Statistical analyses

No statistical analyses for this end point

Secondary: PAP: Mean Spleen Volume at Baseline, Weeks 26, 52

End point title	PAP: Mean Spleen Volume at Baseline, Weeks 26, 52

End point description:

PP population included all subjects who were at least 80% compliant with dosing during PAP, had all of the necessary baseline and Week 52
assessments to evaluate the primary endpoint, and did not have major protocol deviations. Here 'n' signifies number of subjects with available data for specified category for each arm respectively.

End point type	Secondary

End point timeframe:

Baseline, Week 26, Week 52

End point values	PAP, Eliglustat: QD	PAP, Eliglustat: BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	56	59		
Units: MN				
arithmetic mean (standard deviation)				
Baseline (n= 39, 45)	3.309 (± 1.465)	3.787 (± 1.623)		
Week 26 (n= 39, 45)	3.066 (± 1.299)	3.504 (± 1.365)		
Week 52 (n= 39, 45)	3.017 (± 1.381)	3.394 (± 1.305)		

Statistical analyses

No statistical analyses for this end point

Secondary: PAP: Mean Liver Volume at Baseline, Weeks 26, 52

End point title	PAP: Mean Liver Volume at Baseline, Weeks 26, 52

End point description:

PP population included all subjects who were at least 80% compliant with dosing during PAP, had all of the necessary baseline and Week 52
assessments to evaluate the primary endpoint, and did not have major protocol deviations. Here, 'n' signifies number of subjects with available data for specified category for each arm respectively.

End point type	Secondary

End point timeframe:

Baseline, Week 26 and Week 52

End point values	PAP, Eliglustat: QD	PAP, Eliglustat: BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	56	59		
Units: MN				
arithmetic mean (standard deviation)				
Baseline (n=56, 59)	0.981 (± 0.187)	1.04 (± 0.198)		
Week 26 (n=56, 59)	0.987 (± 0.19)	1.024 (± 0.179)		

Week 52 (n=56, 59)	0.97 (± 0.17)	1.009 (± 0.196)		

Statistical analyses

No statistical analyses for this end point

Secondary: PAP: Mean Biomarker (Chitotriosidase) Value at Baseline, Weeks 26 and Week 52

End point title	PAP: Mean Biomarker (Chitotriosidase) Value at Baseline, Weeks 26 and Week 52

End point description:

Chitotriosidase biomarker was assayed from plasma. PP population which all subjects who were at least 80% compliant with dosing during PAP, had all of the necessary Baseline and Week 52 assessments to evaluate the primary endpoint, and did not have major protocol deviations. Here, 'n' signifies number of subjects with available data for specified category for each arm respectively.

End point type	Secondary

End point timeframe:

Baseline, Week 26, Week 52

End point values	PAP, Eliglustat: QD	PAP, Eliglustat: BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	56	59		
Units: nmol/hr/mL				
arithmetic mean (standard deviation)				
Baseline (n=55, 59)	1523.7 (± 2556.6)	1554.9 (± 1895)		
Week 26 (n=52, 54)	1279.6 (± 2328.1)	1242 (± 2012.6)		
Week 52 (n=54, 55)	1076.6 (± 1855.8)	1170.1 (± 1683.3)		

Statistical analyses

No statistical analyses for this end point

Secondary: PAP: Mean Biomarker (GL-1 on DBS) Value at Baseline, Week 26, and Week 52

End point title	PAP: Mean Biomarker (GL-1 on DBS) Value at Baseline, Week 26, and Week 52

End point description:

GL-1 on DBS biomarker was assayed from dried blood spot (DBS). PP population included all subjects who were at least 80% compliant with dosing during PAP, had all of the necessary Baseline and Week 52 assessments to evaluate the primary endpoint, and did not have major protocol deviations. Here 'n' signifies number of subjects with available data at specified time points for each arm respectively.

End point type	Secondary

End point timeframe:

Baseline, Week 26, and Week 52

End point values	PAP, Eliglustat: QD	PAP, Eliglustat: BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	56	59		
Units: mcg/mL				
arithmetic mean (standard deviation)				
GL-1 on DBS: Baseline (n=54, 55)	2.257 (± 0.835)	2.425 (± 1.378)		
GL-1 on DBS: week 26 (n=54, 54)	2.481 (± 1.037)	2.563 (± 1.1)		
GL-1 on DBS: week 52 (n=53, 55)	2.853 (± 1.383)	2.707 (± 1.443)		

Statistical analyses

No statistical analyses for this end point

Secondary: PAP: Mean Biomarker Macrophage Inflammatory Protein-1 Beta (MIP1-beta) Value at Baseline, Weeks 26, 52

End point title	PAP: Mean Biomarker Macrophage Inflammatory Protein-1 Beta (MIP1-beta) Value at Baseline, Weeks 26, 52

End point description:

MIP1-beta biomarker was assayed from plasma. PP population included all subjects who were at least 80% compliant with dosing during PAP, had all of the necessary Baseline and Week 52 assessments to evaluate the primary endpoint, and did not have major protocol deviations. Here, 'n' signifies number of subjects with available data for specified category for each arm respectively.

End point type	Secondary

End point timeframe:

Baseline, Week 26, Week 52

End point values	PAP, Eliglustat: QD	PAP, Eliglustat: BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	56	59		
Units: pg/mL				
arithmetic mean (standard deviation)				
Baseline (n=54, 58)	77.7 (± 74.4)	118.8 (± 156.3)		
Week 26 (n=52, 54)	74.5 (± 68)	121 (± 204.4)		
Week 52 (n=54, 55)	81.3 (± 82.8)	117.9 (± 165.3)		

Statistical analyses

No statistical analyses for this end point

Secondary: PAP: Bone Mineral Density (BMD) at Baseline and Week 52: PP Population

End point title	PAP: Bone Mineral Density (BMD) at Baseline and Week 52: PP Population

End point description:

BMD measurements of the spine and bilateral femur were acquired by dual-energy x-ray absorptiometry (DXA) scan. PP population included all subjects who were at least 80% compliant with dosing during PAP, had all of the necessary Baseline and Week 52 assessments to evaluate the primary endpoint, and did not have major protocol deviations. Here, 'n' signifies number of subjects with available data at specified time points for each arm respectively.

End point type	Secondary

End point timeframe:

Baseline, Week 52

End point values	PAP, Eliglustat: QD	PAP, Eliglustat: BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	56	59		
Units: g/cm^2				
arithmetic mean (standard deviation)				
Lumbar Spine: Baseline (n=51, 55)	1.073 (± 0.177)	1.081 (± 0.172)		
Lumbar Spine: Week 52 (n=51, 55)	1.089 (± 0.183)	1.086 (± 0.177)		
Left Femur: Baseline (n=48, 47)	0.979 (± 0.219)	1 (± 0.199)		
Left Femur: Week 52 (n=48, 47)	0.972 (± 0.211)	0.99 (± 0.196)		
Right Femur: Baseline (n=48, 47)	0.971 (± 0.217)	0.996 (± 0.184)		
Right Femur: Week 52 (n=48, 47)	0.967 (± 0.213)	0.981 (± 0.177)		

Statistical analyses

No statistical analyses for this end point

Secondary: PAP: Total T-Scores for BMD at Baseline and Week 52

End point title	PAP: Total T-Scores for BMD at Baseline and Week 52

End point description:

Images of the spine and bilateral femur were obtained by DXA to determine T-score for each bone area and total bone mineral density. The T-score bone density categories were: normal (score >-1), osteopenia (score -2.5 to <=-1), and osteoporosis (score <= -2.5). PP population included all subjects who were at least 80% compliant with dosing during PAP, had all of the necessary Baseline and Week 52 assessments to evaluate the primary endpoint, and did not have major protocol deviations. Here 'n' signifies number of subjects with available data at specified time points for each arm respectively.

End point type	Secondary

End point timeframe:

Baseline, Week 52

End point values	PAP, Eliglustat: QD	PAP, Eliglustat: BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	56	59		
Units: T-score				
arithmetic mean (standard deviation)				
Lumbar Spine T-Score: Baseline (n=49, 52)	-0.722 (± 1.415)	-0.771 (± 1.217)		
Lumbar Spine T-Score: Week 52 (n=49, 52)	-0.58 (± 1.476)	-0.717 (± 1.271)		
Left Femur T-Score: Baseline (n=46, 44)	-0.459 (± 1.385)	-0.368 (± 1.347)		
Left Femur T-Score: Week 52 (n=46, 44)	-0.509 (± 1.342)	-0.441 (± 1.326)		
Right Femur T-score: Baseline (n=46, 44)	-0.574 (± 1.327)	-0.382 (± 1.282)		
Right Femur T-score: Week 52 (n=46, 44)	-0.607 (± 1.308)	-0.53 (± 1.236)		

Statistical analyses

No statistical analyses for this end point

Secondary: PAP: Total Z-scores for BMD at Baseline and Week 52

End point title	PAP: Total Z-scores for BMD at Baseline and Week 52

End point description:

Images of the spine and bilateral femur were obtained by DXA to determine Z-score for each bone area and total bone mineral density. The Z-score bone density categories are: normal (score >-2) and below normal (score <=-2). PP population included all subjects who were at least 80% compliant with dosing during PAP, had all of the necessary Baseline and Week 52 assessments to evaluate the primary endpoint, and did not have major protocol deviations. Here 'n' signifies number of subjects with available data for specified category for each arm respectively.

End point type	Secondary

End point timeframe:

Baseline, Week 52

End point values	PAP, Eliglustat: QD	PAP, Eliglustat: BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	56	59		
Units: Z-score				
arithmetic mean (standard deviation)				
Lumbar Spine Z-scores: Baseline (n=51, 55)	-0.492 (± 1.517)	-0.609 (± 1.166)		

Lumbar Spine Z-scores: Week 52 (n=51, 55)	-0.324 (± 1.559)	-0.555 (± 1.202)		
Left Femur Z-scores: Baseline (n= 48, 47)	-0.171 (± 1.316)	-0.115 (± 1.294)		
Left Femur Z-scores: Week 52 (n= 48, 47)	-0.202 (± 1.25)	-0.183 (± 1.274)		
Right Femur Z-scores: Baseline (n= 48, 47)	-0.235 (± 1.251)	-0.14 (± 1.194)		
Right Femur Z-scores: Week 52 (n= 48, 47)	-0.248 (± 1.214)	-0.26 (± 1.141)		

Statistical analyses

No statistical analyses for this end point

Secondary: PAP: Number of Subjects With Mobility Status (MS) at Baseline, Weeks 26, and 52

End point title	PAP: Number of Subjects With Mobility Status (MS) at Baseline, Weeks 26, and 52

End point description:

Mobility, i.e., ability to walk was assessed as a part of gaucher disease assessment in subjects. In this endpoint, number of subjects with their different mobility status along with the use of mobility aids (unrestricted mobility, walks with difficulty, walks with orthopaedic aid, requires wheelchair, bedridden) at specified time points were reported. PP population included all subjects who were at least 80% compliant with dosing during PAP, had all of the necessary Baseline and Week 52 assessments to evaluate the primary endpoint, and did not have major protocol deviations. Here 'n' signifies number of subjects with available data at specified time points for each arm respectively.

End point type	Secondary

End point timeframe:

Baseline, Week 26 and Week 52

End point values	PAP, Eliglustat: QD	PAP, Eliglustat: BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	56	59		
Units: subjects				
number (not applicable)				
MS, Unrestricted: Baseline (n=56, 59)	49	59		
MS, Unrestricted: Week 26 (n=55, 57)	46	56		
MS, Unrestricted: Week 52 (n=51, 58)	50	57		
MS, Walks with Difficulty: Baseline (n=56, 59)	6	0		
MS, Walks with Difficulty: Week 26 (n=55, 57)	8	1		
MS, Walks with Difficulty: Week 52 (n=51, 58)	5	1		
MS, Walks with Orthopedic Aid: Baseline (n=56, 59)	1	0		
MS, Walks with Orthopedic Aid: Week 26 (n=55,	1	0		
MS, Walks with Orthopedic Aid: Week 52 (n=51, 58)	0	0		

MS, Required Wheelchair: Baseline (n=56, 59)	0	0		
MS, Required Wheelchair: Week 26 (n=55, 57)	0	0		
MS, Required Wheelchair: Week 52 (n=51, 58)	1	0		
MS, Bedridden: Baseline (n=56, 59)	0	0		
MS, Bedridden: Week 26 (n=55, 57)	0	0		
MS, Bedridden: Week 52 (n=51, 58)	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: PAP: Number of Subjects With Bone Crises Assessment at Baseline, Weeks 26, and 52

End point title	PAP: Number of Subjects With Bone Crises Assessment at Baseline, Weeks 26, and 52

End point description:

Bone crises was assessed as a part of gaucher disease assessment in subjects. Acute, excruciating episodic bone pain is characteristic of Gaucher bone crises, which typically causes debilitation lasting several days or longer and requires treatment with immobilization, hydration, and opioid analgesics. Subjects were categorized as 0= no bone crises, 1= 1 bone crises, 2= 2 bone crises during the assessment period. In this endpoint, number of subjects with different bone crises levels at specified time points were reported. PP population included all subjects who were at least 80% compliant with dosing during PAP, had all of the necessary Baseline and Week 52 assessments to evaluate the primary endpoint, and did not have major protocol deviations. Here 'n' signifies number of subjects with available data at specified time points for each arm respectively.

End point type	Secondary

End point timeframe:

Baseline, Week 26, and Week 52

End point values	PAP, Eliglustat: QD	PAP, Eliglustat: BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	56	59		
Units: subjects				
number (not applicable)				
Bone Crisis (0): Baseline (n=56, 59)	55	57		
Bone Crisis (0): Week 26 (n=55,57)	54	56		
Bone Crisis (0): Week 52 (n=56, 58)	56	57		
Bone Crisis (1): Baseline (n=56, 59)	1	2		
Bone Crisis (1): Week 26 (n=55, 57)	0	1		
Bone Crisis (1): Week 52 (n=56, 58)	0	1		
Bone Crisis (2): Baseline (n=56, 59)	0	0		
Bone Crisis (2): week 26 (n=55, 57)	1	0		
Bone Crisis (2): week 52 (n=56, 58)	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: PAP: Number of Subjects With Bone Pain Levels During the Past 4 Weeks at Baseline, Weeks 26 and Week 52

End point title	PAP: Number of Subjects With Bone Pain Levels During the Past 4 Weeks at Baseline, Weeks 26 and Week 52

End point description:

Bone pain was assessed as a part of gaucher disease assessment in subjects. Subjects were categorized as none (no bone pain), very mild bone pain, mild bone pain, moderate bone pain, severe bone pain and extreme bone pain. In this endpoint, number of subjects with different level of bone pain during the past 4 weeks at specified time points were reported. PP population included all subjects who were at least 80% compliant with dosing during PAP, had all of the necessary Baseline and Week 52 assessments to evaluate the primary endpoint, and did not have major protocol deviations. Here 'n' signifies number of subjects with available data at specified time points for each arm respectively.

End point type	Secondary

End point timeframe:

Baseline, Week 26, and Week 52

End point values	PAP, Eliglustat: QD	PAP, Eliglustat: BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	56	59		
Units: subjects				
number (not applicable)				
None: Baseline (n=56, 59)	42	49		
None: Week 26 (n=55, 57)	42	49		
None: Week 52 (n=56, 58)	41	45		
Very Mild: Baseline (n=56, 59)	2	1		
Very Mild: Week 26 (n=55, 57)	3	4		
Very Mild: Week 52 (n=56, 58)	3	7		
Mild: Baseline (n=56, 59)	7	3		
Mild: Week 26 (n=55, 57)	5	3		
Mild: Week 52 (n=56, 58)	6	2		
Moderate: Baseline (n=56, 59)	4	5		
Moderate: Week 26 (n=55, 57)	5	1		
Moderate: Week 52 (56, 58)	6	2		
Severe: Baseline (n=56, 59)	1	1		
Severe: Week 26 (n=55, 57)	0	0		
Severe: Week 52 (n=56, 58)	0	2		
Extreme: Baseline (n=56, 59)	0	0		
Extreme: Week 26 (n=55, 57)	0	0		
Extreme: Week 52 (n=56, 58)	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: PAP: Total Bone Marrow Burden Score (BMB) at Baseline and 52 weeks

End point title	PAP: Total Bone Marrow Burden Score (BMB) at Baseline and 52 weeks

End point description:

BMB Score was measured using magnetic resonance imaging (MRI), range from 0 (no abnormalities) to 8 points (severe disease) for the lumbar spine and from 0 (no abnormalities) to 8 points (severe disease) for the femurs. The total score was calculated as the sum of scores for femur and lumbar spine regions which ranged from 0 (no abnormalities) -16 (severe disease) points. A higher BMB score signified more severe bone marrow involvement. A higher BMB score signified more severe bone marrow involvement. PP population included all subjects who were at least 80% compliant with dosing during PAP, had all of the necessary Baseline and Week 52 assessments to evaluate the primary endpoint, and did not have major protocol deviations. Here, 'n' signifies number of subjects with available data at specified time points for each arm respectively.

End point type	Secondary

End point timeframe:

Baseline, Week 52

End point values	PAP, Eliglustat: QD	PAP, Eliglustat: BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	56	59		
Units: BMB Score				
arithmetic mean (standard deviation)				
BMB Score: Baseline (n=52, 49)	8.276 (± 2.891)	9.136 (± 2.784)		
BMB Score: week 52 (n=51, 48)	7.971 (± 2.689)	8.705 (± 2.633)		

Statistical analyses

No statistical analyses for this end point

Secondary: LIP: Mean Hemoglobin (Hb) Level at Baseline, Weeks 26, 52 and 78

End point title	LIP: Mean Hemoglobin (Hb) Level at Baseline, Weeks 26, 52 and 78

End point description:

Analysis was performed on all treated (AT) analysis set which included all subjects who received at least 1 dose of eliglustat during lead in period. Here 'n' signifies number of subjects with available data at specified time points.

End point type	Secondary

End point timeframe:

Baseline, Week 26, Week, 52, and Week 78

End point values	LIP, Eliglustat			
Subject group type	Reporting group			
Number of subjects analysed	170			
Units: g/dL				
arithmetic mean (standard deviation)				
Baseline (n=170)	13.435 (± 1.56)			
Week 26 (n=163)	13.443 (± 1.382)			
Week 52 (n=74)	13.434 (± 1.497)			
Week 78 (n=41)	13.329 (± 1.528)			

Statistical analyses

No statistical analyses for this end point

Secondary: LIP: Mean Platelet Count at Baseline, Weeks 26, 52 and 78

End point title	LIP: Mean Platelet Count at Baseline, Weeks 26, 52 and 78

End point description:

Analysis was performed on AT analysis set which included all subjects who received at least 1 dose of eliglustat during LIP. Here 'n' signifies number of subjects with available data at specified time points.

End point type	Secondary

End point timeframe:

Baseline, Week 26, Week 52, Week 78

End point values	LIP, Eliglustat			
Subject group type	Reporting group			
Number of subjects analysed	170			
Units: platelets*10^9 /L				
arithmetic mean (standard deviation)				
Baseline (n=170)	178.653 (± 92.732)			
Week 26 (n=163)	180.021 (± 85.426)			
Week 52 (n=74)	176.378 (± 79.88)			
Week 78 (n=41)	168.72 (± 74.117)			

Statistical analyses

No statistical analyses for this end point

Secondary: LIP: Mean Liver Volume at Baseline, Weeks 26, 52 and 78

End point title	LIP: Mean Liver Volume at Baseline, Weeks 26, 52 and 78

End point description:

Analysis was performed on AT subjects which included all subjects who received at least 1 dose of eliglustat during lead in period. Here, 'n' signifies number of subjects with available data at specified time points.

End point type	Secondary

End point timeframe:

Baseline, Week 26, Week 52, Week 78

End point values	LIP, Eliglustat			
Subject group type	Reporting group			
Number of subjects analysed	170			
Units: MN				
arithmetic mean (standard deviation)				
Baseline (n=170)	1.044 (± 0.243)			
Week 26 (n=149)	1.04 (± 0.229)			
Week 52 (n=68)	1.059 (± 0.242)			
Week 78 (n=39)	1.062 (± 0.236)			

Statistical analyses

No statistical analyses for this end point

Secondary: LIP: Mean Spleen Volume at Baseline, Weeks 26, 52 and 78

End point title	LIP: Mean Spleen Volume at Baseline, Weeks 26, 52 and 78

End point description:

Analysis was performed on AT subjects which included all subjects who received at least 1 dose of eliglustat during lead in period. Here 'n' signifies number of subjects with available data at specified time points for each arm respectively.

End point type	Secondary

End point timeframe:

Baseline, Week 26, Week 52, Week 78

End point values	LIP, Eliglustat			
Subject group type	Reporting group			
Number of subjects analysed	170			
Units: multiples of normal (MN)				
arithmetic mean (standard deviation)				
Baseline (n=119)	4.448 (± 2.314)			
Week 26 (n=106)	3.84 (± 1.801)			
Week 52 (n=52)	4.094 (± 1.767)			

Week 78 (n=30)	4.088 (± 2.089)			

Statistical analyses

No statistical analyses for this end point

Secondary: LIP: Mean Biomarker (Chitotriosidase) Value at Baseline, Weeks 26, 52, and 78

End point title	LIP: Mean Biomarker (Chitotriosidase) Value at Baseline, Weeks 26, 52, and 78

End point description:

Chitotriosidase biomarker was assayed from plasma. Analysis was performed on AT analysis set which included all subjects who received at least 1 dose of eliglustat during LIP. Here 'n' signifies number of subjects with available data at specified time points.

End point type	Secondary

End point timeframe:

Baseline, Week 26, Week 52, and Week 78

End point values	LIP, Eliglustat			
Subject group type	Reporting group			
Number of subjects analysed	170			
Units: nmol/hr/mL				
arithmetic mean (standard deviation)				
Chitotriosidase: Baseline (n=170)	2437.92 (± 3291.25)			
Chitotriosidase: week 26 (n=157)	1802.93 (± 2529.29)			
Chitotriosidase: week 52 (n=72)	1755.7 (± 2649.14)			
Chitotriosidase: week 78 (n=41)	1677.02 (± 2718.75)			

Statistical analyses

No statistical analyses for this end point

Secondary: LIP: Mean Biomarker (GL-1 on DBS) Value at Baseline, week 26, week 52, and week 78

End point title	LIP: Mean Biomarker (GL-1 on DBS) Value at Baseline, week 26, week 52, and week 78

End point description:

GL-1 on DBS biomarker was assayed from dried blood spot. Analysis was performed on AT analysis set which included all subjects who received at least 1 dose of eliglustat during LIP. Here 'n' signifies number of subjects with available data at specified time points.

End point type	Secondary

End point timeframe:

Baseline, Week 26, Week 52, and Week 78

End point values	LIP, Eliglustat			
Subject group type	Reporting group			
Number of subjects analysed	170			
Units: mcg/mL				
arithmetic mean (standard deviation)				
GL-1 on DBS: Baseline (n=159)	4.358 (± 2.155)			
GL-1 on DBS: week 26 (n=144)	2.34 (± 0.868)			
GL-1 on DBS: week 52 (n=68)	2.279 (± 0.73)			
GL-1 on DBS: week 78 (n=39)	2.495 (± 1.5)			

Statistical analyses

No statistical analyses for this end point

Secondary: LIP: Mean Biomarker (MIP1-beta) Value at Baseline, Week 78

End point title	LIP: Mean Biomarker (MIP1-beta) Value at Baseline, Week 78

End point description:

MIP1-beta biomarker was assayed from plasma. Analysis was performed on AT analysis set which included all subjects who received at least 1 dose of eliglustat during LIP. Here 'n' signifies number of subjects with available data at specified time points.

End point type	Secondary

End point timeframe:

Baseline, and week 78

End point values	LIP, Eliglustat			
Subject group type	Reporting group			
Number of subjects analysed	170			
Units: pg/mL				
arithmetic mean (standard deviation)				
MIP-1beta: Baseline (n=170)	142.433 (± 125.961)			
MIP-1beta: 78 weeks (n=41)	132.18 (± 189.454)			

Statistical analyses

No statistical analyses for this end point

Secondary: LIP: Number of Subjects With Mobility Status (MS) at Baseline, Weeks 26, 52 and 78

End point title	LIP: Number of Subjects With Mobility Status (MS) at Baseline, Weeks 26, 52 and 78

End point description:

Mobility, i.e., ability to walk was assessed as a part of gaucher disease assessment in subjects. In this endpoint, number of subjects with their different mobility status along with the use of mobility aids (unrestricted mobility, walks with difficulty, walks with orthopaedic aid, requires wheelchair, bedridden) at specified time points were reported. Analysis was performed on AT analysis set which included all subjects who received at least 1 dose of eliglustat during LIP. Here, 'n' signifies number of subjects with available data at specified time points.

End point type	Secondary

End point timeframe:

Baseline, Week 26, Week 52, Week 78

End point values	LIP, Eliglustat			
Subject group type	Reporting group			
Number of subjects analysed	170			
Units: subjects				
number (not applicable)				
MS,Unrestricted: Baseline (n=163)	146			
MS,Unrestricted: Week 26 (n=161)	153			
MS,Unrestricted: Week 52 (n=72)	70			
MS,Unrestricted: Week 78 (n= 41)	39			
MS, Walks With Difficulty: Baseline (n=163)	12			
MS, Walks With Difficulty: Week 26 (n=161)	6			
MS, Walks With Difficulty: Week 52 (n=72)	1			
MS, Walks With Difficulty: Week 78 (n=41)	2			
MS, Walks With Orthopedic Aid: Baseline (n=163)	3			
MS, Walks With Orthopedic Aid: Week 26 (n=161)	1			
MS, Walks With Orthopedic Aid: Week 52 (n=72)	0			
MS, Walks With Orthopedic Aid: Week 78 (n=41)	0			
MS, Required wheelchair: Baseline (n=163)	2			
MS, Required wheelchair: Week 26 (n=161)	1			
MS, Required wheelchair: Week 52 (n=72)	1			
MS, Required wheelchair: Week 78 (n=41)	0			
MS, Bedridden: Baseline (n=163)	0			
MS, Bedridden: Week 26 (n=161)	0			
MS, Bedridden: Week 52 (n=72)	0			
MS, Bedridden: Week 78 (n=41)	0			

Statistical analyses

No statistical analyses for this end point

Secondary: LIP: Number of Subjects With Bone Crises Assessment at Baseline, Weeks 26, 52 and 78

End point title	LIP: Number of Subjects With Bone Crises Assessment at Baseline, Weeks 26, 52 and 78

End point description:

Bone crises was assessed as a part of gaucher disease assessment in subjects. Acute, excruciating episodic bone pain is characteristic of Gaucher bone crises, which typically causes debilitation lasting several days or longer and requires treatment with immobilization, hydration, and opioid analgesics. Subjects were categorized as 0= no bone crises, 1= 1 bone crises, 2= 2 bone crises, 6= 6 bone crises, 24= 24 bone crises during the assessment period. In this endpoint, number of subjects with different bone crises levels at specified time points were reported. Analysis was performed on AT analysis set which included all subjects who received at least 1 dose of eliglustat during LIP. Here, 'n' signifies number of subjects with available data at specified time points.

End point type	Secondary

End point timeframe:

Baseline, Week 26, Week 52, Week 78

End point values	LIP, Eliglustat			
Subject group type	Reporting group			
Number of subjects analysed	170			
Units: subjects				
number (not applicable)				
Bone Crisis (0): Baseline (n=162)	151			
Bone Crisis (0): Week 26 (n=162)	159			
Bone Crisis (0): Week 52 (n=72)	72			
Bone Crisis (0): Week 78 (n=41)	41			
Bone Crisis (1): Baseline (n=162)	8			
Bone Crisis (1): Week 26 (n=162)	3			
Bone Crisis (1): Week 52 (n=72)	0			
Bone Crisis (1): Week 78 (n=41)	0			
Bone Crisis (2): Baseline (n=162)	1			
Bone Crisis (2): Week 26 (n=162)	0			
Bone Crisis (2): Week 52 (n=72)	0			
Bone Crisis (2): Week 78 (n=41)	0			
Bone Crisis (6): Baseline (n=162)	1			
Bone Crisis (6): Week 26 (n=162)	0			
Bone Crisis (6): Week 52 (n=72)	0			
Bone Crisis (6): Week 78 (n=41)	0			
Bone Crisis (24): Baseline (n=162)	1			
Bone Crisis (24): Week 26 (n=162)	0			

Bone Crisis (24): Week 52 (n=72)	0			
Bone Crisis (24): Week 78 (n=41)	0			

Statistical analyses

No statistical analyses for this end point

Secondary: LIP: Number of Subjects With Bone Pain Levels During the Past 4 Weeks at Baseline, Weeks 26, 52 and 78

End point title	LIP: Number of Subjects With Bone Pain Levels During the Past 4 Weeks at Baseline, Weeks 26, 52 and 78

End point description:

Bone pain was assessed as a part of gaucher disease assessment in subjects. Subjects were categorized as none (no bone pain), very mild bone pain, mild bone pain, moderate bone pain, severe bone pain and extreme bone pain. In this endpoint, number of subjects with different type of bone pain during the past 4 weeks at specified time points were reported. Analysis was performed on AT analysis set which included all subjects who received at least 1 dose of eliglustat during LIP. Here, 'n' signifies number of subjects with available data at specified time points.

End point type	Secondary

End point timeframe:

Baseline, Week 26, Week 52, Week 78

End point values	LIP, Eliglustat			
Subject group type	Reporting group			
Number of subjects analysed	170			
Units: subjects				
number (not applicable)				
None: Baseline (n=163)	112			
None: Week 26 (n=161)	125			
None: Week 52 (n=72)	62			
None: Week 78 (n=41)	39			
Very Mild: Baseline (n=163)	17			
Very Mild: Week 26 (n=161)	14			
Very Mild: Week 52 (n=72)	4			
Very Mild: Week 78 (n=41)	1			
Mild: Baseline (n=163)	22			
Mild: Week 26 (n=161)	10			
Mild: Week 52 (n=72)	3			
Mild: Week 78 (n=41)	0			
Moderate: Baseline (n=163)	8			
Moderate: Week 26 (n=161)	10			
Moderate: Week 52 (n=72)	3			
Moderate: Week 78 (n=41)	1			
Severe: Baseline (n=163)	4			
Severe: Week 26 (n=161)	2			
Severe: Week 52 (n=72)	0			
Severe: Week 78 (n=41)	0			

Extreme: Baseline (n=163)	0			
Extreme: Week 26 (n=161)	0			
Extreme: Week 52 (n=72)	0			
Extreme: Week 78 (n=41)	0			

Statistical analyses

No statistical analyses for this end point

Secondary: LTTP: Percentage of Subjects who Maintained a Stable Bone Criterion, Hemoglobin Level, Platelet Count, Liver Volume and Spleen Volume at 1 Year and 2 Years

End point title	LTTP: Percentage of Subjects who Maintained a Stable Bone Criterion, Hemoglobin Level, Platelet Count, Liver Volume and Spleen Volume at 1 Year and 2 Years

End point description:

Subjects were considered as stable if they met the following criteria: hemoglobin level did not decrease >1.5 g/dL from baseline for PAP, platelet count does not decrease >25% below Baseline for PAP, liver volume does not increase >20% above Baseline for PAP, spleen volume does not increase >25% above Baseline for PAP. Baseline for PAP was defined as last available assessment prior to randomization. Analysis was performed on ITT population which included all subjects who received at least 1 dose of eliglustat after randomization. Here 'n' signifies number of subjects with available data at specified time points.

End point type	Secondary

End point timeframe:

1 Year, 2 Years

End point values	LTTP, Eliglustat			
Subject group type	Reporting group			
Number of subjects analysed	121			
Units: percentage of subjects				
number (confidence interval 95%)				
Bone Criterion Stable at 1 year (n=104)	92.3 (85.4 to 96.6)			
Bone Criterion Stable at 2 years (n=32)	84.4 (67.2 to 94.7)			
Hemoglobin Level Stable at 1 year (n=104)	92.3 (85.4 to 96.6)			
Hemoglobin Level Stable at 2 years (n=32)	81.3 (63.6 to 92.8)			
Platelet Count Stable at 1 year (n=104)	93.3 (86.6 to 97.3)			
Platelet Count Stable at 2 years (n=32)	84.4 (67.2 to 94.7)			
Liver Volume Stable at 1 year (n=103)	93.2 (86.5 to 97.2)			
Liver Volume Stable at 2 years (n=31)	83.9 (66.3 to 94.5)			
Spleen Volume Stable at 1 year (n=72)	95.8 (88.3 to 99.1)			
Spleen Volume Stable at 2 years (n=20)	95 (75.1 to 99.9)			

Statistical analyses

No statistical analyses for this end point

Secondary: LTTP: Number of Subjects With Mobility Status (MS) at Baseline, 1 year, and 2 years

End point title	LTTP: Number of Subjects With Mobility Status (MS) at Baseline, 1 year, and 2 years

End point description:

Mobility, i.e., ability to walk was assessed as a part of gaucher disease assessment in subjects. In this endpoint, number of subjects with their different mobility status along with the use of mobility aids (unrestricted mobility, walks with difficulty, walks with orthopaedic aid, requires wheelchair, bedridden) at specified time points were reported. Analysis was performed on all subjects who received at least one dose of eliglustat during the LTTP. Here, "n" signifies number of subjects with available data at specified time points.

End point type	Secondary

End point timeframe:

Baseline, 1 year, and 2 years

End point values	LTTP, Eliglustat			
Subject group type	Reporting group			
Number of subjects analysed	121			
Units: subjects				
number (not applicable)				
MS, Unrestricted: Baseline (n=120)	111			
MS, Unrestricted: 1 year (n=104)	97			
MS, Unrestricted: 2 years (n=32)	28			
MS, Walks with Difficulty: Baseline (n=120)	7			
MS, Walks with Difficulty: 1 year (n=104)	4			
MS, Walks with Difficulty: 2 years (n=32)	2			
MS, Walks with Orthopedic Aid: Baseline (n=120)	0			
MS, Walks with Orthopedic Aid: 1 year (n=104)	1			
MS, Walks with Orthopedic Aid: 2 years (n=32)	0			
MS, Required Wheelchair: Baseline (n=120)	2			
MS, Required Wheelchair: 1 year (n=104)	2			
MS, Required Wheelchair: 2 years (n=32)	2			
MS, Bedridden: Baseline (n=120)	0			
MS, Bedridden: 1 year (n=104)	0			

MS, Bedridden: 2 years (n=32)	0			

Statistical analyses

No statistical analyses for this end point

Secondary: LTTP: Number of Subjects With Bone Crises Assessment at Baseline, 1 year, and 2 years

End point title	LTTP: Number of Subjects With Bone Crises Assessment at Baseline, 1 year, and 2 years

End point description:

Bone crises was assessed as a part of gaucher disease assessment in subjects. Acute, excruciating episodic bone pain is characteristic of Gaucher bone crises, which typically causes debilitation lasting several days or longer and requires treatment with immobilization, hydration, and opioid analgesics. Subjects were categorized as 0= no bone crises, 1= 1 bone crises during the assessment period. In this endpoint, number of subjects with different bone crises levels at specified time points were reported. Analysis was performed on all subjects who received at least one dose of eliglustat during the LTTP. Here, "n" signifies number of subjects with available data at specified time points.

End point type	Secondary

End point timeframe:

Baseline, 1 year, and 2 years

End point values	LTTP, Eliglustat			
Subject group type	Reporting group			
Number of subjects analysed	121			
Units: subjects				
number (not applicable)				
Bone Crisis (0): Baseline (n=120)	119			
Bone Crisis (0): 1 year (n=104)	104			
Bone Crisis (0): 2 years (n=32)	32			
Bone Crisis (1): Baseline (n=120)	1			
Bone Crisis (1): 1 year (n=104)	0			
Bone Crisis (1): 2 years (n=32)	0			

Statistical analyses

No statistical analyses for this end point

Secondary: LTTP: Number of Subjects With Bone Pain Levels During the Past 4 Weeks at Baseline, 1 year, and 2 years

End point title	LTTP: Number of Subjects With Bone Pain Levels During the Past 4 Weeks at Baseline, 1 year, and 2 years

End point description:

Bone pain was assessed as a part of gaucher disease assessment in subjects. Subjects were categorized

as none (no bone pain), very mild bone pain, mild bone pain, moderate bone pain, severe bone pain and extreme bone pain. In this endpoint, number of subjects with different type of bone pain during the past 4 weeks at specified time points were reported. Analysis was performed on all subjects who received at least one dose of eliglustat during the LTTP. Here, "n" signifies number of subjects with available data at specified time points.

End point type	Secondary

End point timeframe:

Baseline, 1 year, and 2 years

End point values	LTTP, Eliglustat			
Subject group type	Reporting group			
Number of subjects analysed	121			
Units: subjects				
number (not applicable)				
None: Baseline (n=120)	91			
None: 1 year (n=104)	83			
None: 2 years (n=32)	32			
Very Mild: Baseline (n=120)	12			
Very Mild: 1 year (n=104)	9			
Very Mild: 2 years (n=32)	0			
Mild: Baseline (n=120)	8			
Mild: 1 year (n=104)	10			
Mild: 2 years (n=32)	0			
Moderate: Baseline (n=120)	7			
Moderate: 1 year (n=104)	1			
Moderate: 2 years (n=32)	0			
Severe: Baseline (n=120)	2			
Severe: 1 year (n=104)	0			
Severe: 2 years (n=32)	0			
Extreme: Baseline (n=120)	0			
Extreme: 1 year (n=104)	1			
Extreme: 2 years (n=32)	0			

Statistical analyses

No statistical analyses for this end point

Secondary: LTTP: Bone Mineral Density (BMD) at Baseline, 1 year, and 2 years

End point title	LTTP: Bone Mineral Density (BMD) at Baseline, 1 year, and 2 years

End point description:

BMD measurements of the spine and bilateral femur were acquired by dual-energy x-ray absorptiometry (DXA) scan. Analysis was performed on all subjects who received at least one dose of eliglustat during the LTTP. Here, "n" signifies number of subjects with available data at specified time points.

End point type	Secondary

End point timeframe:

Baseline, 1 year, and 2 years

End point values	LTTP, Eliglustat			
Subject group type	Reporting group			
Number of subjects analysed	121			
Units: g/cm^2				
arithmetic mean (standard deviation)				
Lumbar Spine: Baseline (n=113)	1.087 (± 0.182)			
Lumbar Spine: 1 year (n=101)	1.083 (± 0.183)			
Lumbar Spine: 2 years (n=26)	1.082 (± 0.19)			
Left Femur: Baseline (n=107)	0.986 (± 0.205)			
Left Femur: 1 year (n=95)	0.994 (± 0.226)			
Left Femur: 2 years (n=22)	0.95 (± 0.22)			
Right Femur: Baseline (n=103)	0.983 (± 0.201)			
Right Femur: 1 year (n=91)	0.979 (± 0.202)			
Right Femur: 2 years (n=21)	0.908 (± 0.131)			

Statistical analyses

No statistical analyses for this end point

Secondary: LTTP: Total T-Scores for BMD at Baseline, 1 year, and 2 years

End point title	LTTP: Total T-Scores for BMD at Baseline, 1 year, and 2 years

End point description:

Images of the spine and bilateral femur were obtained by DXA to determine T-score for each bone area and total bone mineral density. The T-score bone density categories were: normal (score >-1), osteopenia (score -2.5 to <=-1), and osteoporosis (score <= -2.5). Analysis was performed on all subjects who received at least one dose of eliglustat during the LTTP. Here, "n" signifies number of subjects with available data at specified time points.

End point type	Secondary

End point timeframe:

Baseline, 1 year, and 2 years

End point values	LTTP, Eliglustat			
Subject group type	Reporting group			
Number of subjects analysed	121			
Units: T-score				
arithmetic mean (standard deviation)				
Lumbar Spine T-Score: Baseline (n=110)	-0.674 (± 1.383)			

Lumbar Spine T-Score: 1 year (n=98)	-0.718 (± 1.394)			
Lumbar Spine T-Score: 2 years (n=26)	-0.75 (± 1.37)			
Left Femur T-Score: Baseline (n=103)	-0.421 (± 1.377)			
Left Femur T-Score: 1 year (n=91)	-0.382 (± 1.551)			
Left Femur T-Score: 2 years (n=22)	-0.682 (± 1.532)			
Right Femur T-Score: Baseline (n=99)	-0.461 (± 1.36)			
Right Femur T-Score: 1 year (n=87)	-0.5 (± 1.381)			
Right Femur T-Score: 2 years (n=21)	-1.005 (± 0.931)			

Statistical analyses

No statistical analyses for this end point

Secondary: LTTP: Total Z-scores for BMD at Baseline, 1 year, and 2 years

End point title	LTTP: Total Z-scores for BMD at Baseline, 1 year, and 2 years

End point description:

Images of the spine and bilateral femur were obtained by DXA to determine Z-score for each bone area and total bone mineral density. The Z-score bone density categories are: normal (score >-2) and below normal (score <=-2). Analysis was performed on all subjects who received at least one dose of eliglustat during the LTTP. Here, "n" signifies number of subjects with available data at specified time points.

End point type	Secondary

End point timeframe:

Baseline, 1 year, and 2 years

End point values	LTTP, Eliglustat			
Subject group type	Reporting group			
Number of subjects analysed	121			
Units: Z-score				
arithmetic mean (standard deviation)				
Lumbar Spine Z-Score: Baseline (n=113)	0.46 (± 1.376)			
Lumbar Spine Z-Score: 1 year (n=101)	0.512 (± 1.368)			
Lumbar Spine Z-Score: 2 years (n=26)	0.385 (± 1.316)			
Left Femur Z-Score: Baseline (n=107)	0.164 (± 1.277)			
Left Femur Z-Score: 1 year (n=95)	0.132 (± 1.459)			
Left Femur Z-Score: 2 years (n=22)	0.264 (± 1.525)			
Right Femur Z-Score: Baseline (n=103)	0.214 (± 1.227)			
Right Femur Z-Score: 1 year (n=91)	0.262 (± 1.27)			

Right Femur Z-Score: 2 years (n=21)	0.605 (± 0.957)			

Statistical analyses

No statistical analyses for this end point

Secondary: LTTP: Total Bone Marrow Burden Score (BMB) at Baseline, 1 year, and 2 years

End point title	LTTP: Total Bone Marrow Burden Score (BMB) at Baseline, 1 year, and 2 years

End point description:

BMB Score was measured using MRI, range from 0 (no abnormalities) to 8 points (severe disease) for the lumbar spine and from 0 (no abnormalities) to 8 points (severe disease) for the femurs. The total score was calculated as the sum of scores for femur and lumbar spine regions which ranged from 0-16 points. A higher BMB score signified more severe bone marrow involvement. Analysis was performed on all subjects who received at least one dose of eliglustat during the LTTP. Here, "n" signifies number of subjects with available data at specified time points.

End point type	Secondary

End point timeframe:

Baseline, 1 year, and 2 years

End point values	LTTP, Eliglustat			
Subject group type	Reporting group			
Number of subjects analysed	121			
Units: BMB Score				
arithmetic mean (standard deviation)				
BMB Score: Baseline (n=115)	8.164 (± 2.646)			
BMB Score: 1 year (n=26)	7.853 (± 2.497)			
BMB Score: 2 years (n=17)	8.059 (± 1.918)			

Statistical analyses

No statistical analyses for this end point

Secondary: LTTP: Mean Biomarker (Chitotriosidase) Value at Baseline, 1 year, and 2 years

End point title	LTTP: Mean Biomarker (Chitotriosidase) Value at Baseline, 1 year, and 2 years

End point description:

Chitotriosidase biomarker was assayed from plasma. Analysis was performed on all subjects who received at least one dose of eliglustat during the LTTP. Here, "n" signifies number of subjects with available data at specified time points.

End point type	Secondary

End point timeframe:

Baseline, 1 year, and 2 years

End point values	LTTP, Eliglustat			
Subject group type	Reporting group			
Number of subjects analysed	121			
Units: nmol/hr/mL				
arithmetic mean (standard deviation)				
Chitotriosidase: Baseline (n=118)	1188.983 (± 1857.521)			
Chitotriosidase: 1 year (n=97)	1221.753 (± 2072.446)			
Chitotriosidase: 2 years (n=31)	598.161 (± 1463.603)			

Statistical analyses

No statistical analyses for this end point

Secondary: LTTP: Mean Biomarker (GL-1 on DBS) Value at Baseline, 1 Year, and 2 Years

End point title	LTTP: Mean Biomarker (GL-1 on DBS) Value at Baseline, 1 Year, and 2 Years

End point description:

GL-1 on DBS biomarker was assayed from dried blood spot. Anaysis was performed on all subjects who received at least one dose of eliglustat during the LTTP. Here 'n' signifies number of subjects with available data at specified time points.

End point type	Secondary

End point timeframe:

Baseline, 1 year, and 2 years

End point values	LTTP, Eliglustat			
Subject group type	Reporting group			
Number of subjects analysed	121			
Units: mcg/mL				
arithmetic mean (standard deviation)				
GL-1 on DBS: Baseline (n=114)	2.725 (± 1.35)			
GL-1 on DBS: 1 year (n=98)	2.5 (± 1.031)			
GL-1 on DBS: 2 years (n=29)	2.238 (± 0.658)			

Statistical analyses

No statistical analyses for this end point

Secondary: LTTP: Mean Biomarker (MIP1-beta) Value at Baseline, 1 year, and 2 years

End point title	LTTP: Mean Biomarker (MIP1-beta) Value at Baseline, 1 year, and 2 years

End point description:

MIP1-beta biomarker was assayed from plasma. Analysis was performed on all subjects who received at least one dose of eliglustat during the LTTP. Here, "n" signifies number of subjects with available data at specified time points.

End point type	Secondary

End point timeframe:

Baseline, 1 year, and 2 years

End point values	LTTP, Eliglustat			
Subject group type	Reporting group			
Number of subjects analysed	121			
Units: pg/mL				
arithmetic mean (standard deviation)				
MIP-1beta: Baseline (n=114)	97.857 (± 125.857)			
MIP-1beta: 1 year (n=94)	90.398 (± 90.549)			
MIP-1beta: 2 years (n=31)	68.445 (± 64.774)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All Adverse Events (AE) were collected from signature of the informed consent form up to the final visit regardless of seriousness or relationship to investigational product.

Adverse event reporting additional description:

Reported AEs and deaths are treatment emergent that is AEs that developed/worsened and deaths that is occurred during 'the treatment emergent period' (from the first dose of study drug up to the last dose of study drug + 37 days). Analysis was performed on safety population. Adverse events data was planned to be reported for overall population.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	18.0

Reporting groups

Reporting group title	Eliglustat

Reporting group description: -

Serious adverse events	Eliglustat		
Total subjects affected by serious adverse events			
subjects affected / exposed	40 / 170 (23.53%)		
number of deaths (all causes)	2		
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Lipoma			
subjects affected / exposed	1 / 170 (0.59%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Papillary Thyroid Cancer			
subjects affected / exposed	1 / 170 (0.59%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Aortic Aneurysm			
subjects affected / exposed	1 / 170 (0.59%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hypertension			

subjects affected / exposed	2 / 170 (1.18%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Haemorrhage			
subjects affected / exposed	1 / 170 (0.59%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Pregnancy, puerperium and perinatal conditions			
Ectopic Pregnancy			
subjects affected / exposed	1 / 170 (0.59%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Disuse Syndrome			
subjects affected / exposed	1 / 170 (0.59%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Device Dislocation			
subjects affected / exposed	1 / 170 (0.59%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Impaired Healing			
subjects affected / exposed	1 / 170 (0.59%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Medical Device Pain			
subjects affected / exposed	1 / 170 (0.59%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hernia			
subjects affected / exposed	1 / 170 (0.59%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Reproductive system and breast disorders			
Uterine Polyp			
subjects affected / exposed	1 / 170 (0.59%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Conversion Disorder			
subjects affected / exposed	1 / 170 (0.59%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Major Depression			
subjects affected / exposed	1 / 170 (0.59%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Investigations			
Hepatic Enzyme Increased			
subjects affected / exposed	1 / 170 (0.59%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	1 / 170 (0.59%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Femoral Neck Fracture			
subjects affected / exposed	2 / 170 (1.18%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Femur Fracture			
subjects affected / exposed	1 / 170 (0.59%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Incisional Hernia			

subjects affected / exposed	1 / 170 (0.59%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Forearm Fracture				
subjects affected / exposed	1 / 170 (0.59%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Radius Fracture				
subjects affected / exposed	1 / 170 (0.59%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Spinal Fracture				
subjects affected / exposed	1 / 170 (0.59%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Injury				
subjects affected / exposed	1 / 170 (0.59%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Cardiac disorders				
Arrhythmia				
subjects affected / exposed	1 / 170 (0.59%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Angina Pectoris				
subjects affected / exposed	2 / 170 (1.18%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Cardiac Arrest				
subjects affected / exposed	1 / 170 (0.59%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Nervous system disorders				

Epilepsy			
subjects affected / exposed	2 / 170 (1.18%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Dizziness			
subjects affected / exposed	1 / 170 (0.59%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Presyncope			
subjects affected / exposed	1 / 170 (0.59%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Ischaemic Stroke			
subjects affected / exposed	1 / 170 (0.59%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Seizure			
subjects affected / exposed	1 / 170 (0.59%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Syncope			
subjects affected / exposed	3 / 170 (1.76%)		
occurrences causally related to treatment / all	3 / 3		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Mallory-Weiss Syndrome			
subjects affected / exposed	1 / 170 (0.59%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Abdominal Wall Haematoma			
subjects affected / exposed	1 / 170 (0.59%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			

Cholecystitis			
subjects affected / exposed	1 / 170 (0.59%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cholecystitis Chronic			
subjects affected / exposed	1 / 170 (0.59%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Calculus Urinary			
subjects affected / exposed	1 / 170 (0.59%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Arthritis			
subjects affected / exposed	1 / 170 (0.59%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Arthralgia			
subjects affected / exposed	2 / 170 (1.18%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Muscular Weakness			
subjects affected / exposed	1 / 170 (0.59%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Joint Range Of Motion Decreased			
subjects affected / exposed	1 / 170 (0.59%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Osteonecrosis			
subjects affected / exposed	1 / 170 (0.59%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Osteoarthritis			
subjects affected / exposed	3 / 170 (1.76%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Acute Hepatitis B			
subjects affected / exposed	1 / 170 (0.59%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Appendicitis			
subjects affected / exposed	1 / 170 (0.59%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatitis A			
subjects affected / exposed	1 / 170 (0.59%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Staphylococcal Sepsis			
subjects affected / exposed	1 / 170 (0.59%)		
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	Eliglustat		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	144 / 170 (84.71%)		
Vascular disorders			
Hypertension			
subjects affected / exposed	9 / 170 (5.29%)		
occurrences (all)	11		
Cardiac disorders			
Palpitations			
subjects affected / exposed	11 / 170 (6.47%)		
occurrences (all)	14		

Nervous system disorders			
Headache			
subjects affected / exposed	37 / 170 (21.76%)		
occurrences (all)	99		
Dizziness			
subjects affected / exposed	28 / 170 (16.47%)		
occurrences (all)	33		
Blood and lymphatic system disorders			
Thrombocytopenia			
subjects affected / exposed	9 / 170 (5.29%)		
occurrences (all)	12		
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	17 / 170 (10.00%)		
occurrences (all)	18		
Pyrexia			
subjects affected / exposed	16 / 170 (9.41%)		
occurrences (all)	19		
Gastrointestinal disorders			
Abdominal Distension			
subjects affected / exposed	9 / 170 (5.29%)		
occurrences (all)	9		
Abdominal Pain			
subjects affected / exposed	15 / 170 (8.82%)		
occurrences (all)	20		
Abdominal Pain Upper			
subjects affected / exposed	26 / 170 (15.29%)		
occurrences (all)	36		
Constipation			
subjects affected / exposed	16 / 170 (9.41%)		
occurrences (all)	17		
Gastrooesophageal Reflux Disease			
subjects affected / exposed	9 / 170 (5.29%)		
occurrences (all)	11		
Diarrhoea			

subjects affected / exposed	24 / 170 (14.12%)		
occurrences (all)	29		
Dyspepsia			
subjects affected / exposed	19 / 170 (11.18%)		
occurrences (all)	29		
Nausea			
subjects affected / exposed	18 / 170 (10.59%)		
occurrences (all)	21		
Vomiting			
subjects affected / exposed	14 / 170 (8.24%)		
occurrences (all)	18		
Hepatobiliary disorders			
Hepatomegaly			
subjects affected / exposed	9 / 170 (5.29%)		
occurrences (all)	10		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	21 / 170 (12.35%)		
occurrences (all)	23		
Epistaxis			
subjects affected / exposed	13 / 170 (7.65%)		
occurrences (all)	16		
Oropharyngeal Pain			
subjects affected / exposed	18 / 170 (10.59%)		
occurrences (all)	23		
Psychiatric disorders			
Depression			
subjects affected / exposed	10 / 170 (5.88%)		
occurrences (all)	14		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	30 / 170 (17.65%)		
occurrences (all)	49		
Back Pain			
subjects affected / exposed	29 / 170 (17.06%)		
occurrences (all)	40		

Musculoskeletal Pain			
subjects affected / exposed	10 / 170 (5.88%)		
occurrences (all)	12		
Myalgia			
subjects affected / exposed	11 / 170 (6.47%)		
occurrences (all)	13		
Pain In Extremity			
subjects affected / exposed	24 / 170 (14.12%)		
occurrences (all)	35		
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	52 / 170 (30.59%)		
occurrences (all)	94		
Urinary Tract Infection			
subjects affected / exposed	14 / 170 (8.24%)		
occurrences (all)	22		
Gastroenteritis			
subjects affected / exposed	15 / 170 (8.82%)		
occurrences (all)	24		
Viral Infection			
subjects affected / exposed	10 / 170 (5.88%)		
occurrences (all)	12		
Influenza			
subjects affected / exposed	23 / 170 (13.53%)		
occurrences (all)	28		
Upper Respiratory Tract Infection			
subjects affected / exposed	22 / 170 (12.94%)		
occurrences (all)	38		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
27 June 2011	•Amendment was prepared in response to observed high variability in Genz-99067 plasma concentrations in the Phase 3 studies (GZGD02507 [ENGAGE] and GZGD02607 [ENCORE]) compared to those in the Phase 2 study (GZGD00304). The principal change was the implementation of additional safety monitoring in subjects with a peak Genz-99067 plasma concentration ≥150 ng/mL. It provided details on the management of subjects with peak plasma concentrations ≥150 ng/mL. •Addressed ongoing challenges with recruitment of the target population. It also prepared in response to emerging non-clinical and clinical data for eliglustat, and included the following key changes: •Planned enrollment was reduced from 234 subjects to 131 subjects. •Added additional criteria to be entered into the PAP of the study. •Eliminated the 150 mg BID vs 300 mg QD dose-group pair in the PAP. •Updated guidance on prohibited prior and concomitant medications. •Modified PK sampling and analysis to add peak Genz--99067 plasma concentrations. •Adjusted statistical methodology based on change in sample size, elimination of the 150 mg BID vs. 300 mg QD pair, and change in approach for analyzing organ volumes. •Allowed subjects who had not reached therapeutic goals by N-Month 18 to receive 150 mg BID in the ETP. •Harmonized Japan and outside -Japan protocol versions into a single version. •Updated the risk/benefit and dose rationale information.
23 July 2012	Addressed changes in conduct of the study, including increased enrollment of subjects. Planned enrollment was recalculated from 131 subjects to 170 subjects. The underlying sample size assumptions were unchanged, and the study remained adequately powered for the primary efficacy endpoint. Other key change included: •Extended the maximum duration of a subject's participation in the study to 60 months. •Provided a minimum schedule of assessments for subjects who remained in the study beyond 42 months. •Provided a simplified presentation of concomitant medication guidance. •Clarification that subjects on a dose of 150 mg BID are not eligible for randomization, but will remain in the LIP for the entire 18 months. •Updated benefit/risk summary.
06 February 2013	It provided updated concomitant medication guidelines based on information from Phase 1 drug- drug interaction studies.
31 January 2014	It provided clarification that the assay for GL-1 be performed on plasma samples or DBS.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported