ClinicalTrials.gov Protocol and Results Registration System (PRS) Receipt
Release Date: 08/22/2014

ClinicalTrials.gov ID: NCT00943111

Study Identification

Unique Protocol ID: GZGD02607

Brief Title: A Study of Eliglustat Tartrate (Genz-112638) in Patients With Gaucher Disease Who Have Reached Therapeutic Goals With Enzyme Replacement Therapy (ENCORE)

Official Title: A Phase 3, Randomized, Multi-Center, Multi-National, Open-Label, Active Comparator Study to Evaluate the Efficacy and Safety of Genz-112638 in Patients With Gaucher Disease Type 1 Who Have Reached Therapeutic Goals With Enzyme Replacement Therapy (ENCORE)

Secondary IDs: 2008-005223-28 [EudraCT Number]
EFC12812 [Sanofi]

Study Status

Record Verification: August 2014

Overall Status: Active, not recruiting

Study Start: September 2009

Primary Completion: November 2012 [Actual]

Study Completion: May 2015 [Anticipated]

Sponsor/Collaborators

Sponsor: Genzyme, a Sanofi Company

Responsible Party: Sponsor

Collaborators:

Oversight

FDA Regulated?:	Yes
IND/IDE Protocol?:	Yes
IND/IDE Information:	Grantor: CDER IND/IDE Number: 67,589 Serial Number: 0067 Has Expanded Access? No
Review Board:	Approval Status: Approved Board Name: Board Affiliation: Phone: Email:
Data Monitoring?:	Yes
Oversight Authorities:	United States: Food and Drug Administration Argentina: Administracion Nacional de Medicamentos, Alimentos y Tecnologia Medica Australia: Therapeutic Goods Administration'Brazil: Ministry of Health Brazil: Ministry of Health Canada: Health Canada Egypt: Ministry of Health and Population France: Ministry of Health Germany: Ministry of Health Italy: Ministry of Health Russia: Ministry of Health of the Russian Federation Spain: Ministry of Health United Kingdom: Medicines and Healthcare Products Regulatory Agency

Study Description

Brief Summary:	This Phase 3 study is designed to confirm the efficacy and safety of eliglustat tartrate (Genz-112638) in participants with Gaucher disease type 1 who have reached therapeutic goals with enzyme replacement therapy (ERT).
Detailed Description:	Gaucher disease is characterized by lysosomal accumulation of glucosylceramide due to impaired glucosylceramide hydrolysis. Gaucher disease type 1, which is the most common form, accounts for greater than (>) 90% of cases and does not involve the central nervous system (CNS). Typical manifestations of Gaucher disease type 1 include splenomegaly, hepatomegaly, thrombocytopenia, anemia, bone disease, and decreased quality of life. The disease manifestations are caused by the accumulation of glucosylceramide (storage material) in macrophages (called Gaucher cells) which have infiltrated the spleen and liver as well as other tissues. Eliglustat tartrate is a small molecule drug developed as an oral therapy which acts to specifically inhibit production of this storage material in Gaucher cells.

This study is designed to determine the efficacy, safety, and pharmacokinetics (PK) of eliglustat tartrate in adult participants with Gaucher disease type 1 who have been stabilized on ERT.

Conditions

Conditions: Gaucher Disease, Type 1

Keywords: Gaucher disease,
Genz-112638,
beta-glucosidase,
acid ß-glucosidase,
glucocerebrosidase,
glucosylceramide,
D-glucosyl-N-acylsphingosine glucohydrolase,
substrate reduction therapy

Study Design

Study Type: Interventional

Primary Purpose: Treatment

Study Phase: Phase 3

Intervention Model: Parallel Assignment

Number of Arms: 2

Masking: Open Label

Allocation: Randomized

Endpoint Classification: Safety/Efficacy Study

Enrollment: 160 [Actual]

Arms and Interventions

Arms	Assigned Interventions
Experimental: Investigational Eliglustat tartrate	Drug: Eliglustat tartrate Eliglustat tartrate capsule 50 milligram (mg) twice daily (BID) orally from Day 1 to Week 4 followed by eliglustat tartrate 50 mg or 100 mg capsule BID up to Week 8, and then eliglustat tartrate 50 mg or 100 mg or 150 mg capsule BID up to Week 52. The dose adjustments after Week 4 and Week 8 were based on Genz-99067 (active moiety of eliglustat tartrate

Arms	Assigned Interventions
	in plasma) trough plasma concentrations. If Genz-99067 trough plasma concentration was less than [<] 5 nanogram per milliliter [ng/mL] the next higher dose was administered whereas if the Genz-99067 trough plasma concentration was greater than or equal to [>=] 5 ng/mL the same dose was continued. The pharmacokinetic (PK) assessment at Week 2 and Week 6 were used for dose adjustment after Week 4 and Week 8, respectively. Other Names: • Genz-112638
Active Comparator: Imiglucerase	Drug: Imiglucerase Imiglucerase intravenous infusion every other week (q2w) up to Week 52 in doses equivalent to participant's past ERT dose prior to any unanticipated treatment interruption, dose reduction, or regimen change. Other Names: • Cerezyme®

Outcome Measures

[See Results Section.]

Eligibility

Minimum Age: 18 Years

Maximum Age:

Gender: Both

Accepts Healthy Volunteers?: No

Criteria: Inclusion Criteria:

- The participant (and/or their parent/legal guardian) is willing and able to provide signed informed consent prior to any study-related procedures to be performed
- The participant is at least 18 years old at the time of randomization
- The participant has a confirmed diagnosis of Gaucher disease type 1
- The participant has received treatment with ERT for at least 3 years. Within the 9 months prior to randomization, the participant has received a total monthly dose of 30 to 130 Units/kilogram for at least 6 months
- The participant has reached Gaucher disease therapeutic goals prior to randomization
- Female participants of childbearing potential must have a documented negative pregnancy test prior to dosing. In addition, all female participants of childbearing potential must use a medically accepted form of contraception throughout the study

Exclusion Criteria:

- The participant has had a partial or total splenectomy within 3 years prior to randomization
- The participant has received substrate reduction therapies for Gaucher disease within 6 months prior to randomization
- The participant has Gaucher disease type 2 or 3 or is suspected of having Gaucher disease type 3
- The participant has any clinically significant disease, other than Gaucher disease, including cardiovascular, renal, hepatic, gastrointestinal (GI), pulmonary, neurologic, endocrine, metabolic (e.g. hypokalemia, hypomagnesemia), or psychiatric disease, other medical conditions, or serious intercurrent illnesses that may confound the study results or, in the opinion of the Investigator, may preclude participation in the study
- The participant has tested positive for the human immunodeficiency virus (HIV) antibody, Hepatitis C antibody, or Hepatitis B surface antigen
- The participant has received an investigational product within 30 days prior to randomization
- The participant is pregnant or lactating

Contacts/Locations

Study Officials: Medical Monitor
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References

Citations: Lukina E, Watman N, Arreguin EA, Banikazemi M, Dragosky M, Iastrebner M, Rosenbaum H, Phillips M, Pastores GM, Rosenthal DI, Kaper M, Singh T, Puga AC, Bonate PL, Peterschmitt MJ. A phase 2 study of eliglustat tartrate (Genz-112638), an oral substrate reduction therapy for Gaucher disease type 1. Blood. 2010 Aug 12;116(6):893-9. doi: 10.1182/blood-2010-03-273151. Epub 2010 May 3. PubMed 20439622

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Kamath RS, Lukina E, Watman N, Dragosky M, Pastores GM, Arreguin EA, Rosenbaum H, Zimran A, Aguzzi R, Puga AC, Norfleet AM, Peterschmitt MJ, Rosenthal DI. Skeletal improvement in patients with Gaucher disease type 1: a phase 2 trial of oral eliglustat. Skeletal Radiol. 2014 Oct;43(10):1353-60. doi: 10.1007/s00256-014-1891-9. Epub 2014 May 10. PubMed 24816856

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Links: URL: http://bloodjournal.hematologylibrary.org/cgi/content/full/116/6/893
Description A phase 2 study of eliglustat tartrate (Genz-112638), an oral substrate reduction therapy for Gaucher disease type 1

Participant Flow

Pre-Assignment Details	A total of 209 participants were screened of which 46 participants were screen failure and 3 participants withdrew prior to randomization. A total of 160 participants were enrolled in this study.

Reporting Groups

	Description
Eliglustat	Eliglustat tartrate (Genz-112638) capsule 50 milligram (mg) twice daily (BID) orally from Day 1 to Week 4 followed by eliglustat tartrate 50 mg or 100 mg capsule BID up to Week 8, and then eliglustat tartrate 50 mg or 100 mg or 150 mg capsule BID up to Week 52. The dose adjustments after Week 4 and Week 8 were based on Genz-99067 (active moiety of eliglustat tartrate in plasma) trough plasma concentrations. If Genz-99067 trough plasma concentration was less than [<] 5 nanogram per milliliter [ng/mL] the next higher dose was administered whereas if the Genz-99067 trough plasma concentration was greater than or equal to [>=] 5 ng/mL the same dose was continued. The pharmacokinetic (PK) assessment at Week 2 and Week 6 were used for dose adjustment after Week 4 and Week 8, respectively.
Imiglucerase	Imiglucerase (Cerezyme®) intravenous infusion every other week (q2w) up to Week 52 in doses equivalent to participant's past enzyme replacement therapy (ERT) dose prior to any unanticipated treatment interruption, dose reduction, or regimen change.

Overall Study

	Eliglustat	Imiglucerase
Started	106	54
Treated	106	53
Completed	104	52
Not Completed	2	2
Adverse Event	2	1
Non-compliance with study drug	0	1

Baseline Characteristics

Analysis Population Description

Per protocol population included participants who were at least 80% compliant with treatment during primary analysis period, had no major protocol deviations, and did not exhibit hematological decline as a result of medically determined etiologies other than Gaucher disease.

Reporting Groups

	Description
Eliglustat	Eliglustat tartrate 50 mg capsule BID orally from Day 1 to Week 4, followed by eliglustat tartrate 50, 100 or 150 mg capsule BID orally up to Week 52.
Imiglucerase	Imiglucerase intravenously from Day 1 through Week 52 in a twice weekly regimen equivalent to their ERT dose prior to any unanticipated treatment interruption, dose reduction, or regimen change.

Baseline Measures

	Eliglustat	Imiglucerase	Total
Number of Participants	99	47	146
Age, Continuous [units: years] Mean (Standard Deviation)	37.2 (14.0)	38.6 (15.2)	37.6 (14.4)
Gender, Male/Female [units: participants]			
Female	56	26	82
Male	43	21	64
Race/Ethnicity, Customized [units: participants]			
Race: White	91	45	136
Race: Black or African American	6	2	8
Race: Asian	1	0	1
Race: White/American Indian	1	0	1
Ethnicity: Hispanic or Latino	40	17	57
Ethnicity: Not Hispanic or Latino	59	30	89
Body Mass Index (BMI) [1] [units: kilogram per square meter (kg/m^2)] Mean (Standard Deviation)	25.2 (5.33)	24.4 (4.65)	24.9 (5.12)
Weight [units: kilogram (kg)] Mean (Standard Deviation)	70.8 (17.3)	67.5 (15.0)	69.7 (16.6)

	Eliglustat	Imiglucerase	Total
Height [units: centimeter (cm)] Mean (Standard Deviation)	167.4 (10.10)	166.1 (9.95)	167.0 (10.04)

[1] BMI was calculated as ([weight in kg] divided by [height in cm multiplied by 0.01]^2).

Outcome Measures

1. Primary Outcome Measure:

Measure Title	Percentage of Participants Who Remained Stable for 52 Weeks During the Primary Analysis Period
Measure Description	For a participant to be classified as stable, the participant must have remained stable in hematological parameters (hemoglobin levels and platelet counts) and organ volumes (spleen, when applicable, and liver volumes in multiples of normal [MN]). Stable hematological parameters were defined as hemoglobin level did not decrease more than (>) 1.5 gram per deciliter (g/dL) from baseline and platelet count did not decrease >25% from baseline. Stable organ volumes were defined as spleen volume (in MN) did not increase >25% from baseline, if applicable, and liver volume (in MN) did not increase >20% from baseline.
Time Frame	Baseline up to Week 52
Safety Issue?	No

Analysis Population Description

Per protocol population included participants who were at least 80% compliant with treatment during primary analysis period, had no major protocol deviations, and did not exhibit hematological decline as a result of medically determined etiologies other than Gaucher disease.

Reporting Groups

	Description
Eliglustat	Eliglustat tartrate 50 mg capsule BID orally from Day 1 to Week 4, followed by eliglustat tartrate 50, 100 or 150 mg capsule BID orally up to Week 52.
Imiglucerase	Imiglucerase intravenous infusion q2w up to Week 52 in doses equivalent to participant's past ERT dose prior to any unanticipated treatment interruption, dose reduction, or regimen change.

Measured Values

	Eliglustat	Imiglucerase
Number of Participants Analyzed	99	47
Percentage of Participants Who Remained Stable for 52 Weeks During the Primary Analysis Period [units: percentage of participants] Number (95% Confidence Interval)	84.8 (76.2 to 91.3)	93.6 (82.5 to 98.7)

Statistical Analysis 1 for Percentage of Participants Who Remained Stable for 52 Weeks During the Primary Analysis Period

Statistical Analysis Overview	Comparison Groups	Eliglustat, Imiglucerase
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	Yes
	Comments	The sample size for study was based on expected stability rates of 95% for the Imiglucerase group and 85% for the Eliglustat group, power of 85%, a one-sided significance level of 0.025, a non-inferiority margin of 25%, and a 20% non-evaluable/drop-out rate. Eliglustat was declared non-inferior to Imiglucerase if the lower-bound of the 95% confidence interval for the difference was within the non-inferiority margin of 25%.

Method of Estimation	Estimation Parameter	Other [Difference in Percentage Stable]
	Estimated Value	-8.8
	Confidence Interval	(2-Sided) 95% -17.6 to 4.2
	Estimation Comments	[Not specified]

2. Secondary Outcome Measure:

Measure Title	Total T-Scores for Bone Mineral Density
Measure Description	Images of the spine and bilateral femur were obtained by dual energy X-Ray absorptiometry (DXA) to determine T-score for each bone area and total bone mineral density. T-score compares participant’s bone density with that of healthy young participant. The T-score bone density categories are: normal (score greater than [>]-1), osteopenia (score -2.5 to less than or equal to [<=] -1), and osteoporosis (score <= -2.5).
Time Frame	Baseline
Safety Issue?	No

Analysis Population Description

Per protocol population. Number of participants analyzed = participants with baseline T-score assessment. Here, 'n' signifies participants with baseline T-score assessment for specified bone area.

Reporting Groups

	Description
Eliglustat	Eliglustat tartrate 50 mg capsule BID orally from Day 1 to Week 4, followed by eliglustat tartrate 50, 100 or 150 mg capsule BID orally up to Week 52.

	Description
Imiglucerase	Imiglucerase intravenously from Day 1 through Week 52 in a twice weekly regimen equivalent to their ERT dose prior to any unanticipated treatment interruption, dose reduction, or regimen change.

Measured Values

	Eliglustat	Imiglucerase
Number of Participants Analyzed	81	38
Total T-Scores for Bone Mineral Density [units: T-score] Mean (Standard Deviation)		
Lumbar Spine T-Score (n=81, 38)	-0.56 (1.309)	-0.33 (1.169)
Femur T-Score (n=80, 37)	-0.11 (1.080)	-0.47 (1.293)

3. Secondary Outcome Measure:

Measure Title	Absolute Change From Baseline in Total T-Scores for Bone Mineral Density at Week 52
Measure Description	Images of the spine and bilateral femur were obtained by dual energy X-Ray absorptiometry (DXA) to determine T-score for each bone area and total bone mineral density. T-score compares participant's bone density with that of healthy young participant. The T-score bone density categories are: normal (score greater than [>]-1), osteopenia (score -2.5 to less than or equal to [<=] -1), and osteoporosis (score <= -2.5). Absolute change = T-score at Week 52 minus T-score at baseline.
Time Frame	Baseline, Week 52
Safety Issue?	No

Analysis Population Description

Per protocol population. Number of participants analyzed = participants with both baseline and Week 52 T-score assessment. Here, 'n' signifies participants with both baseline and Week 52 T-score assessment for specified bone area. Eliglustat patients switching to imiglucerase are excluded.

Reporting Groups

	Description
Eliglustat	Eliglustat tartrate 50 mg capsule BID orally from Day 1 to Week 4, followed by eliglustat tartrate 50, 100 or 150 mg capsule BID orally up to Week 52.
Imiglucerase	Imiglucerase intravenously from Day 1 through Week 52 in a twice weekly regimen equivalent to their ERT dose prior to any unanticipated treatment interruption, dose reduction, or regimen change.

Measured Values

	Eliglustat	Imiglucerase
Number of Participants Analyzed	81	38
Absolute Change From Baseline in Total T-Scores for Bone Mineral Density at Week 52 [units: T-score] Least Squares Mean (Standard Error)		
Change in Lumbar Spine T-Score (n=81, 38)	0.04 (0.03)	0.03 (0.05)
Change in Femur T-Score (n=80, 37)	0.00 (0.02)	-0.03 (0.03)

4. Secondary Outcome Measure:

Measure Title	Total Z-Scores for Bone Mineral Density
Measure Description	Images of the spine and bilateral femur were obtained by dual energy X-Ray absorptiometry (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).
Time Frame	Baseline
Safety Issue?	No

Analysis Population Description

Per protocol population. Number of participants analyzed = participants with baseline Z-score assessment. Here, 'n' signifies participants with baseline Z-score assessment for specified bone area.

Reporting Groups

	Description
Eliglustat	Eliglustat tartrate 50 mg capsule BID orally from Day 1 to Week 4, followed by eliglustat tartrate 50, 100 or 150 mg capsule BID orally up to Week 52.
Imiglucerase	Imiglucerase intravenously from Day 1 through Week 52 in a twice weekly regimen equivalent to their ERT dose prior to any unanticipated treatment interruption, dose reduction, or regimen change.

Measured Values

	Eliglustat	Imiglucerase
Number of Participants Analyzed	94	45
Total Z-Scores for Bone Mineral Density [units: Z-score]		

	Eliglustat	Imiglucerase
Mean (Standard Deviation)		
Lumbar Spine Z-Score (n=94, 45)	-0.35 (1.260)	-0.14 (1.108)
Femur Z-Score (n=93, 44)	0.09 (1.020)	-0.18 (1.122)

5. Secondary Outcome Measure:

Measure Title	Absolute Change From Baseline in Total Z-Scores for Bone Mineral Density at Week 52
Measure Description	Images of the spine and bilateral femur were obtained by dual energy X-Ray absorptiometry (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). Absolute change = Z-score at Week 52 minus Z-score at baseline.
Time Frame	Baseline, Week 52
Safety Issue?	No

Analysis Population Description

Per protocol population. Number of participants analyzed = participants with both baseline and Week 52 Z-score assessment. Here, 'n' signifies participants with both baseline and Week 52 Z-score assessment for specified bone area. Eliglustat patients switching to imiglucerase are excluded.

Reporting Groups

	Description
Eliglustat	Eliglustat tartrate 50 mg capsule BID orally from Day 1 to Week 4, followed by eliglustat tartrate 50, 100 or 150 mg capsule BID orally up to Week 52.
Imiglucerase	Imiglucerase intravenously from Day 1 through Week 52 in a twice weekly regimen equivalent to their ERT dose prior to any unanticipated treatment interruption, dose reduction, or regimen change.

Measured Values

	Eliglustat	Imiglucerase
Number of Participants Analyzed	94	45
Absolute Change From Baseline in Total Z-Scores for Bone Mineral Density at Week 52 [units: Z-score] Least Squares Mean (Standard Error)		
Change in Lumbar Spine Z-Score (n=94, 45)	0.06 (0.03)	0.06 (0.04)
Change in Femur Z-Score (n=93, 44)	0.03 (0.02)	0.02 (0.02)

6. Secondary Outcome Measure:

Measure Title	Hemoglobin Level
Measure Description	
Time Frame	Baseline
Safety Issue?	No

Analysis Population Description

Per protocol population. Number of participants analyzed = participants with baseline hemoglobin assessment.

Reporting Groups

	Description
Eliglustat	Eliglustat tartrate 50 mg capsule BID orally from Day 1 to Week 4, followed by eliglustat tartrate 50, 100 or 150 mg capsule BID orally up to Week 52.
Imiglucerase	Imiglucerase intravenously from Day 1 through Week 52 in a twice weekly regimen equivalent to their ERT dose prior to any unanticipated treatment interruption, dose reduction, or regimen change.

Measured Values

	Eliglustat	Imiglucerase
Number of Participants Analyzed	98	47
Hemoglobin Level [units: gram per deciliter (g/dL)] Mean (Standard Deviation)	13.592 (1.2467)	13.797 (1.2234)

7. Secondary Outcome Measure:

Measure Title	Absolute Change From Baseline in Hemoglobin Levels at Week 52
Measure Description	Absolute change = hemoglobin level at Week 52 minus hemoglobin level at baseline.
Time Frame	Baseline, Week 52
Safety Issue?	No

Analysis Population Description

Per protocol population. Number of participants analyzed = participants with both baseline and Week 52 hemoglobin assessment. Eliglustat patients switching to imiglucerase are excluded.

Reporting Groups

	Description
Eliglustat	Eliglustat tartrate 50 mg capsule BID orally from Day 1 to Week 4, followed by eliglustat tartrate 50, 100 or 150 mg capsule BID orally up to Week 52.
Imiglucerase	Imiglucerase intravenous infusion q2w up to Week 52 in doses equivalent to participant's past ERT dose prior to any unanticipated treatment interruption, dose reduction, or regimen change.

Measured Values

	Eliglustat	Imiglucerase
Number of Participants Analyzed	98	47
Absolute Change From Baseline in Hemoglobin Levels at Week 52 [units: g/dL] Least Squares Mean (Standard Error)	-0.22 (0.07)	0.05 (0.10)

8. Secondary Outcome Measure:

Measure Title	Percent Change From Baseline in Platelet Counts at Week 52
Measure Description	Percent change in platelet counts = ([platelet count at Week 52 minus platelet count at baseline] divided by [platelet count at baseline]) multiplied by 100.
Time Frame	Baseline, Week 52
Safety Issue?	No

Analysis Population Description

Per protocol population. Number of participants analyzed = participants with both baseline and Week 52 platelet assessment. Eliglustat patients switching to imiglucerase are excluded.

Reporting Groups

	Description
Eliglustat	Eliglustat tartrate 50 mg capsule BID orally from Day 1 to Week 4, followed by eliglustat tartrate 50, 100 or 150 mg capsule BID orally up to Week 52.
Imiglucerase	Imiglucerase intravenous infusion q2w up to Week 52 in doses equivalent to participant's past ERT dose prior to any unanticipated treatment interruption, dose reduction, or regimen change.

Measured Values

	Eliglustat	Imiglucerase
Number of Participants Analyzed	98	47
Percent Change From Baseline in Platelet Counts at Week 52 [units: percent change] Least Squares Mean (Standard Error)	3.93 (1.71)	2.63 (2.47)

9. Secondary Outcome Measure:

Measure Title	Percent Change From Baseline in Spleen Volume (in Multiplies of Normal [MN]) at Week 52
Measure Description	Percent change in spleen volume = ([spleen volume at Week 52 minus spleen volume at baseline] divided by [spleen volume at baseline]) multiplied by 100, where all volumes are in MN.
Time Frame	Baseline, Week 52
Safety Issue?	No

Analysis Population Description

Per protocol population. Number of participants analyzed = participants with both baseline and Week 52 spleen volume assessment. Eliglustat patients switching to imiglucerase are excluded.

Reporting Groups

	Description
Eliglustat	Eliglustat tartrate 50 mg capsule BID orally from Day 1 to Week 4, followed by eliglustat tartrate 50, 100 or 150 mg capsule BID orally up to Week 52.
Imiglucerase	Imiglucerase intravenous infusion q2w up to Week 52 in doses equivalent to participant's past ERT dose prior to any unanticipated treatment interruption, dose reduction, or regimen change.

Measured Values

	Eliglustat	Imiglucerase
Number of Participants Analyzed	70	39
Percent Change From Baseline in Spleen Volume (in Multiplies of Normal [MN]) at Week 52 [units: percent change] Least Squares Mean (Standard Error)	-6.05 (1.57)	-3.22 (2.13)

10. Secondary Outcome Measure:

Measure Title	Percent Change From Baseline in Liver Volume (in MN) at Week 52
Measure Description	Percent change in liver volume = ([liver volume at Week 52 minus liver volume at baseline] divided by [liver volume at baseline]) multiplied by 100, where all volumes are in multiples of normal.
Time Frame	52 weeks
Safety Issue?	No

Analysis Population Description

Per protocol population. Number of participants analyzed = participants with both baseline and Week 52 liver volume assessment. Eliglustat patients switching to imiglucerase are excluded.

Reporting Groups

	Description
Eliglustat	Eliglustat tartrate 50 mg capsule BID orally from Day 1 to Week 4, followed by eliglustat tartrate 50, 100 or 150 mg capsule BID orally up to Week 52.
Imiglucerase	Imiglucerase intravenous infusion q2w up to Week 52 in doses equivalent to participant's past ERT dose prior to any unanticipated treatment interruption, dose reduction, or regimen change.

Measured Values

	Eliglustat	Imiglucerase
Number of Participants Analyzed	98	47
Percent Change From Baseline in Liver Volume (in MN) at Week 52 [units: percent change] Least Squares Mean (Standard Error)	1.99 (0.94)	3.13 (1.36)

Reported Adverse Events

Time Frame	From signature of informed consent up to 30-37 days after the last dose of treatment (last dose = up to Week 52)
Additional Description	Safety set included all participants who received at least 1 dose of study drug (Eliglustat or Imiglucerase). In the event a single participant experienced both serious and non-serious forms of same adverse events (AE), individual was included in numerator (number of participants affected) of each AE table.

Reporting Groups

	Description
Eliglustat	Eliglustat tartrate 50 mg capsule BID orally from Day 1 to Week 4, followed by eliglustat tartrate 50, 100 or 150 mg capsule BID orally up to Week 52.
Imiglucerase	Imiglucerase (Cerezyme®) intravenous infusion every other week (q2w) up to Week 52 in doses equivalent to participant's past enzyme replacement therapy (ERT) dose prior to any unanticipated treatment interruption, dose reduction, or regimen change.

Serious Adverse Events

	Eliglustat	Imiglucerase
	Affected/At Risk (%)	Affected/At Risk (%)
Total	11/106 (10.38%)	0/53 (0%)
Cardiac disorders		
Myocardial infarction [A] †	1/106 (0.94%)	0/53 (0%)
Gastrointestinal disorders		
Colitis ischaemic [A] †	1/106 (0.94%)	0/53 (0%)
Hepatobiliary disorders		
Cholecystitis [A] †	1/106 (0.94%)	0/53 (0%)
Infections and infestations		
Appendicitis [A] †	1/106 (0.94%)	0/53 (0%)
Diverticulitis [A] †	1/106 (0.94%)	0/53 (0%)
Injury, poisoning and procedural complications		
Joint dislocation [A] †	1/106 (0.94%)	0/53 (0%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)		
Hepatic neoplasm malignant [A] †	1/106 (0.94%)	0/53 (0%)
Uterine leiomyoma [A] †	1/106 (0.94%)	0/53 (0%)
Nervous system disorders		
Syncope [A] †	2/106 (1.89%)	0/53 (0%)

	Eliglustat	Imiglucerase
	Affected/At Risk (%)	Affected/At Risk (%)
Surgical and medical procedures		
Mammoplasty [A] †	1/106 (0.94%)	0/53 (0%)

† Indicates events were collected by systematic assessment.
A Term from vocabulary, MedDRA 15.1

Other Adverse Events

Frequency Threshold Above Which Other Adverse Events are Reported: 0%

	Eliglustat	Imiglucerase
	Affected/At Risk (%)	Affected/At Risk (%)
Total	96/106 (90.57%)	42/53 (79.25%)
Blood and lymphatic system disorders		
Lymphadenopathy [A] †	2/106 (1.89%)	0/53 (0%)
Splenomegaly [A] †	4/106 (3.77%)	1/53 (1.89%)
Thrombocytopenia [A] †	1/106 (0.94%)	2/53 (3.77%)
Cardiac disorders		
Atrioventricular block first degree [A] †	1/106 (0.94%)	0/53 (0%)
Atrioventricular block second degree [A] †	2/106 (1.89%)	0/53 (0%)
Dilatation ventricular [A] †	0/106 (0%)	1/53 (1.89%)
Palpitations [A] †	5/106 (4.72%)	0/53 (0%)
Congenital, familial and genetic disorders		
Porokeratosis [A] †	0/106 (0%)	1/53 (1.89%)
Ear and labyrinth disorders		
Cerumen impaction [A] †	1/106 (0.94%)	0/53 (0%)
Hearing impaired [A] †	1/106 (0.94%)	0/53 (0%)
Hypoacusis [A] †	1/106 (0.94%)	1/53 (1.89%)

	Eliglustat	Imiglucerase
	Affected/At Risk (%)	Affected/At Risk (%)
Middle ear effusion [A] †	1/106 (0.94%)	0/53 (0%)
Motion sickness [A] †	1/106 (0.94%)	0/53 (0%)
Tinnitus [A] †	2/106 (1.89%)	0/53 (0%)
Tympanic membrane perforation [A] †	1/106 (0.94%)	0/53 (0%)
Vertigo [A] †	2/106 (1.89%)	0/53 (0%)
Endocrine disorders		
Hyperthyroidism [A] †	1/106 (0.94%)	0/53 (0%)
Hypothyroidism [A] †	1/106 (0.94%)	0/53 (0%)
Myxoedema [A] †	1/106 (0.94%)	0/53 (0%)
Eye disorders		
Astigmatism [A] †	1/106 (0.94%)	0/53 (0%)
Blindness transient [A] †	0/106 (0%)	1/53 (1.89%)
Cataract [A] †	1/106 (0.94%)	0/53 (0%)
Chalazion [A] †	0/106 (0%)	1/53 (1.89%)
Dry eye [A] †	1/106 (0.94%)	0/53 (0%)
Eye inflammation [A] †	1/106 (0.94%)	0/53 (0%)
Eye pain [A] †	1/106 (0.94%)	0/53 (0%)
Hypermetropia [A] †	0/106 (0%)	1/53 (1.89%)
Iritis [A] †	0/106 (0%)	1/53 (1.89%)
Presbyopia [A] †	1/106 (0.94%)	0/53 (0%)
Scotoma [A] †	1/106 (0.94%)	0/53 (0%)
Visual acuity reduced [A] †	1/106 (0.94%)	0/53 (0%)

	Eliglustat	Imiglucerase
	Affected/At Risk (%)	Affected/At Risk (%)
Gastrointestinal disorders		
Abdominal discomfort [A] †	1/106 (0.94%)	1/53 (1.89%)
Abdominal distension [A] †	3/106 (2.83%)	0/53 (0%)
Abdominal pain [A] †	4/106 (3.77%)	0/53 (0%)
Abdominal pain lower [A] †	2/106 (1.89%)	0/53 (0%)
Abdominal pain upper [A] †	11/106 (10.38%)	0/53 (0%)
Cheilitis [A] †	0/106 (0%)	1/53 (1.89%)
Constipation [A] †	5/106 (4.72%)	0/53 (0%)
Dental caries [A] †	1/106 (0.94%)	1/53 (1.89%)
Diarrhoea [A] †	13/106 (12.26%)	2/53 (3.77%)
Diverticulum [A] †	0/106 (0%)	1/53 (1.89%)
Dry mouth [A] †	3/106 (2.83%)	0/53 (0%)
Duodenogastric reflux [A] †	1/106 (0.94%)	0/53 (0%)
Dyspepsia [A] †	7/106 (6.6%)	1/53 (1.89%)
Dysphagia [A] †	2/106 (1.89%)	0/53 (0%)
Eructation [A] †	1/106 (0.94%)	0/53 (0%)
Flatulence [A] †	3/106 (2.83%)	0/53 (0%)
Food poisoning [A] †	1/106 (0.94%)	1/53 (1.89%)
Gastritis [A] †	1/106 (0.94%)	1/53 (1.89%)
Gastrooesophageal reflux disease [A] †	7/106 (6.6%)	0/53 (0%)
Gingival bleeding [A] †	1/106 (0.94%)	0/53 (0%)
Gingival swelling [A] †	1/106 (0.94%)	1/53 (1.89%)

	Eliglustat	Imiglucerase
	Affected/At Risk (%)	Affected/At Risk (%)
Glossodynia [A] †	1/106 (0.94%)	0/53 (0%)
Haematochezia [A] †	1/106 (0.94%)	0/53 (0%)
Haemorrhoids [A] †	0/106 (0%)	1/53 (1.89%)
Inguinal hernia [A] †	0/106 (0%)	1/53 (1.89%)
Irritable bowel syndrome [A] †	1/106 (0.94%)	0/53 (0%)
Lip oedema [A] †	1/106 (0.94%)	0/53 (0%)
Nausea [A] †	13/106 (12.26%)	0/53 (0%)
Odynophagia [A] †	1/106 (0.94%)	0/53 (0%)
Oesophageal pain [A] †	1/106 (0.94%)	0/53 (0%)
Oesophagitis [A] †	1/106 (0.94%)	0/53 (0%)
Proctalgia [A] †	1/106 (0.94%)	0/53 (0%)
Toothache [A] †	2/106 (1.89%)	3/53 (5.66%)
Vomiting [A] †	4/106 (3.77%)	0/53 (0%)
General disorders		
Asthenia [A] †	9/106 (8.49%)	0/53 (0%)
Chest pain [A] †	4/106 (3.77%)	0/53 (0%)
Extravasation [A] †	0/106 (0%)	1/53 (1.89%)
Face oedema [A] †	1/106 (0.94%)	0/53 (0%)
Fatigue [A] †	15/106 (14.15%)	1/53 (1.89%)
Infusion site induration [A] †	0/106 (0%)	1/53 (1.89%)
Malaise [A] †	1/106 (0.94%)	1/53 (1.89%)
Oedema [A] †	1/106 (0.94%)	0/53 (0%)

	Eliglustat	Imiglucerase
	Affected/At Risk (%)	Affected/At Risk (%)
Oedema peripheral [A] †	3/106 (2.83%)	0/53 (0%)
Pain [A] †	1/106 (0.94%)	0/53 (0%)
Pyrexia [A] †	2/106 (1.89%)	1/53 (1.89%)
Thirst [A] †	1/106 (0.94%)	0/53 (0%)
Unevaluable event [A] †	1/106 (0.94%)	0/53 (0%)
Xerosis [A] †	1/106 (0.94%)	0/53 (0%)
Hepatobiliary disorders		
Biliary colic [A] †	1/106 (0.94%)	0/53 (0%)
Cholecystitis [A] †	1/106 (0.94%)	0/53 (0%)
Cholelithiasis [A] †	1/106 (0.94%)	1/53 (1.89%)
Hepatic steatosis [A] †	1/106 (0.94%)	0/53 (0%)
Hepatomegaly [A] †	1/106 (0.94%)	3/53 (5.66%)
Hepatosplenomegaly [A] †	0/106 (0%)	1/53 (1.89%)
Hepatotoxicity [A] †	0/106 (0%)	1/53 (1.89%)
Jaundice [A] †	0/106 (0%)	1/53 (1.89%)
Immune system disorders		
Hypersensitivity [A] †	1/106 (0.94%)	0/53 (0%)
Seasonal allergy [A] †	2/106 (1.89%)	0/53 (0%)
Infections and infestations		
Abscess [A] †	1/106 (0.94%)	0/53 (0%)
Acarodermatitis [A] †	1/106 (0.94%)	0/53 (0%)
Anal abscess [A] †	1/106 (0.94%)	0/53 (0%)

	Eliglustat	Imiglucerase
	Affected/At Risk (%)	Affected/At Risk (%)
Atypical pneumonia [A] †	1/106 (0.94%)	0/53 (0%)
Bronchitis [A] †	4/106 (3.77%)	0/53 (0%)
Campylobacter gastroenteritis [A] †	1/106 (0.94%)	0/53 (0%)
Cellulitis [A] †	1/106 (0.94%)	0/53 (0%)
Conjunctivitis infective [A] †	0/106 (0%)	1/53 (1.89%)
Ear infection [A] †	2/106 (1.89%)	1/53 (1.89%)
Fungal infection [A] †	1/106 (0.94%)	0/53 (0%)
Fungal skin infection [A] †	1/106 (0.94%)	0/53 (0%)
Furuncle [A] †	1/106 (0.94%)	0/53 (0%)
Gastroenteritis [A] †	3/106 (2.83%)	0/53 (0%)
Gastroenteritis viral [A] †	5/106 (4.72%)	1/53 (1.89%)
Genital herpes [A] †	0/106 (0%)	1/53 (1.89%)
Herpes zoster [A] †	1/106 (0.94%)	0/53 (0%)
Hordeolum [A] †	0/106 (0%)	1/53 (1.89%)
Influenza [A] †	6/106 (5.66%)	2/53 (3.77%)
Lung infection [A] †	1/106 (0.94%)	0/53 (0%)
Molluscum contagiosum [A] †	1/106 (0.94%)	0/53 (0%)
Nail bed infection [A] †	1/106 (0.94%)	0/53 (0%)
Nasopharyngitis [A] †	11/106 (10.38%)	5/53 (9.43%)
Oral herpes [A] †	2/106 (1.89%)	0/53 (0%)
Otitis externa [A] †	1/106 (0.94%)	0/53 (0%)
Otitis media [A] †	1/106 (0.94%)	1/53 (1.89%)

	Eliglustat	Imiglucerase
	Affected/At Risk (%)	Affected/At Risk (%)
Paronychia [A] †	1/106 (0.94%)	0/53 (0%)
Pharyngitis [A] †	1/106 (0.94%)	0/53 (0%)
Pharyngitis streptococcal [A] †	1/106 (0.94%)	1/53 (1.89%)
Pneumonia [A] †	1/106 (0.94%)	0/53 (0%)
Post procedural infection [A] †	0/106 (0%)	1/53 (1.89%)
Respiratory tract infection [A] †	1/106 (0.94%)	0/53 (0%)
Sinusitis [A] †	11/106 (10.38%)	1/53 (1.89%)
Sinusitis bacterial [A] †	1/106 (0.94%)	0/53 (0%)
Skin infection [A] †	1/106 (0.94%)	0/53 (0%)
Staphylococcal skin infection [A] †	0/106 (0%)	1/53 (1.89%)
Streptococcal infection [A] †	2/106 (1.89%)	0/53 (0%)
Tinea pedis [A] †	0/106 (0%)	1/53 (1.89%)
Tonsillitis [A] †	0/106 (0%)	1/53 (1.89%)
Tooth abscess [A] †	1/106 (0.94%)	0/53 (0%)
Tooth infection [A] †	1/106 (0.94%)	1/53 (1.89%)
Upper respiratory tract infection [A] †	11/106 (10.38%)	3/53 (5.66%)
Urinary tract infection [A] †	5/106 (4.72%)	5/53 (9.43%)
Vaginitis gardnerella [A] †	1/106 (0.94%)	0/53 (0%)
Vulvovaginal mycotic infection [A] †	0/106 (0%)	1/53 (1.89%)
Injury, poisoning and procedural complications		
Arthropod bite [A] †	1/106 (0.94%)	0/53 (0%)
Arthropod sting [A] †	0/106 (0%)	1/53 (1.89%)

	Eliglustat	Imiglucerase
	Affected/At Risk (%)	Affected/At Risk (%)
Contusion [A] †	5/106 (4.72%)	0/53 (0%)
Excoriation [A] †	1/106 (0.94%)	0/53 (0%)
Fall [A] †	1/106 (0.94%)	0/53 (0%)
Foreign body [A] †	1/106 (0.94%)	0/53 (0%)
Hand fracture [A] †	1/106 (0.94%)	0/53 (0%)
Joint injury [A] †	1/106 (0.94%)	0/53 (0%)
Laceration [A] †	4/106 (3.77%)	0/53 (0%)
Ligament rupture [A] †	1/106 (0.94%)	0/53 (0%)
Ligament sprain [A] †	4/106 (3.77%)	0/53 (0%)
Limb injury [A] †	1/106 (0.94%)	1/53 (1.89%)
Muscle strain [A] †	1/106 (0.94%)	0/53 (0%)
Post procedural complication [A] †	0/106 (0%)	1/53 (1.89%)
Post-traumatic pain [A] †	1/106 (0.94%)	2/53 (3.77%)
Procedural pain [A] †	2/106 (1.89%)	1/53 (1.89%)
Investigations		
Alanine aminotransferase increased [A] †	2/106 (1.89%)	2/53 (3.77%)
Aspartate aminotransferase increased [A] †	1/106 (0.94%)	1/53 (1.89%)
Blood bilirubin increased [A] †	0/106 (0%)	1/53 (1.89%)
Blood cholesterol increased [A] †	1/106 (0.94%)	2/53 (3.77%)
Blood creatine phosphokinase increased [A] †	7/106 (6.6%)	1/53 (1.89%)
Blood folate decreased [A] †	2/106 (1.89%)	1/53 (1.89%)
Blood homocysteine increased [A] †	3/106 (2.83%)	0/53 (0%)

	Eliglustat	Imiglucerase
	Affected/At Risk (%)	Affected/At Risk (%)
Blood pressure increased [A] †	0/106 (0%)	1/53 (1.89%)
Blood thyroid stimulating hormone decreased [A] †	1/106 (0.94%)	0/53 (0%)
Blood urine present [A] †	1/106 (0.94%)	0/53 (0%)
C-reactive protein increased [A] †	3/106 (2.83%)	0/53 (0%)
Gamma-glutamyltransferase increased [A] †	2/106 (1.89%)	0/53 (0%)
Haematocrit decreased [A] †	1/106 (0.94%)	1/53 (1.89%)
Haemoglobin decreased [A] †	3/106 (2.83%)	1/53 (1.89%)
Hepatic enzyme increased [A] †	0/106 (0%)	2/53 (3.77%)
Mean cell haemoglobin increased [A] †	1/106 (0.94%)	0/53 (0%)
Nerve conduction studies abnormal [A] †	1/106 (0.94%)	0/53 (0%)
Platelet count decreased [A] †	1/106 (0.94%)	1/53 (1.89%)
Red blood cell count decreased [A] †	0/106 (0%)	1/53 (1.89%)
Serum ferritin increased [A] †	1/106 (0.94%)	0/53 (0%)
Urine leukocyte esterase positive [A] †	0/106 (0%)	1/53 (1.89%)
Vitamin B12 decreased [A] †	1/106 (0.94%)	0/53 (0%)
Weight decreased [A] †	2/106 (1.89%)	0/53 (0%)
White blood cell count decreased [A] †	1/106 (0.94%)	0/53 (0%)
White blood cell count increased [A] †	1/106 (0.94%)	0/53 (0%)
Metabolism and nutrition disorders		
Dyslipidaemia [A] †	1/106 (0.94%)	0/53 (0%)
Folate deficiency [A] †	1/106 (0.94%)	0/53 (0%)

	Eliglustat	Imiglucerase
	Affected/At Risk (%)	Affected/At Risk (%)
Hyperglycaemia [A] †	0/106 (0%)	1/53 (1.89%)
Hyperlipidaemia [A] †	2/106 (1.89%)	0/53 (0%)
Iron deficiency [A] †	1/106 (0.94%)	0/53 (0%)
Metabolic syndrome [A] †	1/106 (0.94%)	0/53 (0%)
Type 2 diabetes mellitus [A] †	1/106 (0.94%)	1/53 (1.89%)
Musculoskeletal and connective tissue disorders		
Arthralgia [A] †	16/106 (15.09%)	9/53 (16.98%)
Arthritis [A] †	2/106 (1.89%)	0/53 (0%)
Arthropathy [A] †	1/106 (0.94%)	0/53 (0%)
Back pain [A] †	13/106 (12.26%)	3/53 (5.66%)
Bone cyst [A] †	1/106 (0.94%)	0/53 (0%)
Bone pain [A] †	6/106 (5.66%)	1/53 (1.89%)
Intervertebral disc disorder [A] †	1/106 (0.94%)	0/53 (0%)
Intervertebral disc protrusion [A] †	1/106 (0.94%)	0/53 (0%)
Joint crepitation [A] †	1/106 (0.94%)	0/53 (0%)
Joint stiffness [A] †	4/106 (3.77%)	0/53 (0%)
Muscle spasms [A] †	2/106 (1.89%)	0/53 (0%)
Muscle tightness [A] †	1/106 (0.94%)	0/53 (0%)
Musculoskeletal pain [A] †	2/106 (1.89%)	2/53 (3.77%)
Myalgia [A] †	3/106 (2.83%)	1/53 (1.89%)
Osteopenia [A] †	1/106 (0.94%)	0/53 (0%)
Pain in extremity [A] †	12/106 (11.32%)	1/53 (1.89%)

	Eliglustat	Imiglucerase
	Affected/At Risk (%)	Affected/At Risk (%)
Plantar fasciitis [A] †	1/106 (0.94%)	0/53 (0%)
Spinal osteoarthritis [A] †	1/106 (0.94%)	0/53 (0%)
Temporomandibular joint syndrome [A] †	1/106 (0.94%)	0/53 (0%)
Tendon disorder [A] †	1/106 (0.94%)	1/53 (1.89%)
Tendonitis [A] †	1/106 (0.94%)	1/53 (1.89%)
Torticollis [A] †	1/106 (0.94%)	0/53 (0%)
Upper extremity mass [A] †	1/106 (0.94%)	0/53 (0%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)		
Adenoma benign [A] †	1/106 (0.94%)	0/53 (0%)
Lipoma [A] †	1/106 (0.94%)	0/53 (0%)
Neoplasm skin [A] †	1/106 (0.94%)	0/53 (0%)
Seborrhoeic keratosis [A] †	1/106 (0.94%)	0/53 (0%)
Skin papilloma [A] †	1/106 (0.94%)	0/53 (0%)
Uterine leiomyoma [A] †	1/106 (0.94%)	0/53 (0%)
Nervous system disorders		
Dizziness [A] †	9/106 (8.49%)	0/53 (0%)
Dysaesthesia [A] †	0/106 (0%)	1/53 (1.89%)
Dysgeusia [A] †	2/106 (1.89%)	0/53 (0%)
Headache [A] †	14/106 (13.21%)	1/53 (1.89%)
Hypoaesthesia [A] †	4/106 (3.77%)	0/53 (0%)
Hyposmia [A] †	1/106 (0.94%)	0/53 (0%)
Lumbar radiculopathy [A] †	1/106 (0.94%)	0/53 (0%)

	Eliglustat	Imiglucerase
	Affected/At Risk (%)	Affected/At Risk (%)
Memory impairment [A] †	1/106 (0.94%)	0/53 (0%)
Migraine [A] †	0/106 (0%)	1/53 (1.89%)
Neuralgia [A] †	2/106 (1.89%)	0/53 (0%)
Neuropathy peripheral [A] †	4/106 (3.77%)	0/53 (0%)
Paraesthesia [A] †	3/106 (2.83%)	1/53 (1.89%)
Parkinsonism [A] †	0/106 (0%)	1/53 (1.89%)
Parosmia [A] †	1/106 (0.94%)	0/53 (0%)
Sciatica [A] †	0/106 (0%)	1/53 (1.89%)
Sinus headache [A] †	0/106 (0%)	2/53 (3.77%)
Somnolence [A] †	3/106 (2.83%)	0/53 (0%)
Syncope [A] †	1/106 (0.94%)	0/53 (0%)
Tremor [A] †	3/106 (2.83%)	0/53 (0%)
VIIth nerve paralysis [A] †	1/106 (0.94%)	0/53 (0%)
Psychiatric disorders		
Anxiety [A] †	2/106 (1.89%)	2/53 (3.77%)
Apathy [A] †	1/106 (0.94%)	0/53 (0%)
Confusional state [A] †	1/106 (0.94%)	0/53 (0%)
Depression [A] †	1/106 (0.94%)	0/53 (0%)
Panic attack [A] †	0/106 (0%)	1/53 (1.89%)
Psychotic disorder [A] †	0/106 (0%)	1/53 (1.89%)
Restlessness [A] †	1/106 (0.94%)	0/53 (0%)
Stress [A] †	1/106 (0.94%)	0/53 (0%)

	Eliglustat	Imiglucerase
	Affected/At Risk (%)	Affected/At Risk (%)
Renal and urinary disorders		
Haematuria [A] †	2/106 (1.89%)	1/53 (1.89%)
Nephrolithiasis [A] †	1/106 (0.94%)	0/53 (0%)
Proteinuria [A] †	1/106 (0.94%)	0/53 (0%)
Renal pain [A] †	0/106 (0%)	1/53 (1.89%)
Reproductive system and breast disorders		
Breast cyst [A] †	1/106 (0.94%)	0/53 (0%)
Breast mass [A] †	1/106 (0.94%)	0/53 (0%)
Dysmenorrhoea [A] †	3/106 (2.83%)	0/53 (0%)
Menorrhagia [A] †	1/106 (0.94%)	0/53 (0%)
Menstruation irregular [A] †	1/106 (0.94%)	0/53 (0%)
Metrorrhagia [A] †	2/106 (1.89%)	1/53 (1.89%)
Polycystic ovaries [A] †	1/106 (0.94%)	0/53 (0%)
Pruritus genital [A] †	1/106 (0.94%)	0/53 (0%)
Vaginal haemorrhage [A] †	1/106 (0.94%)	1/53 (1.89%)
Respiratory, thoracic and mediastinal disorders		
Cough [A] †	7/106 (6.6%)	2/53 (3.77%)
Dysphonia [A] †	1/106 (0.94%)	0/53 (0%)
Dyspnoea [A] †	2/106 (1.89%)	0/53 (0%)
Epistaxis [A] †	5/106 (4.72%)	0/53 (0%)
Nasal congestion [A] †	1/106 (0.94%)	0/53 (0%)
Nasal septum deviation [A] †	1/106 (0.94%)	0/53 (0%)

	Eliglustat	Imiglucerase
	Affected/At Risk (%)	Affected/At Risk (%)
Oropharyngeal pain [A] †	4/106 (3.77%)	0/53 (0%)
Pulmonary hypertension [A] †	1/106 (0.94%)	0/53 (0%)
Rhinitis allergic [A] †	2/106 (1.89%)	0/53 (0%)
Throat irritation [A] †	2/106 (1.89%)	0/53 (0%)
Skin and subcutaneous tissue disorders		
Acne [A] †	1/106 (0.94%)	0/53 (0%)
Dermatitis contact [A] †	1/106 (0.94%)	2/53 (3.77%)
Dry skin [A] †	2/106 (1.89%)	0/53 (0%)
Ecchymosis [A] †	2/106 (1.89%)	0/53 (0%)
Eczema [A] †	1/106 (0.94%)	0/53 (0%)
Increased tendency to bruise [A] †	1/106 (0.94%)	0/53 (0%)
Petechiae [A] †	1/106 (0.94%)	0/53 (0%)
Pruritus [A] †	1/106 (0.94%)	1/53 (1.89%)
Psoriasis [A] †	1/106 (0.94%)	0/53 (0%)
Rash [A] †	5/106 (4.72%)	0/53 (0%)
Rosacea [A] †	1/106 (0.94%)	0/53 (0%)
Skin hyperpigmentation [A] †	1/106 (0.94%)	0/53 (0%)
Skin hypopigmentation [A] †	1/106 (0.94%)	0/53 (0%)
Sunburn [A] †	1/106 (0.94%)	0/53 (0%)
Swelling face [A] †	1/106 (0.94%)	0/53 (0%)
Urticaria [A] †	1/106 (0.94%)	0/53 (0%)
Social circumstances		

	Eliglustat	Imiglucerase
	Affected/At Risk (%)	Affected/At Risk (%)
Menopause [A] †	1/106 (0.94%)	0/53 (0%)
Surgical and medical procedures		
Catheter removal [A] †	1/106 (0.94%)	0/53 (0%)
Vascular disorders		
Aortic dilatation [A] †	0/106 (0%)	1/53 (1.89%)
Essential hypertension [A] †	1/106 (0.94%)	0/53 (0%)
Flushing [A] †	3/106 (2.83%)	0/53 (0%)
Hot flush [A] †	1/106 (0.94%)	0/53 (0%)
Hypertension [A] †	0/106 (0%)	1/53 (1.89%)
Hypotension [A] †	2/106 (1.89%)	0/53 (0%)

† Indicates events were collected by systematic assessment.
A Term from vocabulary, MedDRA 15.1

Limitations and Caveats

The results include data up to the end of primary analysis period (Week 52).

More Information

Certain Agreements:

Principal Investigators are NOT employed by the organization sponsoring the study.

There IS an agreement between the Principal Investigator and the Sponsor (or its agents) that restricts the PI's rights to discuss or publish trial results after the trial is completed.

If no publication has occurred within 12 months of the completion of the study, the Investigator shall have the right to publish/present independently the results of the study. The Investigator shall provide the Sponsor with a copy of any such presentation/publication for comment at least 30 days before any presentation/submission for publication. If requested by the Sponsor, any presentation/submission shall be delayed up to 90 days, to allow the Sponsor to preserve its proprietary rights.

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