Clinical trial results:
A Multicenter, Randomized, Double-Blind, Parallel-Group Study of Gene-Activated® Human Glucocerebrosidase (GA-GCB) Enzyme Replacement Therapy Compared with Imiglucerase in Patients with Type I Gaucher Disease

Summary

EudraCT number	2007-002840-21
Trial protocol	ES GB IT
Global end of trial date	05 May 2009

Results information

Result version number	v1 (current)
This version publication date	04 September 2018
First version publication date	31 May 2015

Trial information

Trial identification

Sponsor protocol code	HGT-GCB-039

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00553631
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Shire
Sponsor organisation address	300 Shire Way, Lexington, Massachusetts, United States, 02421
Public contact	Tiffany Crump, Medical Communications Manager, Shire HGT, +1 484-595-8850, tcrump@shire.com
Scientific contact	Tiffany Crump, Medical Communications Manager, Shire HGT, +1 484-595-8850, tcrump@shire.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-000556-PIP01-09
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?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	05 May 2009
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	05 May 2009
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study was to compare the effects of velaglucerase alfa and imiglucerase on hemoglobin concentration in subjects with type 1 Gaucher disease.

Protection of trial subjects:

This study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki. This study was also conducted in accordance with local country regulations and International Conference on Harmonisation (ICH) Good Clinical Practice (GCP) E6 guidelines.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	29 January 2008
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Spain: 3
Country: Number of subjects enrolled	United Kingdom: 1
Country: Number of subjects enrolled	Paraguay: 5
Country: Number of subjects enrolled	Argentina: 3
Country: Number of subjects enrolled	Israel: 4
Country: Number of subjects enrolled	Russian Federation: 4
Country: Number of subjects enrolled	Tunisia: 6
Country: Number of subjects enrolled	United States: 1
Country: Number of subjects enrolled	India: 8
Worldwide total number of subjects	35
EEA total number of subjects	4

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)	7
Adolescents (12-17 years)	2
Adults (18-64 years)	25
From 65 to 84 years	1
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted in multiple sites from 29 January 2008 (first subject first enrolled) to 05 May 2009 (last subject completed).

Pre-assignment

Screening details:

Subjects at least 2 years of age with type 1 Gaucher disease.Gaucher-disease-related anemia and at least 1 of the following: moderate splenomegaly, Gaucher-disease-related thrombocytopenia, readily palpable enlarged liver. Subjects had not received treatment for Gaucher disease within 12 months prior to study entry.

Period 1

Period 1 title	Overall study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Gene-Activated Human Glucocerebrosidase (GA-GCB)

Arm description:

Velaglucerase alfa 60 unit per kilogram (U/kg) administered intravenously (IV) every other week for 39 weeks.

Arm type	Experimental
Investigational medicinal product name	velaglucerase alfa
Investigational medicinal product code	GA-GCB
Other name	VPRIV™, gene-activated human glucocerebrosidase
Pharmaceutical forms	Powder for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Velaglucerase alfa 60 U/kg administered IV every other week for 39 weeks.

Arm title	Imiglucerase

Arm description:

Imiglucerase 60 U/kg administered IV every other week for 39 weeks.

Arm type	Active comparator
Investigational medicinal product name	Imiglucerase
Investigational medicinal product code	
Other name	Cerezyme
Pharmaceutical forms	Powder for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Imiglucerase 60 U/kg administered IV every other week for 39 weeks.

Number of subjects in period 1[1]	Gene-Activated Human Glucocerebrosidase (GA-GCB)	Imiglucerase
Started	17	17
Completed	16	16
Not completed	1	1
Consent withdrawn by subject	-	1
Lost to follow-up	1	-

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: The baseline included only subjects who received treatment. Since 1 subject from the 35 randomized subjects did not receive treatment hence it was excluded.

Baseline characteristics

Reporting groups	
Reporting group title	Gene-Activated Human Glucocerebrosidase (GA-GCB)
Reporting group description:	
Velaglucerase alfa 60 unit per kilogram (U/kg) administered intravenously (IV) every other week for 39 weeks.	
Reporting group title	Imiglucerase
Reporting group description:	
Imiglucerase 60 U/kg administered IV every other week for 39 weeks.	

Reporting group values	Gene-Activated Human Glucocerebrosidase (GA-GCB)	Imiglucerase	Total
Number of subjects	17	17	34
Age categorical Units: Subjects			
Less than equal to (<=)18 years	4	5	9
Between 18 and 65 years	13	11	24
Greater than equal to (>=) 65 years	0	1	1
Age continuous			
Age at the time of consent.			
Units: years			
median	36	27	
full range (min-max)	7 to 60	3 to 37	-
Gender categorical Units: Subjects			
Female	9	9	18
Male	8	8	16

End points

End points reporting groups

Reporting group title	Gene-Activated Human Glucocerebrosidase (GA-GCB)
Reporting group description:	
Velaglucerase alfa 60 unit per kilogram (U/kg) administered intravenously (IV) every other week for 39 weeks.	
Reporting group title	Imiglucerase
Reporting group description:	
Imiglucerase 60 U/kg administered IV every other week for 39 weeks.	

Primary: Mean Change From Baseline to Month 9 in Hemoglobin (Hgb) Concentration for Each Treatment Group

End point title	Mean Change From Baseline to Month 9 in Hemoglobin (Hgb) Concentration for Each Treatment Group[1]
End point description:	
Intent-to-treat (ITT) population comprised of all randomized subjects who received at least 1 full or partial dose of study drug.	
End point type	Primary
End point timeframe:	
Baseline to Month 9	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Descriptive statistical analysis was only performed and inferential statistical analysis was not performed for this endpoint.

End point values	Gene-Activated Human Glucocerebrosidase (GA-GCB)	Imiglucerase		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	17	17		
Units: gram per deciliter (g/dl)				
arithmetic mean (standard error)	1.624 (± 0.223)	1.488 (± 0.281)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline to Month 9 in Platelet Counts for Each Treatment Group

End point title	Change From Baseline to Month 9 in Platelet Counts for Each Treatment Group
End point description:	
Values shown are observed change from Baseline to Month 9. ITT population	
End point type	Secondary

End point timeframe:

Baseline to Month 9

End point values	Gene-Activated Human Glucocerebrosidase (GA-GCB)	Imiglucerase		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	17	17		
Units: 10^9 per liter (10^9/L)				
arithmetic mean (standard error)	110.41 (± 17.159)	144.38 (± 22.76)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline to Month 9 in Normalized Liver Volume (Percent (%) Body Weight) for Each Treatment Group

End point title	Change From Baseline to Month 9 in Normalized Liver Volume (Percent (%) Body Weight) for Each Treatment Group

End point description:

Values shown are observed change from Baseline to Month 9. Measured by Magnetic resonance imaging (MRI). Liver volume has been normalized for percent (%) body weight for each treatment arm. Liver size relative to body weight = (Liver volume [cubic centimeter (cc)]/Body weight [kg]*1000. ITT population.

End point type	Secondary

End point timeframe:

Baseline to Month 9

End point values	Gene-Activated Human Glucocerebrosidase (GA-GCB)	Imiglucerase		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	17	17		
Units: cubic centimeter (cm^3)				
arithmetic mean (standard error)	-1.31 (± 0.347)	-1.1 (± 0.182)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline to Month 9 in Normalized Spleen Volume (Percent

(%) Body Weight) for Each Treatment Group

End point title	Change From Baseline to Month 9 in Normalized Spleen Volume (Percent (%) Body Weight) for Each Treatment Group

End point description:

Values shown are observed change from Baseline to month 9. Measured by Magnetic resonance imaging (MRI). Spleen volume was normalized for percent (%) of body weight for each treatment arm. Spleen size relative to body weight = (Spleen volume [cc]/Body weight [kg])*100. Ten subjects in each treatment group underwent splenectomy, and therefore, were excluded from the analysis. ITT population. Number of subjects analysed signifies subjects evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Baseline to Month 9

End point values	Gene-Activated Human Glucocerebrosidase (GA-GCB)	Imiglucerase		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7	7		
Units: cm^3				
arithmetic mean (standard error)	-1.34 (± 0.424)	-2.46 (± 0.966)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline to Month 9 in Plasma Chitotriosidase for Each Treatment Group

End point title	Change From Baseline to Month 9 in Plasma Chitotriosidase for Each Treatment Group

End point description:

Values shown are observed change from Baseline to Month 9. Chitotriosidase levels were measured in 10 subjects in the velaglucerase alfa group and 11 subjects in the imiglucerase group. Units of measure is defined as nanomole per milliliter per hour. ITT population. Number of subjects analysed signifies subjects evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Baseline to Month 9

End point values	Gene-Activated Human Glucocerebrosidase (GA-GCB)	Imiglucerase		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	11		
Units: nanomole/milliliter/hour (nmol/mL/h)				

arithmetic mean (standard error)	-34711.9 (± 6887.77)	-35109.5 (± 7310.22)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline to Month 9 in Plasma Chemokine (C-C Motif) Ligand 18 (CCL18) for Each Treatment Group

End point title	Change From Baseline to Month 9 in Plasma Chemokine (C-C Motif) Ligand 18 (CCL18) for Each Treatment Group

End point description:

Values shown are observed change from Baseline to Month 9. ITT population.

End point type	Secondary

End point timeframe:

Baseline to Month 9

End point values	Gene-Activated Human Glucocerebrosidase (GA-GCB)	Imiglucerase		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	17	17		
Units: nanogram per milliliter (ng/mL)				
arithmetic mean (standard error)	-926.2 (± 113.29)	-1153.4 (± 269.63)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects Who Developed Antibody for Each Treatment Group

End point title	Number of Subjects Who Developed Antibody for Each Treatment Group

End point description:

Measure type is actual number of subjects who developed antibodies to treatment; GA-GCB or imiglucerase. Antibody detection was based upon serum samples collected at various time points throughout the study. Serum samples were screened using an enzyme-linked immunosorbent assay (ELISA) and positive antibody confirmation was determined using a radioimmunoprecipitation assay (RIP); positive samples were also tested for enzyme neutralizing activity. Subject samples were compared to internal assay controls (positive/negative), positive samples were determined based upon individual assay criteria.

Safety population comprised of all randomized subjects who received at least 1 full or partial dose of study drug.

End point type	Secondary

End point timeframe:

Baseline to Month 9

End point values	Gene-Activated Human Glucocerebrosidase (GA-GCB)	Imiglucerase		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	17	17		
Units: subjects	0	4		

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Response- Comparison of GA-GCB and Imiglucerase on the Earliest Time to Respond as Assessed Via Hemoglobin Concentration

End point title	Time to Response- Comparison of GA-GCB and Imiglucerase on the Earliest Time to Respond as Assessed Via Hemoglobin Concentration

End point description:

Time to response was defined as a ≥ 1 g/dL improvement in hemoglobin levels relative to Baseline. Units (%) correlates to the percentage of subjects who had a change of ≥ 1 g/dL improvement in hemoglobin levels relative to Baseline during their participation in the study. ITT population.

End point type	Secondary

End point timeframe:

Response rate at Month 9 compared to Baseline

End point values	Gene-Activated Human Glucocerebrosidase (GA-GCB)	Imiglucerase		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	17	17		
Units: percentage of participants				
number (not applicable)	92.9	100		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events (AE) monitored from time informed consent/assent obtained through 30 days after the last infusion. For patients (pt) who completed this study and elected to enroll in the long-term extension study, AEs were monitored through the Week 41.

Adverse event reporting additional description:

AE may have been discovered via observation, examination, questioning or complaint by subjects. Unexpected laboratory values that became significantly out of range and determined to be clinically significant by the investigator could have been reported as AEs. Other AE were determined to be possibly/probably related to GA-GCB by the investigator.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	9.0

Reporting groups

Reporting group title	Gene-Activated Human Glucocerebrosidase (GA-GCB)

Reporting group description:

Velaglucerase alfa 60 U/kg administered IV every other week for 39 weeks.

Reporting group title	Imiglucerase

Reporting group description:

Imiglucerase 60 U/kg administered IV every other week for 39 weeks.

Serious adverse events	Gene-Activated Human Glucocerebrosidase (GA-GCB)	Imiglucerase	
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 17 (17.65%)	0 / 17 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
Nervous system disorders			
Convulsion			
subjects affected / exposed	1 / 17 (5.88%)	0 / 17 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Thrombocytopenia			
subjects affected / exposed	1 / 17 (5.88%)	0 / 17 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			

Dermatitis allergic			
subjects affected / exposed	1 / 17 (5.88%)	0 / 17 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Gene-Activated Human Glucocerebrosidase (GA-GCB)	Imiglucerase	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	16 / 17 (94.12%)	16 / 17 (94.12%)	
Vascular disorders			
Flushing			
subjects affected / exposed	0 / 17 (0.00%)	1 / 17 (5.88%)	
occurrences (all)	0	2	
Hypertension			
subjects affected / exposed	1 / 17 (5.88%)	0 / 17 (0.00%)	
occurrences (all)	1	0	
Hypotension			
subjects affected / exposed	1 / 17 (5.88%)	1 / 17 (5.88%)	
occurrences (all)	1	1	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 17 (5.88%)	0 / 17 (0.00%)	
occurrences (all)	1	0	
Axillary pain			
subjects affected / exposed	1 / 17 (5.88%)	0 / 17 (0.00%)	
occurrences (all)	1	0	
Chills			
subjects affected / exposed	0 / 17 (0.00%)	1 / 17 (5.88%)	
occurrences (all)	0	2	
Face oedema			
subjects affected / exposed	1 / 17 (5.88%)	0 / 17 (0.00%)	
occurrences (all)	1	0	
Fatigue			

subjects affected / exposed	0 / 17 (0.00%)	1 / 17 (5.88%)	
occurrences (all)	0	1	
Feeling abnormal			
subjects affected / exposed	0 / 17 (0.00%)	1 / 17 (5.88%)	
occurrences (all)	0	1	
Feeling cold			
subjects affected / exposed	0 / 17 (0.00%)	1 / 17 (5.88%)	
occurrences (all)	0	3	
Feeling hot			
subjects affected / exposed	0 / 17 (0.00%)	1 / 17 (5.88%)	
occurrences (all)	0	2	
Hunger			
subjects affected / exposed	0 / 17 (0.00%)	1 / 17 (5.88%)	
occurrences (all)	0	1	
Inflammatory pain			
subjects affected / exposed	0 / 17 (0.00%)	1 / 17 (5.88%)	
occurrences (all)	0	1	
Influenza like illness			
subjects affected / exposed	0 / 17 (0.00%)	2 / 17 (11.76%)	
occurrences (all)	0	4	
Injection site haemorrhage			
subjects affected / exposed	1 / 17 (5.88%)	1 / 17 (5.88%)	
occurrences (all)	1	1	
Oedema peripheral			
subjects affected / exposed	3 / 17 (17.65%)	0 / 17 (0.00%)	
occurrences (all)	3	0	
Pain			
subjects affected / exposed	0 / 17 (0.00%)	1 / 17 (5.88%)	
occurrences (all)	0	1	
Pyrexia			
subjects affected / exposed	4 / 17 (23.53%)	2 / 17 (11.76%)	
occurrences (all)	4	3	
Immune system disorders			
Food allergy			
subjects affected / exposed	1 / 17 (5.88%)	0 / 17 (0.00%)	
occurrences (all)	1	0	

Hypersensitivity			
subjects affected / exposed	2 / 17 (11.76%)	0 / 17 (0.00%)	
occurrences (all)	2	0	
Reproductive system and breast disorders			
Pelvic pain			
subjects affected / exposed	1 / 17 (5.88%)	0 / 17 (0.00%)	
occurrences (all)	1	0	
Vaginal discharge			
subjects affected / exposed	0 / 17 (0.00%)	1 / 17 (5.88%)	
occurrences (all)	0	2	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	2 / 17 (11.76%)	2 / 17 (11.76%)	
occurrences (all)	2	2	
Dyspnoea			
subjects affected / exposed	0 / 17 (0.00%)	1 / 17 (5.88%)	
occurrences (all)	0	1	
Epistaxis			
subjects affected / exposed	2 / 17 (11.76%)	2 / 17 (11.76%)	
occurrences (all)	2	7	
Pharyngolaryngeal pain			
subjects affected / exposed	1 / 17 (5.88%)	1 / 17 (5.88%)	
occurrences (all)	1	1	
Respiratory disorder			
subjects affected / exposed	1 / 17 (5.88%)	0 / 17 (0.00%)	
occurrences (all)	1	0	
Rhinorrhoea			
subjects affected / exposed	1 / 17 (5.88%)	1 / 17 (5.88%)	
occurrences (all)	1	1	
Stridor			
subjects affected / exposed	0 / 17 (0.00%)	1 / 17 (5.88%)	
occurrences (all)	0	1	
Psychiatric disorders			
Insomnia			
subjects affected / exposed	1 / 17 (5.88%)	0 / 17 (0.00%)	
occurrences (all)	1	0	

Investigations			
Blood potassium increased			
subjects affected / exposed	0 / 17 (0.00%)	1 / 17 (5.88%)	
occurrences (all)	0	1	
Activated partial thromboplastin time prolonged			
subjects affected / exposed	1 / 17 (5.88%)	0 / 17 (0.00%)	
occurrences (all)	1	0	
Blood pressure systolic increased			
subjects affected / exposed	0 / 17 (0.00%)	1 / 17 (5.88%)	
occurrences (all)	0	2	
Electrocardiogram abnormal			
subjects affected / exposed	0 / 17 (0.00%)	1 / 17 (5.88%)	
occurrences (all)	0	1	
Laboratory test abnormal			
subjects affected / exposed	1 / 17 (5.88%)	1 / 17 (5.88%)	
occurrences (all)	1	1	
Oxygen saturation decreased			
subjects affected / exposed	0 / 17 (0.00%)	1 / 17 (5.88%)	
occurrences (all)	0	1	
Prothrombin time prolonged			
subjects affected / exposed	1 / 17 (5.88%)	0 / 17 (0.00%)	
occurrences (all)	1	0	
Serum ferritin increased			
subjects affected / exposed	1 / 17 (5.88%)	0 / 17 (0.00%)	
occurrences (all)	1	0	
Injury, poisoning and procedural complications			
Injury			
subjects affected / exposed	1 / 17 (5.88%)	0 / 17 (0.00%)	
occurrences (all)	1	0	
Post-Traumatic pain			
subjects affected / exposed	0 / 17 (0.00%)	1 / 17 (5.88%)	
occurrences (all)	0	1	
Tongue injury			
subjects affected / exposed	1 / 17 (5.88%)	0 / 17 (0.00%)	
occurrences (all)	1	0	
Cardiac disorders			

Sinus bradycardia			
subjects affected / exposed	1 / 17 (5.88%)	0 / 17 (0.00%)	
occurrences (all)	1	0	
Sinus tachycardia			
subjects affected / exposed	0 / 17 (0.00%)	1 / 17 (5.88%)	
occurrences (all)	0	1	
Nervous system disorders			
Carpal tunnel syndrome			
subjects affected / exposed	0 / 17 (0.00%)	1 / 17 (5.88%)	
occurrences (all)	0	1	
Convulsion			
subjects affected / exposed	0 / 17 (0.00%)	1 / 17 (5.88%)	
occurrences (all)	0	1	
Dizziness			
subjects affected / exposed	1 / 17 (5.88%)	2 / 17 (11.76%)	
occurrences (all)	1	3	
Headache			
subjects affected / exposed	3 / 17 (17.65%)	3 / 17 (17.65%)	
occurrences (all)	7	6	
Hemiparesis			
subjects affected / exposed	1 / 17 (5.88%)	0 / 17 (0.00%)	
occurrences (all)	1	0	
Migraine			
subjects affected / exposed	0 / 17 (0.00%)	1 / 17 (5.88%)	
occurrences (all)	0	2	
Paraesthesia			
subjects affected / exposed	2 / 17 (11.76%)	1 / 17 (5.88%)	
occurrences (all)	2	1	
Tremor			
subjects affected / exposed	0 / 17 (0.00%)	1 / 17 (5.88%)	
occurrences (all)	0	1	
Blood and lymphatic system disorders			
Spontaneous haematoma			
subjects affected / exposed	0 / 17 (0.00%)	1 / 17 (5.88%)	
occurrences (all)	0	1	
Thrombocythaemia			

subjects affected / exposed	1 / 17 (5.88%)	1 / 17 (5.88%)	
occurrences (all)	1	1	
Thrombocytopenia			
subjects affected / exposed	0 / 17 (0.00%)	1 / 17 (5.88%)	
occurrences (all)	0	1	
Eye disorders			
Conjunctivitis			
subjects affected / exposed	1 / 17 (5.88%)	0 / 17 (0.00%)	
occurrences (all)	1	0	
Dry eye			
subjects affected / exposed	1 / 17 (5.88%)	0 / 17 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	0 / 17 (0.00%)	1 / 17 (5.88%)	
occurrences (all)	0	1	
Abdominal pain			
subjects affected / exposed	1 / 17 (5.88%)	2 / 17 (11.76%)	
occurrences (all)	2	3	
Abdominal pain upper			
subjects affected / exposed	1 / 17 (5.88%)	3 / 17 (17.65%)	
occurrences (all)	1	4	
Aphthous stomatitis			
subjects affected / exposed	1 / 17 (5.88%)	0 / 17 (0.00%)	
occurrences (all)	1	0	
Constipation			
subjects affected / exposed	0 / 17 (0.00%)	1 / 17 (5.88%)	
occurrences (all)	0	1	
Diarrhoea			
subjects affected / exposed	3 / 17 (17.65%)	1 / 17 (5.88%)	
occurrences (all)	4	1	
Food poisoning			
subjects affected / exposed	1 / 17 (5.88%)	0 / 17 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorder			

subjects affected / exposed	1 / 17 (5.88%)	0 / 17 (0.00%)	
occurrences (all)	1	0	
Gingival bleeding			
subjects affected / exposed	0 / 17 (0.00%)	1 / 17 (5.88%)	
occurrences (all)	0	1	
Nausea			
subjects affected / exposed	1 / 17 (5.88%)	0 / 17 (0.00%)	
occurrences (all)	3	0	
Odynophagia			
subjects affected / exposed	1 / 17 (5.88%)	0 / 17 (0.00%)	
occurrences (all)	1	0	
Tooth loss			
subjects affected / exposed	1 / 17 (5.88%)	0 / 17 (0.00%)	
occurrences (all)	1	0	
Toothache			
subjects affected / exposed	1 / 17 (5.88%)	0 / 17 (0.00%)	
occurrences (all)	1	0	
Vomiting			
subjects affected / exposed	1 / 17 (5.88%)	2 / 17 (11.76%)	
occurrences (all)	2	2	
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	1 / 17 (5.88%)	1 / 17 (5.88%)	
occurrences (all)	1	1	
Dermatitis allergic			
subjects affected / exposed	1 / 17 (5.88%)	0 / 17 (0.00%)	
occurrences (all)	1	0	
Lichen planus			
subjects affected / exposed	0 / 17 (0.00%)	1 / 17 (5.88%)	
occurrences (all)	0	1	
Pruritus			
subjects affected / exposed	2 / 17 (11.76%)	0 / 17 (0.00%)	
occurrences (all)	3	0	
Rash			
subjects affected / exposed	1 / 17 (5.88%)	0 / 17 (0.00%)	
occurrences (all)	1	0	

Rash pruritic			
subjects affected / exposed	0 / 17 (0.00%)	1 / 17 (5.88%)	
occurrences (all)	0	1	
Swelling face			
subjects affected / exposed	1 / 17 (5.88%)	0 / 17 (0.00%)	
occurrences (all)	2	0	
Urticaria			
subjects affected / exposed	2 / 17 (11.76%)	1 / 17 (5.88%)	
occurrences (all)	2	2	
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	1 / 17 (5.88%)	1 / 17 (5.88%)	
occurrences (all)	1	1	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	4 / 17 (23.53%)	3 / 17 (17.65%)	
occurrences (all)	11	21	
Arthritis			
subjects affected / exposed	0 / 17 (0.00%)	1 / 17 (5.88%)	
occurrences (all)	0	1	
Arthropathy			
subjects affected / exposed	0 / 17 (0.00%)	1 / 17 (5.88%)	
occurrences (all)	0	1	
Back pain			
subjects affected / exposed	2 / 17 (11.76%)	2 / 17 (11.76%)	
occurrences (all)	2	3	
Bone pain			
subjects affected / exposed	2 / 17 (11.76%)	3 / 17 (17.65%)	
occurrences (all)	4	3	
Muscle spasms			
subjects affected / exposed	1 / 17 (5.88%)	2 / 17 (11.76%)	
occurrences (all)	1	2	
Myalgia			
subjects affected / exposed	2 / 17 (11.76%)	1 / 17 (5.88%)	
occurrences (all)	2	1	
Neck pain			

subjects affected / exposed	2 / 17 (11.76%)	1 / 17 (5.88%)	
occurrences (all)	2	1	
Pain in extremity			
subjects affected / exposed	1 / 17 (5.88%)	1 / 17 (5.88%)	
occurrences (all)	1	3	
Shoulder pain			
subjects affected / exposed	0 / 17 (0.00%)	1 / 17 (5.88%)	
occurrences (all)	0	1	
Infections and infestations			
Bronchitis			
subjects affected / exposed	1 / 17 (5.88%)	2 / 17 (11.76%)	
occurrences (all)	1	2	
Bronchitis acute			
subjects affected / exposed	1 / 17 (5.88%)	1 / 17 (5.88%)	
occurrences (all)	2	1	
Cystitis			
subjects affected / exposed	2 / 17 (11.76%)	1 / 17 (5.88%)	
occurrences (all)	2	1	
Cervicitis			
subjects affected / exposed	1 / 17 (5.88%)	0 / 17 (0.00%)	
occurrences (all)	1	0	
Ear infection			
subjects affected / exposed	1 / 17 (5.88%)	0 / 17 (0.00%)	
occurrences (all)	1	0	
Gastroenteritis			
subjects affected / exposed	1 / 17 (5.88%)	0 / 17 (0.00%)	
occurrences (all)	1	0	
Helminthic infection			
subjects affected / exposed	1 / 17 (5.88%)	0 / 17 (0.00%)	
occurrences (all)	1	0	
Herpes simplex			
subjects affected / exposed	0 / 17 (0.00%)	1 / 17 (5.88%)	
occurrences (all)	0	1	
Infection parasitic			
subjects affected / exposed	0 / 17 (0.00%)	1 / 17 (5.88%)	
occurrences (all)	0	1	

Influenza			
subjects affected / exposed	3 / 17 (17.65%)	4 / 17 (23.53%)	
occurrences (all)	4	6	
Nasopharyngitis			
subjects affected / exposed	3 / 17 (17.65%)	3 / 17 (17.65%)	
occurrences (all)	3	3	
Otitis externa			
subjects affected / exposed	1 / 17 (5.88%)	0 / 17 (0.00%)	
occurrences (all)	1	0	
Paronychia			
subjects affected / exposed	1 / 17 (5.88%)	0 / 17 (0.00%)	
occurrences (all)	1	0	
Pulpitis dental			
subjects affected / exposed	1 / 17 (5.88%)	0 / 17 (0.00%)	
occurrences (all)	1	0	
Respiratory tract infection			
subjects affected / exposed	0 / 17 (0.00%)	1 / 17 (5.88%)	
occurrences (all)	0	1	
Rhinitis			
subjects affected / exposed	3 / 17 (17.65%)	1 / 17 (5.88%)	
occurrences (all)	3	1	
Sinusitis			
subjects affected / exposed	1 / 17 (5.88%)	0 / 17 (0.00%)	
occurrences (all)	1	0	
Skin bacterial infection			
subjects affected / exposed	0 / 17 (0.00%)	1 / 17 (5.88%)	
occurrences (all)	0	1	
Tinea versicolour			
subjects affected / exposed	2 / 17 (11.76%)	0 / 17 (0.00%)	
occurrences (all)	2	0	
Staphylococcal infection			
subjects affected / exposed	0 / 17 (0.00%)	1 / 17 (5.88%)	
occurrences (all)	0	1	
Tonsillitis			
subjects affected / exposed	1 / 17 (5.88%)	0 / 17 (0.00%)	
occurrences (all)	2	0	

Tooth infection			
subjects affected / exposed	0 / 17 (0.00%)	1 / 17 (5.88%)	
occurrences (all)	0	1	
Upper respiratory tract infection			
subjects affected / exposed	0 / 17 (0.00%)	1 / 17 (5.88%)	
occurrences (all)	0	1	
Urinary tract infection			
subjects affected / exposed	2 / 17 (11.76%)	0 / 17 (0.00%)	
occurrences (all)	2	0	
Viral infection			
subjects affected / exposed	0 / 17 (0.00%)	1 / 17 (5.88%)	
occurrences (all)	0	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
13 February 2007	• Change the cytokine assessment used from Macrophage Colony Stimulating Factor (MCSF) to Granulocyte Macrophage Colony Stimulating Factor (GM-CSF). • The requirement for pregnancy testing was changed from a urine and a serum test at all visits during the treatment phase to a urine test followed by a serum test only if the urine test was positive. • Change collection of adverse event information from time of first infusion to time of informed consent.
10 June 2008	• The language describing the primary endpoint was modified to: The primary endpoint of this study is to measure the mean change from Baseline to Week 41/End of Study (EOS) in hemoglobin concentration between the two treatment groups. Previously it was not specified that the change was to Week 41. • The language describing the tertiary endpoint of evaluating cytokine parameters was changed to indicate that this would only occur in subjects who were ≥ 18 years of age. • The inclusion criteria defining Gaucher-disease-related anemia, was altered by removing the definition of "being at least 0.5 g/dL" below the lower limit of normal for age and gender. • The inclusion criterion regarding the need for contraception during study participation had the text added for clarification regarding contraception requirements for men in the study to specify that male subjects must use a medically acceptable method of birth control throughout their participation in the study and must report pregnancy of a partner. • The text in Exclusion Criterion 2 has had text added for clarification regarding immunogenic reactions. In addition to being antibody positive or experiencing an anaphylactic reaction, it was specified that a subject could not be anaphylactoid. • Clarifying text was added to Exclusion Criterion 4. The example of erythropoietin for a red blood cell growth factor was added and it was specified that the use of inhaled corticosteroid therapy and intermittent corticosteroids was permitted in certain circumstances. • An additional exclusion criterion was added, specifying that pregnant or lactating women were excluded. • Additional blood sampling for subjects ≥18 years of age was added for immune and inflammatory response testing. • Frequency of chitotriosidase and CCL18 measurement was changed from every study visit (excluding Week 1 and Week 41) to every other week (including Week 1 and Week 41)

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

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

Subjects aged 2-4 years: 4 subjects (23.5%) in the imiglucerase group and 0 subjects in the GA-GCB group.

Notes: