Clinical trial results:
An Open-Label Extension Study of Gene-Activated® Human Glucocerebrosidase (GA-GCB) Enzyme Replacement Therapy in Patients with Type 1 Gaucher Disease

Summary

EudraCT number	2008-001965-27
Trial protocol	GB ES
Global end of trial date	28 December 2012

Results information

Result version number	v1 (current)
This version publication date	04 September 2018
First version publication date	20 March 2015

Trial information

Trial identification

Sponsor protocol code	HGT-GCB-044

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00635427
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Shire Human Genetic Therapies (HGT), Inc.
Sponsor organisation address	300 Shire Way, Lexington, MA, United States, 02421
Public contact	MedInfo, Shire, +1 8668880660, US_ShireHGT_Medicalinformation@shire.com
Scientific contact	MedInfo, Shire, +1 8668880660, US_ShireHGT_Medicalinformation@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?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	28 December 2012
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	28 December 2012
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this Phase III clinical study was to evaluate the long-term safety of velaglucerase alfa when administered every other week (EOW) intravenously (IV) 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 and that are consistent with Good Clinical Practice (GCP) and applicable regulatory requirements. Known instances of non-conformance were documented and are not considered to have had an impact on the overall conclusions of this study.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	13 March 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	United Kingdom: 4
Country: Number of subjects enrolled	Tunisia: 9
Country: Number of subjects enrolled	Spain: 4
Country: Number of subjects enrolled	Korea, Republic of: 1
Country: Number of subjects enrolled	Russian Federation: 7
Country: Number of subjects enrolled	Poland: 5
Country: Number of subjects enrolled	Paraguay: 16
Country: Number of subjects enrolled	Israel: 18
Country: Number of subjects enrolled	India: 7
Country: Number of subjects enrolled	United States: 21
Country: Number of subjects enrolled	Argentina: 3
Worldwide total number of subjects	95
EEA total number of subjects	13

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)	13
Adolescents (12-17 years)	11
Adults (18-64 years)	68
From 65 to 84 years	3
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The first subject was enrolled in the study on 13 March 2008 and the last subject completed study procedures on 28 December 2012.

Pre-assignment

Screening details: -

Pre-assignment period milestones

Number of subjects started	95
Intermediate milestone: Number of subjects	Intent-to-treat (ITT) population: 93
Intermediate milestone: Number of subjects	Safety population: 95
Number of subjects completed	93

Pre-assignment subject non-completion reasons

Reason: Number of subjects	Did not have type 1 Gaucher disease: 2

Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	VPRIV 60 U/kg (Parent Study VPRIV (45 U/kg)-TKT032)

Arm description:

VPRIV 45 units per kilogram (U/kg), IV, EOW for 51 weeks in parent study TKT032 (2008-001965-27) and switched to 60 U/kg in HGT-GCB-044.

Arm type	Experimental
Investigational medicinal product name	Velaglucerase alfa
Investigational medicinal product code	
Other name	VPRIV®, Gene-Activated Human Glucocerebrosidase (GA-GCB)
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

VPRIV 45 U/kg, IV, EOW for 51 weeks in parent study TKT032 (2008-001965-27) and switched to 60 U/kg in HGT-GCB-044.

Arm title	VPRIV 60 U/kg (Parent Study VPRIV (60 U/kg)-TKT032)

Arm description:

VPRIV 60 U/kg, IV, EOW for 51 weeks in parent study TKT032 (2008-001965-27).

Arm type	Experimental
Investigational medicinal product name	Velaglucerase alfa
Investigational medicinal product code	
Other name	VPRIV®, Gene-Activated Human Glucocerebrosidase (GA-GCB)
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

VPRIV 60 U/kg, IV, EOW for 51 weeks in parent study TKT032 (2008-001965-27).

Arm title	VPRIV 60 U/kg (Parent Study VPRIV (60U/kg) HGT-GCB-039)

Arm description:

VPRIV 60 U/kg, IV, EOW for 39 weeks in parent study HGT-GCB-039 (NCT00553631, 2007-002840-21).

Arm type	Experimental
Investigational medicinal product name	Velaglucerase alfa
Investigational medicinal product code	
Other name	VPRIV®, Gene-Activated Human Glucocerebrosidase (GA-GCB)
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

VPRIV 60 U/kg, IV, EOW for 39 weeks in parent study HGT-GCB-039 (NCT00553631, 2007-002840-21).

Arm title	VPRIV 60 U/kg (Parent Study imiglucerase(60 U/kg) HGT-GCB-039)

Arm description:

Imiglucerase 60 U/kg, IV, EOW for 39 weeks in parent study HGT-GCB-039 (NCT00553631, 2007-002840-21) and switched to 60 U/kg VPRIV in HGT-GCB-044.

Arm type	Experimental
Investigational medicinal product name	Velaglucerase alfa
Investigational medicinal product code	
Other name	VPRIV®, Gene-Activated Human Glucocerebrosidase (GA-GCB)
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Imiglucerase 60 U/kg, IV, EOW for 39 weeks in parent study HGT-GCB-039 (NCT00553631, 2007-002840-21) and switched 60 U/kg VPRIV in HGT-GCB-044.

Arm title	VPRIV 15-60 U/kg (Parent Study VPRIV (15-60 U/kg)-TKT034)

Arm description:

VPRIV 15-60 U/kg, IV, EOW for 51 weeks in parent study TKT034 (NCT00478647, 2006-006304-11) and continued in HGT-GCB-044 at the same dose as prescribed in TKT034.

Arm type	Experimental
Investigational medicinal product name	Velaglucerase alfa
Investigational medicinal product code	
Other name	VPRIV®, Gene-Activated Human Glucocerebrosidase (GA-GCB)
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

VPRIV 15-60 U/kg, IV, EOW for 51 weeks in parent study TKT034 (NCT00478647, 2006-006304-11) and continued in HGT-GCB-044 at the same dose as prescribed in TKT034.

Number of subjects in period 1[1]	VPRIV 60 U/kg (Parent Study VPRIV (45 U/kg)-TKT032)	VPRIV 60 U/kg (Parent Study VPRIV (60 U/kg)-TKT032)	VPRIV 60 U/kg (Parent Study VPRIV (60U/kg) HGT-GCB-039)
Started	12	11	16
Completed	1	6	5
Not completed	11	5	11
Consent withdrawn by subject	-	-	-
Death	-	-	-
'Refusal of required diagnostic evaluation '	-	-	1
Termination of study by sponsor	11	5	10

Number of subjects in period 1[1]	VPRIV 60 U/kg (Parent Study imiglucerase(60 U/kg) HGT-GCB-039)	VPRIV 15-60 U/kg (Parent Study VPRIV (15-60 U/kg)-TKT034)
Started	16	38
Completed	7	30
Not completed	9	8
Consent withdrawn by subject	2	2
Death	1	-
'Refusal of required diagnostic evaluation '	-	-
Termination of study by sponsor	6	6

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: Two subjects who did not have type 1 Gaucher disease were withdrawn from the ITT population as per statistical analysis plan (SAP) definition and removed from the long-term efficacy analyses in this study, needed to support the interpretation of the long-term efficacy results. Hence, 93 of 95 enrolled subjects worldwide were included in the baseline period which consisted of HGT-GCB-044 ITT population.

Baseline characteristics

Reporting groups	
Reporting group title	VPRIV 60 U/kg (Parent Study VPRIV (45 U/kg)-TKT032)
Reporting group description:	
VPRIV 45 units per kilogram (U/kg), IV, EOW for 51 weeks in parent study TKT032 (2008-001965-27) and switched to 60 U/kg in HGT-GCB-044.	
Reporting group title	VPRIV 60 U/kg (Parent Study VPRIV (60 U/kg)-TKT032)
Reporting group description:	
VPRIV 60 U/kg, IV, EOW for 51 weeks in parent study TKT032 (2008-001965-27).	
Reporting group title	VPRIV 60 U/kg (Parent Study VPRIV (60U/kg) HGT-GCB-039)
Reporting group description:	
VPRIV 60 U/kg, IV, EOW for 39 weeks in parent study HGT-GCB-039 (NCT00553631, 2007-002840-21).	
Reporting group title	VPRIV 60 U/kg (Parent Study imiglucerase(60 U/kg) HGT-GCB-039)
Reporting group description:	
Imiglucerase 60 U/kg, IV, EOW for 39 weeks in parent study HGT-GCB-039 (NCT00553631, 2007-002840-21) and switched to 60 U/kg VPRIV in HGT-GCB-044.	
Reporting group title	VPRIV 15-60 U/kg (Parent Study VPRIV (15-60 U/kg)-TKT034)
Reporting group description:	
VPRIV 15-60 U/kg, IV, EOW for 51 weeks in parent study TKT034 (NCT00478647, 2006-006304-11) and continued in HGT-GCB-044 at the same dose as prescribed in TKT034.	

Reporting group values	VPRIV 60 U/kg (Parent Study VPRIV (45 U/kg)-TKT032)	VPRIV 60 U/kg (Parent Study VPRIV (60 U/kg)-TKT032)	VPRIV 60 U/kg (Parent Study VPRIV (60U/kg) HGT-GCB-039)
Number of subjects	12	11	16
Age categorical			
ITT population included all enrolled subjects who had type 1 Gaucher disease. Age at the time the informed consent was obtained in the core study.			
Units: Subjects			
At least 18 years	2	3	3
Between 18 and 65 years	10	8	13
Greater than or equal to 65 years	0	0	0
Age continuous			
ITT population. Age at the time the informed consent was obtained in the core study.			
Units: years			
arithmetic mean	32.5	22	32.9
standard deviation	± 16.75	± 11.08	± 16.14
Gender categorical			
ITT population.			
Units: Subjects			
Female	7	6	8
Male	5	5	8
Splenectomy status			
ITT population.			
Units: Subjects			
Yes	0	0	9
No	12	11	7

Baseline hemoglobin concentration per treatment group			
ITT population. Baseline was defined as data collected prior to the first dose in the core study (TKT032, TKT034, and HGT-GCB-039).			
Units: gram per deciliter			
arithmetic mean	10.68	10.68	11.56
full range (min-max)	8.5 to 12.9	7.1 to 12.3	9.7 to 14.4
Baseline platelet counts per treatment group			
ITT population. Baseline was defined as data collected prior to the first dose in the core study (TKT032, TKT034, and HGT-GCB-039).			
Units: x10^9/L			
arithmetic mean	69.3	79.4	160.1
full range (min-max)	13 to 146	47 to 139	44 to 310
Baseline liver volume per treatment group			
ITT population. Baseline was defined as data collected prior to the first dose in the core study (TKT032, TKT034, and HGT-GCB-039). Normal liver volume is defined as 2.5 percent of body weight.			
Units: Percent (%) body weight			
arithmetic mean	1.64	1.63	1.59
full range (min-max)	1.1 to 2.9	1 to 3.2	0.8 to 2.2
Baseline Spleen volume per treatment group			
ITT population. Baseline was defined as data collected prior to the first dose in the core study (TKT032, TKT034, and HT-GCB-039). Normal spleen volume is defined as 0.2 percentage of body weight.			
Units: Multiple of Normal (MN)			
arithmetic mean	23.08	18.48	12.69
full range (min-max)	4.8 to 65.1	5.7 to 36.9	7.2 to 31.6

Reporting group values	VPRIV 60 U/kg (Parent Study imiglucerase(60 U/kg) HGT-GCB-039)	VPRIV 15-60 U/kg (Parent Study VPRIV (15-60 U/kg)-TKT034)	Total
Number of subjects	16	38	93
Age categorical			
ITT population included all enrolled subjects who had type 1 Gaucher disease. Age at the time the informed consent was obtained in the core study.			
Units: Subjects			
At least 18 years	5	9	22
Between 18 and 65 years	11	26	68
Greater than or equal to 65 years	0	3	3
Age continuous			
ITT population. Age at the time the informed consent was obtained in the core study.			
Units: years			
arithmetic mean	25	34.3	
standard deviation	± 17.33	± 17.94	-
Gender categorical			
ITT population.			
Units: Subjects			
Female	7	18	46
Male	9	20	47
Splenectomy status			
ITT population.			
Units: Subjects			
Yes	10	3	22

No	6	35	71

Baseline hemoglobin concentration per treatment group			
ITT population. Baseline was defined as data collected prior to the first dose in the core study (TKT032, TKT034, and HGT-GCB-039).			
Units: gram per deciliter			
arithmetic mean	10.58	13.82	
full range (min-max)	8.1 to 13.1	10.7 to 16.5	-
Baseline platelet counts per treatment group			
ITT population. Baseline was defined as data collected prior to the first dose in the core study (TKT032, TKT034, and HGT-GCB-039).			
Units: x10^9/L			
arithmetic mean	186.3	165.4	
full range (min-max)	63 to 430	29 to 399	-
Baseline liver volume per treatment group			
ITT population. Baseline was defined as data collected prior to the first dose in the core study (TKT032, TKT034, and HGT-GCB-039). Normal liver volume is defined as 2.5 percent of body weight.			
Units: Percent (%) body weight			
arithmetic mean	1.68	0.82	
full range (min-max)	0.7 to 2.8	0.6 to 1.3	-
Baseline Spleen volume per treatment group			
ITT population. Baseline was defined as data collected prior to the first dose in the core study (TKT032, TKT034, and HT-GCB-039). Normal spleen volume is defined as 0.2 percentage of body weight.			
Units: Multiple of Normal (MN)			
arithmetic mean	23.52	4.1	
full range (min-max)	3.1 to 44.4	1.2 to 15.8	-

End points

End points reporting groups

Reporting group title	VPRIV 60 U/kg (Parent Study VPRIV (45 U/kg)-TKT032)
Reporting group description:	
VPRIV 45 units per kilogram (U/kg), IV, EOW for 51 weeks in parent study TKT032 (2008-001965-27) and switched to 60 U/kg in HGT-GCB-044.	
Reporting group title	VPRIV 60 U/kg (Parent Study VPRIV (60 U/kg)-TKT032)
Reporting group description:	
VPRIV 60 U/kg, IV, EOW for 51 weeks in parent study TKT032 (2008-001965-27).	
Reporting group title	VPRIV 60 U/kg (Parent Study VPRIV (60U/kg) HGT-GCB-039)
Reporting group description:	
VPRIV 60 U/kg, IV, EOW for 39 weeks in parent study HGT-GCB-039 (NCT00553631, 2007-002840-21).	
Reporting group title	VPRIV 60 U/kg (Parent Study imiglucerase(60 U/kg) HGT-GCB-039)
Reporting group description:	
Imiglucerase 60 U/kg, IV, EOW for 39 weeks in parent study HGT-GCB-039 (NCT00553631, 2007-002840-21) and switched to 60 U/kg VPRIV in HGT-GCB-044.	
Reporting group title	VPRIV 15-60 U/kg (Parent Study VPRIV (15-60 U/kg)-TKT034)
Reporting group description:	
VPRIV 15-60 U/kg, IV, EOW for 51 weeks in parent study TKT034 (NCT00478647, 2006-006304-11) and continued in HGT-GCB-044 at the same dose as prescribed in TKT034.	
Subject analysis set title	VPRIV 60 U/kg(Parent Study VPRIV(45 or 60 U/kg) TKT032,GCB039)
Subject analysis set type	Safety analysis
Subject analysis set description:	
This arm is the Overall velaglucerase alfa (VPRIV) 60 U/kg and includes subjects from the following groups: VPRIV 45 U/kg or 60 U/kg, IV, EOW for 51 weeks in parent study TKT032 (2008-001965-27) and switched to 60 U/kg in HGT-GCB-044 to maintain blindness or 60 U/kg, IV, EOW for 39 weeks in parent study HGT-GCB-039 (NCT00553631, 2007-002840-21).	

Primary: Overall Summary of Treatment Emergent Adverse Events (TEAEs)

End point title	Overall Summary of Treatment Emergent Adverse Events (TEAEs)[1][2]
End point description:	
Safety was evaluated by an analysis of adverse events (AEs), concomitant medication use, clinical laboratory tests, vital signs during the infusion of study drug, physical examination, and the development of anti-velaglucerase alfa. No formal comparisons or statistical tests were applied for the safety analyses, including for differences between the groups. All subjects who received at least 1 infusion (full or partial) of study drug were evaluated for safety (that is, were included in the safety population). There were 95 subjects in the safety population.	
End point type	Primary
End point timeframe:	
Baseline to termination of study	

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: Inferential statistical analysis was not planned for this endpoint. Only descriptive statistics were reported.
[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: A subject analysis set "VPRIV 60 U/kg (Parent Study VPRIV(45 or 60 U/kg) TKT032, GCB039)" was created by combining 3 reporting groups [VPRIV 60 U/kg (Parent Study VPRIV (45 U/kg)-TKT032); VPRIV 60 U/kg (Parent Study VPRIV (60 U/kg)-TKT032); VPRIV 60 U/kg (Parent Study VPRIV (60U/kg) HGT-GCB-039)] of the baseline period and reported statistics for this endpoint as planned.

End point values	VPRIV 60 U/kg (Parent Study imiglucerase(60 U/kg) HGT-GCB-039)	VPRIV 15-60 U/kg (Parent Study VPRIV (15-60 U/kg)-TKT034)	VPRIV 60 U/kg(Parent Study VPRIV(45 or 60 U/kg)	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	16	38	41	
Units: Subjects				
Experienced no AEs	1	3	3	
Experienced at least 1 AE	15	35	38	
Experienced at least 1 drug-related (DR) AE	7	8	9	
Experienced at least 1 infusion-related AE	1	5	5	
Experienced at least 1 severe AE	3	4	4	
Experienced at least 1 DR severe AE	0	0	0	
Experienced at least 1 Life-threatening AE	0	0	0	
Experienced at least 1 DR Life-threatening AE	0	0	0	
Experienced at least 1 serious AE	4	6	6	
Experienced at least 1 DR serious AE	0	0	0	
Discontinued due to an AE	0	0	0	
Deaths	1	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline to 24 Months in Hemoglobin Concentration for Each Treatment Group

End point title	Change From Baseline to 24 Months in Hemoglobin Concentration for Each Treatment Group[3]

End point description:

ITT population included all enrolled subjects who had type 1 Gaucher disease.

End point type	Secondary

End point timeframe:

Baseline to 24 months

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: A subject analysis set "VPRIV 60 U/kg (Parent Study VPRIV(45 or 60 U/kg) TKT032, GCB039)" was created by combining 3 reporting groups [VPRIV 60 U/kg (Parent Study VPRIV (45 U/kg)-TKT032); VPRIV 60 U/kg (Parent Study VPRIV (60 U/kg)-TKT032); VPRIV 60 U/kg (Parent Study VPRIV (60U/kg) HGT-GCB-039)] of the baseline period and reported statistics for this endpoint as planned.

End point values	VPRIV 60 U/kg (Parent Study imiglucerase(60 U/kg) HGT-GCB-039)	VPRIV 15-60 U/kg (Parent Study VPRIV (15-60 U/kg)-TKT034)	VPRIV 60 U/kg(Parent Study VPRIV(45 or 60 U/kg)	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	16	38	39	
Units: gram per deciliter				
arithmetic mean (confidence interval	2 (1.25 to	-0.05 (-0.34 to	2.75 (2.28 to	

95%)	2.75)	0.25)	3.22)

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline to 24 Months in Platelet Counts for Each Treatment Group

End point title	Change From Baseline to 24 Months in Platelet Counts for Each Treatment Group[4]
End point description:	
ITT population.	
End point type	Secondary
End point timeframe:	
Baseline to 24 months	

Notes:

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: A subject analysis set "VPRIV 60 U/kg (Parent Study VPRIV(45 or 60 U/kg) TKT032, GCB039)" was created by combining 3 reporting groups [VPRIV 60 U/kg (Parent Study VPRIV (45 U/kg)-TKT032); VPRIV 60 U/kg (Parent Study VPRIV (60 U/kg)-TKT032); VPRIV 60 U/kg (Parent Study VPRIV (60U/kg) HGT-GCB-039)] of the baseline period and reported statistics for this endpoint as planned.

End point values	VPRIV 60 U/kg (Parent Study imiglucerase(60 U/kg) HGT-GCB-039)	VPRIV 15-60 U/kg (Parent Study VPRIV (15-60 U/kg)-TKT034)	VPRIV 60 U/kg(Parent Study VPRIV(45 or 60 U/kg)	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	16	38	39	
Units: 10^9 per liter				
arithmetic mean (confidence interval 95%)	160.94 (117.22 to 204.66)	9.03 (-2.6 to 20.66)	87.85 (72.69 to 103)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline to 24 Months in Normalized Liver Volume for Each Treatment Group

End point title	Change From Baseline to 24 Months in Normalized Liver Volume for Each Treatment Group[5]
End point description:	
ITT population.	
End point type	Secondary
End point timeframe:	
Baseline to 24 months	

Notes:

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: A subject analysis set "VPRIV 60 U/kg (Parent Study VPRIV(45 or 60 U/kg) TKT032, GCB039)" was created by combining 3 reporting groups [VPRIV 60 U/kg (Parent Study VPRIV (45 U/kg)-TKT032); VPRIV 60 U/kg (Parent Study VPRIV (60 U/kg)-TKT032); VPRIV 60 U/kg (Parent Study VPRIV (60U/kg) HGT-GCB-039)] of the baseline period and reported statistics for this endpoint as planned.

End point values	VPRIV 60 U/kg (Parent Study imiglucerase(60 U/kg) HGT-GCB-039)	VPRIV 15-60 U/kg (Parent Study VPRIV (15-60 U/kg)-TKT034)	VPRIV 60 U/kg(Parent Study VPRIV(45 or 60 U/kg)	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	16	38	39	
Units: Percent (%) Body weight				
arithmetic mean (confidence interval 95%)	-1.688 (-2.164 to -1.211)	-0.026 (-0.1 to 0.047)	-1.206 (-1.501 to -0.912)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage Change From Baseline to 24 Months in Normalized Spleen Volume for Each Treatment Group

End point title	Percentage Change From Baseline to 24 Months in Normalized Spleen Volume for Each Treatment Group[6]
End point description:	
ITT population.	
End point type	Secondary
End point timeframe:	
Baseline to 24 months	

Notes:

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: A subject analysis set "VPRIV 60 U/kg (Parent Study VPRIV(45 or 60 U/kg) TKT032, GCB039)" was created by combining 3 reporting groups [VPRIV 60 U/kg (Parent Study VPRIV (45 U/kg)-TKT032); VPRIV 60 U/kg (Parent Study VPRIV (60 U/kg)-TKT032); VPRIV 60 U/kg (Parent Study VPRIV (60U/kg) HGT-GCB-039)] of the baseline period and reported statistics for this endpoint as planned.

End point values	VPRIV 60 U/kg (Parent Study imiglucerase(60 U/kg) HGT-GCB-039)	VPRIV 15-60 U/kg (Parent Study VPRIV (15-60 U/kg)-TKT034)	VPRIV 60 U/kg(Parent Study VPRIV(45 or 60 U/kg)	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	16	38	39	
Units: Percent (%) change				
arithmetic mean (confidence interval 95%)	-63.82 (-89.65 to -37.98)	-8.04 (-14 to -2.08)	-64.49 (-69.26 to -59.73)	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

TEAEs were defined as AEs which occurred on or after the time of the first infusion in HGT-GCB-044, until 30 days after the subject's last study infusion

Adverse event reporting additional description:

AEs may have been discovered through observation or examination of the subject, questioning of the subject, complaint by the subject, or by an abnormal clinical laboratory value. Severity of AEs was to be assessed by the investigator and recorded on the electronic case report form regardless of the severity or relationship to study drug.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	9.0

Reporting groups

Reporting group title	VPRIV 15-60 U/kg (Parent Study VPRIV (15-60 U/kg) TKT034)

Reporting group description:

VPRIV 15-60 U/kg, IV, EOW for 51 weeks in parent study TKT034 (NCT00478647, 2006-006304-11) and continued in HGT-GCB-044 at the same dose as prescribed in TKT034.

Reporting group title	VPRIV 60 U/kg (Parent Study-imiglucerase(60 U/kg) HGT-GCB-039)

Reporting group description:

Imiglucerase 60 U/kg, IV, EOW for 39 weeks in parent study HGT-GCB-039 (NCT00553631, 2007-002840-21) and switched to 60 U/kg VPRIV in HGT-GCB-044.

Reporting group title	VPRIV 60 U/kg(VPRIV Parent Study 45 or 60 U/kg-TKT032,GCB039)

Reporting group description:

This arm is the Overall velaglucerase alfa (VPRIV) 60 U/kg and includes subjects from the following groups:
VPRIV 45 U/kg or 60 U/kg, IV, EOW for 51 weeks in parent study TKT032 (2008-001965-27) and switched to 60 U/kg in HGT-GCB-044 to maintain blindness or 60 U/kg, IV, EOW for 39 weeks in parent study HGT-GCB-039 (NCT00553631, 2007-002840-21).

Serious adverse events	VPRIV 15-60 U/kg (Parent Study VPRIV (15-60 U/kg) TKT034)	VPRIV 60 U/kg (Parent Study-imiglucerase(60 U/kg) HGT-GCB-039)	VPRIV 60 U/kg(VPRIV Parent Study 45 or 60 U/kg-
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 38 (15.79%)	4 / 16 (25.00%)	6 / 41 (14.63%)
number of deaths (all causes)	0	1	0
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Benign renal neoplasm			
subjects affected / exposed	0 / 38 (0.00%)	0 / 16 (0.00%)	1 / 41 (2.44%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Injury, poisoning and procedural complications			
Lower limb fracture			
subjects affected / exposed	0 / 38 (0.00%)	0 / 16 (0.00%)	1 / 41 (2.44%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post procedural haematoma			
subjects affected / exposed	1 / 38 (2.63%)	0 / 16 (0.00%)	0 / 41 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Phlebitis			
subjects affected / exposed	1 / 38 (2.63%)	0 / 16 (0.00%)	0 / 41 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Convulsion			
subjects affected / exposed	0 / 38 (0.00%)	1 / 16 (6.25%)	0 / 41 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Syncope			
subjects affected / exposed	1 / 38 (2.63%)	0 / 16 (0.00%)	0 / 41 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pregnancy, puerperium and perinatal conditions			
Abortion			
subjects affected / exposed	0 / 38 (0.00%)	0 / 16 (0.00%)	1 / 41 (2.44%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oligohydramnios			
subjects affected / exposed	1 / 38 (2.63%)	0 / 16 (0.00%)	0 / 41 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Splenomegaly			

subjects affected / exposed	1 / 38 (2.63%)	0 / 16 (0.00%)	0 / 41 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Non-Cardiac chest pain			
subjects affected / exposed	0 / 38 (0.00%)	0 / 16 (0.00%)	1 / 41 (2.44%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal hernia			
subjects affected / exposed	1 / 38 (2.63%)	0 / 16 (0.00%)	0 / 41 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Umbilical hernia			
subjects affected / exposed	0 / 38 (0.00%)	1 / 16 (6.25%)	0 / 41 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	0 / 38 (0.00%)	1 / 16 (6.25%)	1 / 41 (2.44%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Renal colic			
subjects affected / exposed	0 / 38 (0.00%)	0 / 16 (0.00%)	1 / 41 (2.44%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 38 (2.63%)	0 / 16 (0.00%)	1 / 41 (2.44%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lumbar spinal stenosis			

subjects affected / exposed	1 / 38 (2.63%)	0 / 16 (0.00%)	0 / 41 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteonecrosis			
subjects affected / exposed	0 / 38 (0.00%)	2 / 16 (12.50%)	2 / 41 (4.88%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Bronchopneumonia			
subjects affected / exposed	0 / 38 (0.00%)	1 / 16 (6.25%)	0 / 41 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis acute			
subjects affected / exposed	0 / 38 (0.00%)	0 / 16 (0.00%)	1 / 41 (2.44%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory tract infection			
subjects affected / exposed	0 / 38 (0.00%)	1 / 16 (6.25%)	0 / 41 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	1 / 38 (2.63%)	0 / 16 (0.00%)	0 / 41 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	VPRIV 15-60 U/kg (Parent Study VPRIV (15-60 U/kg) TKT034)	VPRIV 60 U/kg (Parent Study-imiglucerase(60 U/kg) HGT-GCB-039)	VPRIV 60 U/kg(VPRIV Parent Study 45 or 60 U/kg-
Total subjects affected by non-serious adverse events			
subjects affected / exposed	35 / 38 (92.11%)	15 / 16 (93.75%)	35 / 41 (85.37%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			

Lentigo			
subjects affected / exposed	0 / 38 (0.00%)	1 / 16 (6.25%)	0 / 41 (0.00%)
occurrences (all)	0	1	0
Vascular disorders			
Haematoma			
subjects affected / exposed	2 / 38 (5.26%)	0 / 16 (0.00%)	1 / 41 (2.44%)
occurrences (all)	2	0	1
Hypertension			
subjects affected / exposed	4 / 38 (10.53%)	0 / 16 (0.00%)	5 / 41 (12.20%)
occurrences (all)	6	0	6
General disorders and administration site conditions			
Adverse drug reaction			
subjects affected / exposed	2 / 38 (5.26%)	0 / 16 (0.00%)	0 / 41 (0.00%)
occurrences (all)	2	0	0
Fatigue			
subjects affected / exposed	7 / 38 (18.42%)	0 / 16 (0.00%)	3 / 41 (7.32%)
occurrences (all)	8	0	3
Chest discomfort			
subjects affected / exposed	0 / 38 (0.00%)	1 / 16 (6.25%)	0 / 41 (0.00%)
occurrences (all)	0	1	0
Gait disturbance			
subjects affected / exposed	0 / 38 (0.00%)	1 / 16 (6.25%)	0 / 41 (0.00%)
occurrences (all)	0	1	0
Influenza like illness			
subjects affected / exposed	2 / 38 (5.26%)	0 / 16 (0.00%)	0 / 41 (0.00%)
occurrences (all)	3	0	0
Pyrexia			
subjects affected / exposed	2 / 38 (5.26%)	1 / 16 (6.25%)	6 / 41 (14.63%)
occurrences (all)	2	1	10
Reproductive system and breast disorders			
Galactorrhoea			
subjects affected / exposed	0 / 38 (0.00%)	1 / 16 (6.25%)	0 / 41 (0.00%)
occurrences (all)	0	1	0
Respiratory, thoracic and mediastinal disorders			

Cough			
subjects affected / exposed	5 / 38 (13.16%)	3 / 16 (18.75%)	0 / 41 (0.00%)
occurrences (all)	6	4	0
Dysphonia			
subjects affected / exposed	2 / 38 (5.26%)	0 / 16 (0.00%)	0 / 41 (0.00%)
occurrences (all)	2	0	0
Epistaxis			
subjects affected / exposed	1 / 38 (2.63%)	1 / 16 (6.25%)	0 / 41 (0.00%)
occurrences (all)	2	1	0
Dyspnoea			
subjects affected / exposed	1 / 38 (2.63%)	1 / 16 (6.25%)	0 / 41 (0.00%)
occurrences (all)	2	3	0
Pharyngolaryngeal pain			
subjects affected / exposed	5 / 38 (13.16%)	0 / 16 (0.00%)	3 / 41 (7.32%)
occurrences (all)	8	0	4
Postnasal drip			
subjects affected / exposed	2 / 38 (5.26%)	0 / 16 (0.00%)	0 / 41 (0.00%)
occurrences (all)	2	0	0
Productive cough			
subjects affected / exposed	0 / 38 (0.00%)	0 / 16 (0.00%)	4 / 41 (9.76%)
occurrences (all)	0	0	5
Rhinitis allergic			
subjects affected / exposed	0 / 38 (0.00%)	1 / 16 (6.25%)	1 / 41 (2.44%)
occurrences (all)	0	3	1
Sinus congestion			
subjects affected / exposed	3 / 38 (7.89%)	0 / 16 (0.00%)	0 / 41 (0.00%)
occurrences (all)	3	0	0
Tachypnoea			
subjects affected / exposed	0 / 38 (0.00%)	1 / 16 (6.25%)	0 / 41 (0.00%)
occurrences (all)	0	2	0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	2 / 38 (5.26%)	1 / 16 (6.25%)	0 / 41 (0.00%)
occurrences (all)	2	1	0
Aspartate aminotransferase increased			

subjects affected / exposed	1 / 38 (2.63%)	1 / 16 (6.25%)	0 / 41 (0.00%)
occurrences (all)	1	1	0
Blood creatine phosphokinase increased			
subjects affected / exposed	2 / 38 (5.26%)	0 / 16 (0.00%)	1 / 41 (2.44%)
occurrences (all)	2	0	3
Blood urine present			
subjects affected / exposed	0 / 38 (0.00%)	1 / 16 (6.25%)	1 / 41 (2.44%)
occurrences (all)	0	1	1
Haemoglobin decreased			
subjects affected / exposed	0 / 38 (0.00%)	1 / 16 (6.25%)	0 / 41 (0.00%)
occurrences (all)	0	1	0
Mean cell volume increased			
subjects affected / exposed	0 / 38 (0.00%)	1 / 16 (6.25%)	0 / 41 (0.00%)
occurrences (all)	0	1	0
Neutrophil count increased			
subjects affected / exposed	0 / 38 (0.00%)	1 / 16 (6.25%)	0 / 41 (0.00%)
occurrences (all)	0	1	0
Red blood cell count decreased			
subjects affected / exposed	0 / 38 (0.00%)	1 / 16 (6.25%)	0 / 41 (0.00%)
occurrences (all)	0	1	0
Red blood cells urine positive			
subjects affected / exposed	0 / 38 (0.00%)	1 / 16 (6.25%)	1 / 41 (2.44%)
occurrences (all)	0	1	1
White blood cell count increased			
subjects affected / exposed	0 / 38 (0.00%)	1 / 16 (6.25%)	0 / 41 (0.00%)
occurrences (all)	0	1	0
White blood cells urine positive			
subjects affected / exposed	2 / 38 (5.26%)	1 / 16 (6.25%)	0 / 41 (0.00%)
occurrences (all)	2	1	0
Injury, poisoning and procedural complications			
Anaemia postoperative			
subjects affected / exposed	0 / 38 (0.00%)	1 / 16 (6.25%)	1 / 41 (2.44%)
occurrences (all)	0	1	1
Burns first degree			

subjects affected / exposed	0 / 38 (0.00%)	0 / 16 (0.00%)	3 / 41 (7.32%)
occurrences (all)	0	0	5
Contusion			
subjects affected / exposed	1 / 38 (2.63%)	1 / 16 (6.25%)	0 / 41 (0.00%)
occurrences (all)	2	1	0
Excoriation			
subjects affected / exposed	1 / 38 (2.63%)	1 / 16 (6.25%)	0 / 41 (0.00%)
occurrences (all)	1	1	0
Injury			
subjects affected / exposed	0 / 38 (0.00%)	1 / 16 (6.25%)	2 / 41 (4.88%)
occurrences (all)	0	1	2
Joint injury			
subjects affected / exposed	0 / 38 (0.00%)	1 / 16 (6.25%)	0 / 41 (0.00%)
occurrences (all)	0	1	0
Muscle strain			
subjects affected / exposed	2 / 38 (5.26%)	0 / 16 (0.00%)	0 / 41 (0.00%)
occurrences (all)	2	0	0
Procedural pain			
subjects affected / exposed	3 / 38 (7.89%)	0 / 16 (0.00%)	0 / 41 (0.00%)
occurrences (all)	6	0	0
Skin laceration			
subjects affected / exposed	0 / 38 (0.00%)	1 / 16 (6.25%)	0 / 41 (0.00%)
occurrences (all)	0	1	0
Nervous system disorders			
Convulsion			
subjects affected / exposed	0 / 38 (0.00%)	1 / 16 (6.25%)	0 / 41 (0.00%)
occurrences (all)	0	1	0
Dizziness			
subjects affected / exposed	0 / 38 (0.00%)	1 / 16 (6.25%)	3 / 41 (7.32%)
occurrences (all)	0	3	3
Drop attacks			
subjects affected / exposed	0 / 38 (0.00%)	1 / 16 (6.25%)	0 / 41 (0.00%)
occurrences (all)	0	1	0
Headache			
subjects affected / exposed	6 / 38 (15.79%)	4 / 16 (25.00%)	7 / 41 (17.07%)
occurrences (all)	10	6	16

Hypoaesthesia			
subjects affected / exposed	0 / 38 (0.00%)	1 / 16 (6.25%)	0 / 41 (0.00%)
occurrences (all)	0	1	0
Paraesthesia			
subjects affected / exposed	2 / 38 (5.26%)	1 / 16 (6.25%)	2 / 41 (4.88%)
occurrences (all)	2	3	2
Sciatica			
subjects affected / exposed	0 / 38 (0.00%)	1 / 16 (6.25%)	0 / 41 (0.00%)
occurrences (all)	0	1	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 38 (2.63%)	1 / 16 (6.25%)	0 / 41 (0.00%)
occurrences (all)	1	2	0
Leukocytosis			
subjects affected / exposed	0 / 38 (0.00%)	1 / 16 (6.25%)	0 / 41 (0.00%)
occurrences (all)	0	1	0
Lymphadenitis			
subjects affected / exposed	0 / 38 (0.00%)	1 / 16 (6.25%)	0 / 41 (0.00%)
occurrences (all)	0	1	0
Splenomegaly			
subjects affected / exposed	0 / 38 (0.00%)	0 / 16 (0.00%)	3 / 41 (7.32%)
occurrences (all)	0	0	3
Eye disorders			
Conjunctivitis allergic			
subjects affected / exposed	0 / 38 (0.00%)	1 / 16 (6.25%)	0 / 41 (0.00%)
occurrences (all)	0	2	0
Dry eye			
subjects affected / exposed	2 / 38 (5.26%)	0 / 16 (0.00%)	0 / 41 (0.00%)
occurrences (all)	2	0	0
Visual acuity reduced			
subjects affected / exposed	0 / 38 (0.00%)	1 / 16 (6.25%)	1 / 41 (2.44%)
occurrences (all)	0	1	1
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	2 / 38 (5.26%)	1 / 16 (6.25%)	3 / 41 (7.32%)
occurrences (all)	2	1	3
Abdominal pain upper			

subjects affected / exposed	3 / 38 (7.89%)	2 / 16 (12.50%)	4 / 41 (9.76%)
occurrences (all)	4	2	6
Diarrhoea			
subjects affected / exposed	2 / 38 (5.26%)	1 / 16 (6.25%)	2 / 41 (4.88%)
occurrences (all)	2	1	3
Dyspepsia			
subjects affected / exposed	2 / 38 (5.26%)	0 / 16 (0.00%)	3 / 41 (7.32%)
occurrences (all)	4	0	3
Rectal haemorrhage			
subjects affected / exposed	1 / 38 (2.63%)	1 / 16 (6.25%)	0 / 41 (0.00%)
occurrences (all)	1	1	0
Toothache			
subjects affected / exposed	2 / 38 (5.26%)	2 / 16 (12.50%)	6 / 41 (14.63%)
occurrences (all)	3	2	7
Vomiting			
subjects affected / exposed	2 / 38 (5.26%)	0 / 16 (0.00%)	1 / 41 (2.44%)
occurrences (all)	2	0	1
Hepatobiliary disorders			
Biliary colic			
subjects affected / exposed	0 / 38 (0.00%)	1 / 16 (6.25%)	0 / 41 (0.00%)
occurrences (all)	0	2	0
Cholelithiasis			
subjects affected / exposed	0 / 38 (0.00%)	2 / 16 (12.50%)	0 / 41 (0.00%)
occurrences (all)	0	2	0
Cytolytic hepatitis			
subjects affected / exposed	0 / 38 (0.00%)	0 / 16 (0.00%)	3 / 41 (7.32%)
occurrences (all)	0	0	6
Liver disorder			
subjects affected / exposed	0 / 38 (0.00%)	1 / 16 (6.25%)	0 / 41 (0.00%)
occurrences (all)	0	1	0
Skin and subcutaneous tissue disorders			
Dermatitis allergic			
subjects affected / exposed	2 / 38 (5.26%)	0 / 16 (0.00%)	0 / 41 (0.00%)
occurrences (all)	2	0	0
Dermatitis contact			

subjects affected / exposed	0 / 38 (0.00%)	1 / 16 (6.25%)	0 / 41 (0.00%)
occurrences (all)	0	1	0
Erythema			
subjects affected / exposed	0 / 38 (0.00%)	1 / 16 (6.25%)	0 / 41 (0.00%)
occurrences (all)	0	1	0
Rash vesicular			
subjects affected / exposed	0 / 38 (0.00%)	1 / 16 (6.25%)	0 / 41 (0.00%)
occurrences (all)	0	7	0
Pruritus generalised			
subjects affected / exposed	1 / 38 (2.63%)	1 / 16 (6.25%)	0 / 41 (0.00%)
occurrences (all)	1	1	0
Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	0 / 38 (0.00%)	1 / 16 (6.25%)	0 / 41 (0.00%)
occurrences (all)	0	1	0
Endocrine disorders			
Hyperprolactinaemia			
subjects affected / exposed	0 / 38 (0.00%)	1 / 16 (6.25%)	0 / 41 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	9 / 38 (23.68%)	2 / 16 (12.50%)	14 / 41 (34.15%)
occurrences (all)	13	34	33
Arthritis			
subjects affected / exposed	1 / 38 (2.63%)	2 / 16 (12.50%)	0 / 41 (0.00%)
occurrences (all)	1	2	0
Back pain			
subjects affected / exposed	4 / 38 (10.53%)	1 / 16 (6.25%)	5 / 41 (12.20%)
occurrences (all)	7	1	6
Bone pain			
subjects affected / exposed	7 / 38 (18.42%)	2 / 16 (12.50%)	7 / 41 (17.07%)
occurrences (all)	12	7	20
Myalgia			
subjects affected / exposed	2 / 38 (5.26%)	0 / 16 (0.00%)	3 / 41 (7.32%)
occurrences (all)	3	0	3
Muscle spasms			

subjects affected / exposed	0 / 38 (0.00%)	1 / 16 (6.25%)	0 / 41 (0.00%)
occurrences (all)	0	1	0
Osteoarthritis			
subjects affected / exposed	3 / 38 (7.89%)	0 / 16 (0.00%)	1 / 41 (2.44%)
occurrences (all)	3	0	1
Pain in extremity			
subjects affected / exposed	4 / 38 (10.53%)	1 / 16 (6.25%)	5 / 41 (12.20%)
occurrences (all)	6	1	6
Shoulder pain			
subjects affected / exposed	3 / 38 (7.89%)	1 / 16 (6.25%)	2 / 41 (4.88%)
occurrences (all)	4	2	4
Infections and infestations			
Bronchitis			
subjects affected / exposed	1 / 38 (2.63%)	1 / 16 (6.25%)	5 / 41 (12.20%)
occurrences (all)	1	1	13
Bronchitis acute			
subjects affected / exposed	0 / 38 (0.00%)	1 / 16 (6.25%)	5 / 41 (12.20%)
occurrences (all)	0	1	5
Dental caries			
subjects affected / exposed	0 / 38 (0.00%)	1 / 16 (6.25%)	1 / 41 (2.44%)
occurrences (all)	0	1	1
Diarrhoea infectious			
subjects affected / exposed	2 / 38 (5.26%)	0 / 16 (0.00%)	0 / 41 (0.00%)
occurrences (all)	2	0	0
Gastroenteritis			
subjects affected / exposed	2 / 38 (5.26%)	1 / 16 (6.25%)	7 / 41 (17.07%)
occurrences (all)	2	1	10
Hepatitis a			
subjects affected / exposed	0 / 38 (0.00%)	1 / 16 (6.25%)	0 / 41 (0.00%)
occurrences (all)	0	1	0
Hordeolum			
subjects affected / exposed	1 / 38 (2.63%)	1 / 16 (6.25%)	2 / 41 (4.88%)
occurrences (all)	1	1	3
Influenza			
subjects affected / exposed	4 / 38 (10.53%)	4 / 16 (25.00%)	6 / 41 (14.63%)
occurrences (all)	6	12	10

Nasopharyngitis			
subjects affected / exposed	16 / 38 (42.11%)	3 / 16 (18.75%)	11 / 41 (26.83%)
occurrences (all)	31	4	20
Lower respiratory tract infection			
subjects affected / exposed	0 / 38 (0.00%)	1 / 16 (6.25%)	0 / 41 (0.00%)
occurrences (all)	0	1	0
Pharyngitis			
subjects affected / exposed	5 / 38 (13.16%)	1 / 16 (6.25%)	2 / 41 (4.88%)
occurrences (all)	11	1	2
Pyelonephritis acute			
subjects affected / exposed	0 / 38 (0.00%)	1 / 16 (6.25%)	0 / 41 (0.00%)
occurrences (all)	0	1	0
Respiratory tract infection			
subjects affected / exposed	1 / 38 (2.63%)	2 / 16 (12.50%)	0 / 41 (0.00%)
occurrences (all)	2	3	0
Rhinitis			
subjects affected / exposed	0 / 38 (0.00%)	1 / 16 (6.25%)	3 / 41 (7.32%)
occurrences (all)	0	1	3
Sinusitis			
subjects affected / exposed	3 / 38 (7.89%)	0 / 16 (0.00%)	0 / 41 (0.00%)
occurrences (all)	5	0	0
Tinea versicolour			
subjects affected / exposed	0 / 38 (0.00%)	1 / 16 (6.25%)	4 / 41 (9.76%)
occurrences (all)	0	2	13
Staphylococcal infection			
subjects affected / exposed	0 / 38 (0.00%)	1 / 16 (6.25%)	0 / 41 (0.00%)
occurrences (all)	0	1	0
Tonsillitis			
subjects affected / exposed	1 / 38 (2.63%)	0 / 16 (0.00%)	4 / 41 (9.76%)
occurrences (all)	1	0	4
Upper respiratory tract infection			
subjects affected / exposed	9 / 38 (23.68%)	6 / 16 (37.50%)	4 / 41 (9.76%)
occurrences (all)	9	14	7
Urinary tract infection			
subjects affected / exposed	3 / 38 (7.89%)	0 / 16 (0.00%)	3 / 41 (7.32%)
occurrences (all)	5	0	5

Vaginal infection			
subjects affected / exposed	3 / 38 (7.89%)	0 / 16 (0.00%)	1 / 41 (2.44%)
occurrences (all)	3	0	1
Varicella			
subjects affected / exposed	0 / 38 (0.00%)	1 / 16 (6.25%)	0 / 41 (0.00%)
occurrences (all)	0	1	0
Vulvovaginal mycotic infection			
subjects affected / exposed	2 / 38 (5.26%)	0 / 16 (0.00%)	1 / 41 (2.44%)
occurrences (all)	2	0	1

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
09 October 2008	Amendment 1 was revised from the original version to update the background information and contact information for serious adverse event reporting, and included several clarifications. The major clarification was that subjects completing TKT034 were permitted to continue to receive home infusions or were able to begin home infusions at any time.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported