Clinical trial results:
An Open-label Study Investigating the Safety and Efficacy of rhPTH(1-84) in Subjects with Hypoparathyroidism

Summary

EudraCT number	2017-003067-36
Trial protocol	HU DK
Global end of trial date	14 April 2020

Results information

Result version number	v1 (current)
This version publication date	30 April 2021
First version publication date	30 April 2021

Trial information

Trial identification

Sponsor protocol code	SHP634-404

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03364738
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Shire
Sponsor organisation address	300 Shire Way, Lexington, United States, MA 02421
Public contact	Study Director, Shire, ClinicalTransparency@takeda.com
Scientific contact	Study Director, Shire, ClinicalTransparency@takeda.com

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	14 April 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	14 April 2020
Global end of trial reached?	Yes
Global end of trial date	14 April 2020
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 evaluate the proportion of subjects who achieved total serum calcium (albumin corrected) values in the range of 7.5 mg/dL (1.875 mmol/L) – upper limit of normal (ULN) and to further characterize the safety of rhPTH(1-84) in adult subjects with hypoparathyroidism (HPT).

Protection of trial subjects:

The study was conducted in accordance with the ethical principles that have their origins in the Declaration of Helsinki and in compliance with all applicable industry regulations, International Conference on Harmonisation (ICH) Good Clinical Practice (GCP) Guideline E6 (1996), European Union (EU) Directive 2001/20/EC, as well as all applicable national and local laws and regulations.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	26 September 2018
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	Canada: 5
Country: Number of subjects enrolled	Denmark: 2
Country: Number of subjects enrolled	Hungary: 9
Country: Number of subjects enrolled	United States: 6
Worldwide total number of subjects	22
EEA total number of subjects	11

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0

Adults (18-64 years)	19
From 65 to 84 years	3
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Subjects with HPT who completed SHP634-101 (2015-004757-40) study were eligible and enrolled in this extension study which was conducted at 10 sites in the United States, Denmark, Hungary and Canada between 26 September 2018 (first participant first visit) and 14 April 2020 (last participant last visit).

Pre-assignment

Screening details:

A total of 22 subjects were enrolled and treated in the study, of which 14 subjects completed the study.

Period 1

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

Arms

Arm title	rhPTH(1-84)

Arm description:

Subjects received recombinant human parathyroid hormone (rhPTH) (1-84) (Natpara) 50 microgram (mcg), injection, subcutaneously, once daily in the thigh (alternate thigh every day) up to 52 weeks (end of treatment [EOT])/ early termination (ET). Dose escalation was done up to 100 mcg in increments of 25 mcg no more frequently than every 2 to 4 weeks, with the goal of achieving or maintaining albumin-corrected serum calcium (ACSC) levels in the range of 2-2.25 millimoles per liter (mmol/L) (8-9 milligrams per deciliter [mg/dL]). Administered dose was maintained once a participant achieved a stable ACSC level of 2-2.25 mmol/L (8-9 mg/dL) and had minimized supplement (active vitamin D and calcium supplement) doses. If ACSC was greater than (>) 2.25 mmol/L (>9.0 mg/dL), a starting dose of 25 mcg was administered.

Arm type	Experimental
Investigational medicinal product name	Human recombinant parathyroid Hormone
Investigational medicinal product code	SHP634
Other name	Natpara
Pharmaceutical forms	Powder and solvent for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Subjects received rhPTH(1-84) 50 mcg, injection, subcutaneously, once daily in the thigh (alternate thigh every day) up to Week 52 (end of treatment [EOT]).

Number of subjects in period 1	rhPTH(1-84)
Started	22
Completed	14
Not completed	8
Consent withdrawn by subject	1
Adverse event, non-fatal	1
Early termination due to FDA recall of rhPTH(1-84)	6

Baseline characteristics

Reporting groups	
Reporting group title	rhPTH(1-84)

Reporting group description:

Subjects received recombinant human parathyroid hormone (rhPTH) (1-84) (Natpara) 50 microgram (mcg), injection, subcutaneously, once daily in the thigh (alternate thigh every day) up to 52 weeks (end of treatment [EOT])/ early termination (ET). Dose escalation was done up to 100 mcg in increments of 25 mcg no more frequently than every 2 to 4 weeks, with the goal of achieving or maintaining albumin-corrected serum calcium (ACSC) levels in the range of 2-2.25 millimoles per liter (mmol/L) (8-9 milligrams per deciliter [mg/dL]). Administered dose was maintained once a participant achieved a stable ACSC level of 2-2.25 mmol/L (8-9 mg/dL) and had minimized supplement (active vitamin D and calcium supplement) doses. If ACSC was greater than (>) 2.25 mmol/L (>9.0 mg/dL), a starting dose of 25 mcg was administered.

Reporting group values	rhPTH(1-84)	Total	
Number of subjects	22	22	
Age categorical Units: Subjects			
Age Continuous Units: years			
arithmetic mean	50		
standard deviation	± 11.39	-	
Sex: Female, Male Units: Subjects			
Female	18	18	
Male	4	4	
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	0	0	
Not Hispanic or Latino	21	21	
Unknown or Not Reported	1	1	
Race/Ethnicity, Customized Units: Subjects			
American Indian or Alaska Native	0	0	
Asian	0	0	
Black or African American	1	1	
White	20	20	
Native Hawaiian or other Pacific Islander	0	0	
Native American And Caucasian	1	1	

End points

End points reporting groups

Reporting group title	rhPTH(1-84)

Reporting group description:

Subjects received recombinant human parathyroid hormone (rhPTH) (1-84) (Natpara) 50 microgram (mcg), injection, subcutaneously, once daily in the thigh (alternate thigh every day) up to 52 weeks (end of treatment [EOT])/ early termination (ET). Dose escalation was done up to 100 mcg in increments of 25 mcg no more frequently than every 2 to 4 weeks, with the goal of achieving or maintaining albumin-corrected serum calcium (ACSC) levels in the range of 2-2.25 millimoles per liter (mmol/L) (8-9 milligrams per deciliter [mg/dL]). Administered dose was maintained once a participant achieved a stable ACSC level of 2-2.25 mmol/L (8-9 mg/dL) and had minimized supplement (active vitamin D and calcium supplement) doses. If ACSC was greater than (>) 2.25 mmol/L (>9.0 mg/dL), a starting dose of 25 mcg was administered.

Primary: Percentage of Subjects who Achieved Total Albumin-corrected Serum Calcium (ACSC) Values Greater Than or Equal to (>=) to the Range of 7.5 mg/dL (1.875 mmol/L) and less Than or Equal to (<=) Upper Limit of Normal (ULN) at Week 24

End point title	Percentage of Subjects who Achieved Total Albumin-corrected Serum Calcium (ACSC) Values Greater Than or Equal to (>=) to the Range of 7.5 mg/dL (1.875 mmol/L) and less Than or Equal to (<=) Upper Limit of Normal (ULN) at Week 24[1]

End point description:

Percentage of subjects who achieved ACSC values >= to range of 1.875 mmol/L and <= ULN at Week 24 was reported. Safety analysis population consisted of all subjects who had received at least 1 dose of rhPTH(1-84). Here, "number of subjects analysed" were subjects who were evaluable for this end point.

End point type	Primary

End point timeframe:

At Week 24

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: Only descriptive data was planned to be analyzed for this endpoint.

End point values	rhPTH(1-84)			
Subject group type	Reporting group			
Number of subjects analysed	21			
Units: percentage of subjects	100			

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With Total ACSC Values >= to the Range of 7.5 mg/dL (1.875 mmol/L) and <=ULN at Week 52 (End-of-treatment [EOT])

End point title	Percentage of Subjects With Total ACSC Values >= to the Range of 7.5 mg/dL (1.875 mmol/L) and <=ULN at Week 52 (End-of-treatment [EOT])[2]

End point description:

Percentage of subjects who achieved ACSC values >= to range of 1.875 mmol/L and <= ULN at Week

52 (EOT) was reported. Safety analysis population consisted of all subjects who had received at least 1 dose of rhPTH(1-84).

End point type	Primary

End point timeframe:

At Week 52 (EOT)

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive data was planned to be analyzed for this endpoint.

End point values	rhPTH(1-84)			
Subject group type	Reporting group			
Number of subjects analysed	22			
Units: percentage of subjects				
number (not applicable)	95.5			

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Treatment-emergent Adverse Events (TEAEs) and Serious TEAEs

End point title	Number of Subjects With Treatment-emergent Adverse Events (TEAEs) and Serious TEAEs[3]

End point description:

An adverse event (AE) was any untoward medical occurrence in a clinical investigation participant administered a pharmaceutical product and that does not necessarily have a causal relationship with this treatment. A Serious Adverse Event (SAE) was any untoward medical occurrence (whether considered to be related to investigational product or not) that at any dose: results in death, is life-threatening, requires inpatient hospitalization or prolongation of existing hospitalization, results in persistent or significant disability/incapacity, is a congenital abnormality/birth defect, and is an important medical event. TEAEs were defined as AEs with a start date on or after the first dose of investigational product or a start date before the date of the first dose of investigational product that increased in severity or after the date of the first dose. Safety analysis population consisted of all subjects who had received at least 1 dose of rhPTH(1-84).

End point type	Primary

End point timeframe:

From start of study drug administration to end of study (Week 56)

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive data was planned to be analyzed for this endpoint.

End point values	rhPTH(1-84)			
Subject group type	Reporting group			
Number of subjects analysed	22			
Units: Subjects				
Subjects with TEAEs	17			
Subjects with serious TEAEs	4			

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Clinically Significant Change in Clinical Laboratory Values

End point title	Number of Subjects With Clinically Significant Change in Clinical Laboratory Values[4]

End point description:

Clinical laboratory assessment included hematology, serum chemistry, urine chemistry and urinalysis. The investigator will assess out-of-range clinical laboratory values for clinical significance, to indicate whether or not the values are clinically significant. Any changes in clinical laboratory results which were deemed clinically significant by the investigator was reported. Safety analysis population consisted of all subjects who had received at least 1 dose of rhPTH(1-84).

End point type	Primary

End point timeframe:

From start of study drug administration to end of study (Week 56)

Notes:

[4] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive data was planned to be analyzed for this endpoint.

End point values	rhPTH(1-84)			
Subject group type	Reporting group			
Number of subjects analysed	22			
Units: Subjects	0			

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Clinically Significant Change in Vital Sign

End point title	Number of Subjects With Clinically Significant Change in Vital Sign[5]

End point description:

Vital sign parameters included: temperature, pulse rate, respiration rate, systolic and diastolic blood pressure. Any changes in vital signs which were deemed clinically significant by the investigator was reported. Safety analysis population consisted of all subjects who had received at least 1 dose of rhPTH(1-84).

End point type	Primary

End point timeframe:

From start of study drug administration to end of study (Week 56)

Notes:

[5] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive data was planned to be analyzed for this endpoint.

End point values	rhPTH(1-84)			
Subject group type	Reporting group			
Number of subjects analysed	22			
Units: Subjects	0			

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Clinically Significant Change in Electrocardiogram (ECG) Parameters

End point title	Number of Subjects With Clinically Significant Change in Electrocardiogram (ECG) Parameters[6]

End point description:

Twelve-lead ECGs was performed in triplicate with a minimum 2-minute gap between traces. The participant rested in the supine position for at least 5 minutes before collecting the ECG. Assessment of ECG parameters included: heart rate, RR interval, PR interval, QRS interval, QT interval, and QTc interval. Any change in ECG assessments which were deemed clinically significant by the investigator was reported. Safety analysis population consisted of all subjects who had received at least 1 dose of rhPTH(1-84).

End point type	Primary

End point timeframe:

From start of study drug administration to end of study (Week 56)

Notes:

[6] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive data was planned to be analyzed for this endpoint.

End point values	rhPTH(1-84)			
Subject group type	Reporting group			
Number of subjects analysed	22			
Units: Subjects	0			

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Clinically Significant Change in Estimated Glomerular Filtration Rate (eGFR) Values

End point title	Number of Subjects With Clinically Significant Change in Estimated Glomerular Filtration Rate (eGFR) Values[7]

End point description:

Estimated glomerular filtration rate (eGFR) was calculated using the chronic kidney disease epidemiology (CDK-epi) formula. Safety analysis population consisted of all subjects who had received at least 1 dose of rhPTH(1-84).

End point type	Primary

End point timeframe:

From start of study drug administration to end of study (Week 56)

Notes:

[7] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive data was planned to be analyzed for this endpoint.

End point values	rhPTH(1-84)			
Subject group type	Reporting group			
Number of subjects analysed	22			
Units: Subjects	0			

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Clinically Significant Change in Serum Creatinine Value

End point title	Number of Subjects With Clinically Significant Change in Serum Creatinine Value[8]

End point description:

eGFR was assessed by measuring serum creatinine. Serum creatinine level was obtained directly from laboratory results. Safety analysis population consisted of all subjects who had received at least 1 dose of rhPTH(1-84).

End point type	Primary

End point timeframe:

From start of study drug administration to end of study (Week 56)

Notes:

[8] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive data was planned to be analyzed for this endpoint.

End point values	rhPTH(1-84)			
Subject group type	Reporting group			
Number of subjects analysed	22			
Units: Subjects	0			

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Positive Anti-Parathyroid Hormone Antibodies at Week 24

End point title	Number of Subjects With Positive Anti-Parathyroid Hormone Antibodies at Week 24[9]

End point description:

Number of participants with positive anti-parathyroid hormone antibodies at Week 24 was reported. Safety analysis population consisted of all subjects who had received at least 1 dose of rhPTH(1-84). Here "number of subjects analysed" were subjects who were evaluable for this end point.

End point type	Primary

End point timeframe:

Week 24

Notes:

[9] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive data was planned to be analyzed for this endpoint.

End point values	rhPTH(1-84)			
Subject group type	Reporting group			
Number of subjects analysed	21			
Units: Subjects	0			

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Positive Anti-Parathyroid Hormone Antibodies at Week 52 (EOT)

End point title	Number of Subjects With Positive Anti-Parathyroid Hormone Antibodies at Week 52 (EOT)[10]

End point description:

Number of subjects with positive anti-parathyroid hormone antibodies at Week 52 (EOT) was reported. Safety analysis population consisted of all subjects who had received at least 1 dose of rhPTH(1-84). Here "number of subjects analysed" were subjects who were evaluable for this end point.

End point type	Primary

End point timeframe:

Week 52 (EOT)

Notes:

[10] - 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: Only descriptive data was planned to be analyzed for this endpoint.

End point values	rhPTH(1-84)			
Subject group type	Reporting group			
Number of subjects analysed	21			
Units: Subjects	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Albumin Corrected Serum Calcium (ACSC) Concentration at Weeks 24 and 52 (EOT)

End point title	Change From Baseline in Albumin Corrected Serum Calcium (ACSC) Concentration at Weeks 24 and 52 (EOT)

End point description:

Change from baseline in ACSC concentration at Weeks 24 and 52 (EOT) was reported. Safety analysis population consisted of all subjects who had received at least 1 dose of rhPTH(1-84). Here "n" were subjects who were evaluable for the end point at given time points.

End point type	Secondary

End point timeframe:

Baseline, Weeks 24 and 52 (EOT)

End point values	rhPTH(1-84)			
Subject group type	Reporting group			
Number of subjects analysed	22			
Units: mmol/L				
arithmetic mean (standard deviation)				
Change at Week 24 (n =21)	-0.024 (± 0.2065)			
Change at Week 52 (EOT) (n =22)	-0.076 (± 0.1497)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Serum Phosphate Concentration at Weeks 4, 8, 16, 24, 32, 40 and 52 (EOT)

End point title	Change From Baseline in Serum Phosphate Concentration at Weeks 4, 8, 16, 24, 32, 40 and 52 (EOT)

End point description:

Change from baseline in serum phosphate concentration at Weeks 4, 8, 16, 24, 32, 40 and 52 (EOT) was reported. Safety analysis population consisted of all subjects who had received at least 1 dose of rhPTH(1-84). Here "n" were subjects who were evaluable for the end point at given time points.

End point type	Secondary

End point timeframe:

Baseline, Weeks 4, 8, 16, 24, 32, 40 and 52 (EOT)

End point values	rhPTH(1-84)			
Subject group type	Reporting group			
Number of subjects analysed	22			
Units: mmol/L				
arithmetic mean (standard deviation)				
Change at Week 4 (n =21)	-0.167 (± 0.1816)			
Change at Week 8 (n =21)	-0.124 (± 0.2252)			
Change at Week 16 (n =21)	-0.107 (± 0.2583)			
Change at Week 24 (n =21)	-0.160 (± 0.2303)			
Change at Week 32 (n =20)	-0.089 (± 0.1809)			
Change at Week 40 (n =17)	-0.121 (± 0.2542)			

Change at Week 52 (EOT) (n =22)	-0.114 (± 0.2590)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in ACSC-phosphate Product at Weeks 4, 8, 16, 24, 32, 40 and 52 (EOT)

End point title	Change From Baseline in ACSC-phosphate Product at Weeks 4, 8, 16, 24, 32, 40 and 52 (EOT)

End point description:

Change from baseline in ACSC-phosphate product at Weeks 4, 8, 16, 24, 32, 40 and 52 (EOT) was reported. Here "mmol^2/L^2" is abbreviated as millimoles square per liter square. Safety analysis population consisted of all subjects who had received at least 1 dose of rhPTH(1-84). Here “n” were subjects who were evaluable for the end point at given time points.

End point type	Secondary

End point timeframe:

Baseline, Weeks 4, 8, 16, 24, 32, 40 and 52 (EOT)

End point values	rhPTH(1-84)			
Subject group type	Reporting group			
Number of subjects analysed	22			
Units: mmol^2/L^2				
arithmetic mean (standard deviation)				
Change at Week 4 (n =21)	-0.31 (± 0.462)			
Change at Week 8 (n =21)	-0.19 (± 0.537)			
Change at Week 16 (n =21)	-0.16 (± 0.609)			
Change at Week 24 (n =21)	-0.38 (± 0.556)			
Change at Week 32 (n =20)	-0.29 (± 0.456)			
Change at Week 40 (n =17)	-0.29 (± 0.572)			
Change at Week 52 (EOT) (n =22)	-0.34 (± 0.539)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in 24-hour Urine Calcium Excretion at Weeks 16, 32 and 52 (EOT)

End point title	Change From Baseline in 24-hour Urine Calcium Excretion at Weeks 16, 32 and 52 (EOT)

End point description:

Change from baseline in 24-hour urine calcium excretion at Weeks 16, 32 and 52 (EOT) was reported. Safety analysis population consisted of all subjects who had received at least 1 dose of rhPTH(1-84). Here "number of subjects analysed" were subjects who were evaluable for this end point and "n" were subjects who were evaluable for the end point at given time points.

End point type	Secondary

End point timeframe:

Baseline, Weeks 16, 32 and 52 (EOT)

End point values	rhPTH(1-84)			
Subject group type	Reporting group			
Number of subjects analysed	21			
Units: millimoles per day (mmol/day)				
arithmetic mean (standard deviation)				
Change at Week 16 (n =21)	-0.22 (± 4.741)			
Change at Week 32 (n =20)	-3.13 (± 4.103)			
Change at Week 52 (EOT) (n =20)	-2.53 (± 4.421)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage Change From Baseline in Prescribed Supplemental Oral Calcium Dose at Weeks 4, 8, 16, 24, 32, 40, 52 (EOT) and 56 (End of Study [EOS])

End point title	Percentage Change From Baseline in Prescribed Supplemental Oral Calcium Dose at Weeks 4, 8, 16, 24, 32, 40, 52 (EOT) and 56 (End of Study [EOS])

End point description:

Percentage change from baseline in prescribed supplemental oral calcium dose at Weeks 4, 8, 16, 24, 32, 40, 52 (EOT) and 56 (EOS) were reported. Safety analysis population consisted of all subjects who had received at least 1 dose of rhPTH(1-84). Here "n" were subjects who were evaluable for the end point at given time points. Data for Week 56 was not collected as study was early terminated due to FDA recall of rhPTH(1-84) (Natpara). Here "99999" refers to data not available and we have added it as space-fillers.

End point type	Secondary

End point timeframe:

Baseline and at Weeks 4, 8, 16, 24, 32, 40, 52 (EOT) and 56 (EOS)

End point values	rhPTH(1-84)			
Subject group type	Reporting group			
Number of subjects analysed	22			
Units: percentage change				
arithmetic mean (standard deviation)				
Percentage change at Week 4 (n =21)	-14.30 (± 34.269)			
Percentage change at Week 8 (n =21)	-29.08 (± 38.019)			
Percentage change at Week 16 (n =21)	-36.94 (± 45.665)			
Percentage change at Week 24 (n =21)	-49.05 (± 49.049)			
Percentage change at Week 32 (n =20)	-55.58 (± 44.268)			
Percentage change at Week 40 (n =17)	-56.36 (± 45.168)			
Percentage change at Week 52 (EOT) (n =22)	-48.55 (± 45.237)			
Percentage change at Week 56 (EOS) (n =0)	99999 (± 99999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage Change From Baseline in Prescribed Supplemental Active Vitamin D Dose at Weeks 4, 8, 16, 24, 32, 40, 52 (EOT) and 56 (EOS)

End point title	Percentage Change From Baseline in Prescribed Supplemental Active Vitamin D Dose at Weeks 4, 8, 16, 24, 32, 40, 52 (EOT) and 56 (EOS)

End point description:

Percentage change from baseline in prescribed supplemental oral calcium dose at Weeks 4, 8, 16, 24, 32, 40, 52 (EOT) and 56 (EOS) were reported. Safety analysis population consisted of all subjects who had received at least 1 dose of rhPTH(1-84). Here “number of subjects analysed” were subjects who were evaluable for this end point and “n” were subjects who were evaluable for the end point at given time points. Data for Week 56 was not collected as study was early terminated due to FDA recall of rhPTH(1-84) (Natpara). Here "99999" refers to data not available and we have added it as space-fillers.

End point type	Secondary

End point timeframe:

Baseline, Weeks 4, 8, 16, 24, 32, 40, 52 (EOT) and 56 (EOS)

End point values	rhPTH(1-84)			
Subject group type	Reporting group			
Number of subjects analysed	21			
Units: percentage change				
arithmetic mean (standard deviation)				
Percentage change at Week 4 (n =20)	-57.50 (± 40.995)			
Percentage change at Week 8 (n =20)	-70.00 (± 39.217)			

Percentage change at Week 16 (n =20)	-80.83 (± 27.185)			
Percentage change at Week 24 (n =20)	-85.42 (± 25.055)			
Percentage change at Week 32 (n =19)	-90.79 (± 17.324)			
Percentage change at Week 40 (n =16)	-90.10 (± 18.564)			
Percentage change at Week 52 (EOT) (n =21)	-77.38 (± 43.870)			
Percentage change at Week 56 (EOS) (n =0)	99999 (± 99999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage Change From Baseline in Serum Bone-specific Alkaline Phosphatase at Weeks 8, 24 and 52 (EOT)

End point title	Percentage Change From Baseline in Serum Bone-specific Alkaline Phosphatase at Weeks 8, 24 and 52 (EOT)

End point description:

Percentage change from baseline in serum bone-specific alkaline phosphatase at Weeks 8, 24 and 52 (EOT) was reported. Safety analysis population consisted of all subjects who had received at least 1 dose of rhPTH(1-84). Here "n" were subjects who were evaluable for the end point at given time points.

End point type	Secondary

End point timeframe:

Baseline, Weeks 8, 24 and 52 (EOT)

End point values	rhPTH(1-84)			
Subject group type	Reporting group			
Number of subjects analysed	22			
Units: percentage change				
arithmetic mean (standard deviation)				
Percentage change at Week 8 (n =20)	29.90 (± 31.575)			
Percentage change at Week 24 (n =21)	89.14 (± 54.452)			
Percentage change at Week 52 (EOT) (n =22)	94.08 (± 75.066)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage Change From Baseline in Serum Osteocalcin at Weeks 8, 24 and 52 (EOT)

End point title	Percentage Change From Baseline in Serum Osteocalcin at

	Weeks 8, 24 and 52 (EOT)

End point description:

Percentage change from baseline in serum osteocalcin at Weeks 8, 24 and 52 (EOT) was reported. Safety analysis population consisted of all subjects who had received at least 1 dose of rhPTH(1-84). Here "n" were subjects who were evaluable for the end point at given time points.

End point type	Secondary

End point timeframe:

Baseline, Weeks 8, 24 and 52 (EOT)

End point values	rhPTH(1-84)			
Subject group type	Reporting group			
Number of subjects analysed	22			
Units: percentage change				
arithmetic mean (standard deviation)				
Percentage change at Week 8 (n =21)	61.74 (± 68.363)			
Percentage change at Week 24 (n =21)	225.91 (± 130.798)			
Percentage change at Week 52 (EOT) (n =22)	294.93 (± 215.100)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage Change From Baseline in Procollagen 1 N-Terminal Propeptide at Weeks 8, 24 and 52 (EOT)

End point title	Percentage Change From Baseline in Procollagen 1 N-Terminal Propeptide at Weeks 8, 24 and 52 (EOT)

End point description:

Percentage change from baseline in procollagen 1 N-terminal propeptide at Weeks 8, 24 and 52 (EOT) was reported. Safety analysis population consisted of all subjects who had received at least 1 dose of rhPTH(1-84). Here "n" were subjects who were evaluable for the end point at given time points.

End point type	Secondary

End point timeframe:

Baseline, Weeks 8, 24 and 52 (EOT)

End point values	rhPTH(1-84)			
Subject group type	Reporting group			
Number of subjects analysed	22			
Units: percentage change				
median (standard deviation)				
Percentage change at Week 8 (n =21)	119.98 (± 161.156)			
Percentage change at Week 24 (n =21)	412.46 (± 248.423)			

Percentage change at Week 52 (EOT) (n =22)	476.07 (± 377.383)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage Change From Baseline in Type I Collagen C-Telopeptides at Weeks 8, 24 and 52 (EOT)

End point title	Percentage Change From Baseline in Type I Collagen C-Telopeptides at Weeks 8, 24 and 52 (EOT)

End point description:

Percentage change from baseline in type I collagen C-telopeptides at Week 8, 24 and 52 (EOT) was reported. Safety analysis population consisted of all subjects who had received at least 1 dose of rhPTH(1-84). Here "n" were subjects who were evaluable for the end point at given time points.

End point type	Secondary

End point timeframe:

Baseline, Weeks 8, 24 and 52 (EOT)

End point values	rhPTH(1-84)			
Subject group type	Reporting group			
Number of subjects analysed	22			
Units: percentage change				
arithmetic mean (standard deviation)				
Percentage change at Week 8 (n =21)	124.62 (± 160.564)			
Percentage change at Week 24 (n =21)	254.26 (± 198.947)			
Percentage change at Week 52 (EOT) (n =22)	227.13 (± 182.262)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage Change From Baseline in Type I Collagen N-Telopeptides at Weeks 8, 24 and 52 (EOT)

End point title	Percentage Change From Baseline in Type I Collagen N-Telopeptides at Weeks 8, 24 and 52 (EOT)

End point description:

Percentage change from baseline in type I collagen N-telopeptides at Week 8, 24 and 52 (EOT) was reported. Safety analysis population consisted of all subjects who had received at least 1 dose of rhPTH(1-84). Here "n" were subjects who were evaluable for the end point at given time points.

End point type	Secondary

End point timeframe:

Baseline, Weeks 8, 24 and 52 (EOT)

End point values	rhPTH(1-84)			
Subject group type	Reporting group			
Number of subjects analysed	22			
Units: percentage change				
arithmetic mean (standard deviation)				
Percentage change at Week 8 (n =21)	71.33 (± 99.933)			
Percentage change at Week 24 (n =21)	183.23 (± 160.350)			
Percentage change at Week 52 (EOT) (n =22)	231.80 (± 270.229)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From start of screening up to end of study (Week 56)

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	20.1

Reporting groups

Reporting group title	rhPTH(1-84)

Reporting group description:

Subjects received rhPTH(1-84) (Natpara) 50 mcg, injection, subcutaneously, once daily in the thigh (alternate thigh every day) up to 52 weeks (EOT/ET). Dose escalation was done up to 100 mcg in increments of 25 mcg no more frequently than every 2 to 4 weeks, with the goal of achieving or maintaining ACSC levels in the range of 2-2.25 mmol/L (8-9 mg/dL). Administered dose was maintained once a participant achieved a stable ACSC level of 2-2.25 mmol/L (8-9 mg/dL) and had minimized supplement (active vitamin D and calcium supplement) doses. If ACSC was >2.25 mmol/L (>9.0 mg/dL), a starting dose of 25 mcg was administered.

Serious adverse events	rhPTH(1-84)		
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 22 (18.18%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Breast cancer			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Cerebellar haemorrhage			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			

Appendicitis			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	rhPTH(1-84)		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	10 / 22 (45.45%)		
Nervous system disorders			
Headache			
subjects affected / exposed	3 / 22 (13.64%)		
occurrences (all)	7		
Migraine			
subjects affected / exposed	2 / 22 (9.09%)		
occurrences (all)	3		
Paraesthesia			
subjects affected / exposed	2 / 22 (9.09%)		
occurrences (all)	2		
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	4 / 22 (18.18%)		
occurrences (all)	5		
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	6 / 22 (27.27%)		
occurrences (all)	7		
Vomiting			
subjects affected / exposed	2 / 22 (9.09%)		
occurrences (all)	4		
Psychiatric disorders			
Anxiety			
subjects affected / exposed	2 / 22 (9.09%)		
occurrences (all)	2		
Musculoskeletal and connective tissue disorders			

Muscle spasms subjects affected / exposed occurrences (all)	3 / 22 (13.64%) 6		
Myalgia subjects affected / exposed occurrences (all)	2 / 22 (9.09%) 2		
Osteoarthritis subjects affected / exposed occurrences (all)	2 / 22 (9.09%) 2		
Tendonitis subjects affected / exposed occurrences (all)	2 / 22 (9.09%) 2		
Infections and infestations Nasopharyngitis subjects affected / exposed occurrences (all)	3 / 22 (13.64%) 3		
Metabolism and nutrition disorders Hypercalcaemia subjects affected / exposed occurrences (all)	4 / 22 (18.18%) 5		
Hypocalcaemia subjects affected / exposed occurrences (all)	2 / 22 (9.09%) 4		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported