Clinical trial results:
A Phase 3, Multicenter, Randomized, Double-Blind, Placebo-Controlled, Parallel Group Trial, with an Open-Label Extension, Investigating the Safety, Tolerability and Efficacy of TransCon PTH Administered Subcutaneously Daily in Adults with Hypoparathyroidism

Summary

EudraCT number	2020-003380-26
Trial protocol	DK NO FR DE HU IT
Global end of trial date	21 January 2025

Results information

Result version number	v2 (current)
This version publication date	06 February 2026
First version publication date	27 April 2023
Version creation reason	• New data added to full data set Update to include OLE safety data.

Trial information

Trial identification

Sponsor protocol code	TCP-304

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04701203
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Ascendis Pharma Bone Diseases A/S
Sponsor organisation address	Tuborg Boulevard 12, Hellerup, Denmark, DK 2900
Public contact	Clinical Trial Information Desk , Ascendis Pharma Bone Diseases A/S, 45 70222244, clinhelpdesk@ascendispharma.com
Scientific contact	Clinical Trial Information Desk , Ascendis Pharma Bone Diseases A/S, 45 70222244, clinhelpdesk@ascendispharma.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	09 October 2025
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	21 January 2025
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the treatment effect of daily TransCon PTH on serum calcium levels, and therapeutic doses of active vitamin D (i.e., calcitriol or alfacalcidol) and calcium at 26 weeks of treatment.

Protection of trial subjects:

Written informed consent was obtained from all subjects prior to enrollment into the trial, as dictated by the Declaration of Helsinki.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	28 December 2020
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
Long term follow-up duration	3 Years
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United States: 30
Country: Number of subjects enrolled	Canada: 21
Country: Number of subjects enrolled	Norway: 1
Country: Number of subjects enrolled	Denmark: 11
Country: Number of subjects enrolled	Germany: 1
Country: Number of subjects enrolled	Hungary: 7
Country: Number of subjects enrolled	Italy: 11
Worldwide total number of subjects	82
EEA total number of subjects	31

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	0

months)	
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	72
From 65 to 84 years	10
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Overall, 82 subjects were enrolled and dosed. Enrollment of subjects occurred in seven countries: Canada, Denmark, Germany, Italy, Hungary, Norway, and the United States.

Pre-assignment

Screening details:

A total of 106 subjects were screened and 84 of these met eligibility criteria and were enrolled into the study. Two subjects randomised to TransCon PTH were not treated. A total of 82 subjects were therefore included in the ITT and the Safety analysis populations.

Period 1

Period 1 title	Blinded Treatment Period (Weeks 0 to 26)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Double Blind: TransCon PTH

Arm description:

TransCon PTH at a starting dose of 18 mcg delivered once daily by subcutaneous injection and titrated to an optimal dose.

Arm type	Experimental
Investigational medicinal product name	TransCon PTH
Investigational medicinal product code	ACP-014
Other name	Palopegteriparatide
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

TransCon PTH drug product was supplied as a clear solution containing palopegteriparatide with a nominal PTH(1-34) content of 0.3 mg/mL in a pre-filled pen intended for subcutaneous injection. All subjects were initially prescribed TransCon PTH 18 µg PTH(1-34)/d and were individually and progressively titrated to an optimal dose (allowable range 6–60 µg/d) in increments of 3 µg/d. Titration of study drug and conventional therapy was performed according to a protocol-specified algorithm guided by serum calcium values.

Arm title	Double Blind: Placebo

Arm description:

Once daily subcutaneous administration of placebo for TransCon PTH to mimick the dose of investigational product.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Placebo for TransCon PTH drug product was supplied as a clear solution containing placebo liquid to match the investigational product in a pre-filled pen intended for subcutaneous injection.

Number of subjects in period 1	Double Blind: TransCon PTH	Double Blind: Placebo
Started	61	21
Completed	60	19
Not completed	1	2
Adverse event, serious fatal	1	-
Consent withdrawn by subject	-	1
Adverse event, non-fatal	-	1

Period 2

Period 2 title	Open-Label Period (Weeks 26 to 182)
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Open-Label Extension Period: TransCon PTH

Arm description:

Subjects who completed the 26-week double treatment period, continued into the open-label extension period and received treatment with TransCon PTH up to Week 182. All participants received individualized doses of TransCon PTH (allowable dose range: 6 to 60 mcg/day).

Arm type	Experimental
Investigational medicinal product name	TransCon PTH
Investigational medicinal product code	ACP-014
Other name	Palopegteriparatide
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

TransCon PTH drug product was supplied as a clear solution containing palopegteriparatide with a nominal PTH (1-34) content of 0.3 mg/mL in a pre-filled pen intended for subcutaneous injection. All subjects received individualized doses of TransCon PTH (allowable dose range: 6 to 60 µg/day).

Number of subjects in period 2	Open-Label Extension Period: TransCon PTH
Started	79
Completed	73
Not completed	6
Consent withdrawn by subject	5
Pregnancy	1

Baseline characteristics

Reporting groups	
Reporting group title	Double Blind: TransCon PTH
Reporting group description:	
TransCon PTH at a starting dose of 18 mcg delivered once daily by subcutaneous injection and titrated to an optimal dose.	
Reporting group title	Double Blind: Placebo
Reporting group description:	
Once daily subcutaneous administration of placebo for TransCon PTH to mimick the dose of investigational product.	

Reporting group values	Double Blind: TransCon PTH	Double Blind: Placebo	Total
Number of subjects	61	21	82
Age categorical			
Units: Subjects			
Age continuous			
Units: years			
arithmetic mean	49.0	47.3	
standard deviation	± 13.13	± 11.43	-
Gender categorical			
Units: Subjects			
Female	46	18	64
Male	15	3	18
Race			
Units: Subjects			
Asian	3	2	5
White	57	19	76
Other	1	0	1
Ethnicity			
Units: Subjects			
Not Hispanic or Latino	57	18	75
Not Reported	3	1	4
Unknown	1	2	3
Height			
Units: cm			
arithmetic mean	168.22	166.67	
standard deviation	± 8.353	± 8.831	-
Weight			
Units: kg			
arithmetic mean	77.18	81.61	
standard deviation	± 17.335	± 15.631	-
Body Mass Index			
Units: kg/m^2			
arithmetic mean	27.27	29.47	
standard deviation	± 5.813	± 5.691	-

End points

End points reporting groups

Reporting group title	Double Blind: TransCon PTH
Reporting group description:	
TransCon PTH at a starting dose of 18 mcg delivered once daily by subcutaneous injection and titrated to an optimal dose.	
Reporting group title	Double Blind: Placebo
Reporting group description:	
Once daily subcutaneous administration of placebo for TransCon PTH to mimick the dose of investigational product.	
Reporting group title	Open-Label Extension Period: TransCon PTH
Reporting group description:	
Subjects who completed the 26-week double treatment period, continued into the open-label extension period and received treatment with TransCon PTH up to Week 182. All participants received individualized doses of TransCon PTH (allowable dose range: 6 to 60 mcg/day).	

Primary: Efficacy - Primary Endpoint During the Blinded Period

End point title	Efficacy - Primary Endpoint During the Blinded Period
End point description:	
The primary endpoint was a multi-component endpoint that included the percentage of subjects who met the following criteria at 26 weeks of blinded treatment: 1) albumin-adjusted serum calcium measured within 4 weeks prior to and on Week 26 visit within the normal range (8.3 to 10.6 mg/dL), and 2) independence from active vitamin D within 4 weeks prior to Week 26 visit (i.e., all daily standing dose of active vitamin D equal to zero AND use of PRN ≤7 days during the 4 weeks), and 3) independence from therapeutic doses of calcium within 4 weeks prior to Week 26 visit (i.e., average daily standing dose of elemental calcium ≤600 mg AND use of PRN doses on ≤7 days during the 4 weeks) and, 4) no increase in prescribed study drug within 4 weeks prior to Week 26 visit.	
End point type	Primary
End point timeframe:	
26 weeks	

End point values	Double Blind: TransCon PTH	Double Blind: Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	61	21		
Units: Percentage of subjects				
number (confidence interval 95%)	78.7 (66.3 to 88.1)	4.8 (0.1 to 23.8)		

Statistical analyses

Statistical analysis title	Primary efficacy endpoint
Statistical analysis description:	
For the primary efficacy endpoint, the Cochran–Mantel Haenszel test stratified by etiology of hypoparathyroidism (postsurgical or other) was used to compare the proportion of participants meeting the multi-component primary endpoint in the TransCon PTH versus placebo groups. Participants without week 26 albumin-adjusted serum calcium or with >25% (ie, >7 days) missing diary data of active	

vitamin D or elemental calcium during the 4 weeks before week 26 were considered non-responders.

Comparison groups	Double Blind: TransCon PTH v Double Blind: Placebo
Number of subjects included in analysis	82
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	t-test, 2-sided

Secondary: Change From Baseline to Week 26 in HPES Symptom - Physical Domain Score

End point title	Change From Baseline to Week 26 in HPES Symptom - Physical Domain Score

End point description:

Change from baseline in Hypoparathyroidism Patient Experience Scale (HPES) Symptom - Physical Domain score, a disease-specific patient reported outcome, at 26 weeks of treatment. The measure uses a scale of 0-100 and values represent the change in scores from baseline. A decrease in HPES score denotes an improvement in hypoparathyroidism disease related physical symptoms.

End point type	Secondary

End point timeframe:

Week 26

End point values	Double Blind: TransCon PTH	Double Blind: Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	59	19		
Units: units on a scale				
least squares mean (confidence interval 95%)	-21.01 (-25.41 to -16.60)	-4.81 (-15.22 to 5.59)		

Statistical analyses

Statistical analysis title	HPES - Symptom - Physical Domain Score

Statistical analysis description:

ANCOVA model with unequal variance was used to analyze the key secondary Endpoints. The change from baseline is variable of interest at week 26 and was included in the model as response variables. Treatment assignment and etiology of hypoparathyroidism were entered as fixed effects and baseline value of the variable of interest was entered as a covariate.

Comparison groups	Double Blind: TransCon PTH v Double Blind: Placebo
Number of subjects included in analysis	78
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.0038
Method	t-test, 2-sided

Secondary: Change From Baseline to Week 26 in HPES Symptom - Cognitive Domain Score

End point title	Change From Baseline to Week 26 in HPES Symptom - Cognitive Domain Score

End point description:

Change from baseline in Hypoparathyroidism Patient Experience Scale (HPES) Symptom - Cognitive Domain score, a disease-specific patient reported outcome, at 26 weeks of treatment. The measure uses a scale of 0-100 and values represent the change in scores from baseline. A decrease in HPES score denotes an improvement in hypoparathyroidism disease related cognitive symptoms.

End point type	Secondary

End point timeframe:

Week 26

End point values	Double Blind: TransCon PTH	Double Blind: Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	59	19		
Units: units on a scale				
least squares mean (confidence interval 95%)	-20.49 (-25.67 to -15.31)	-6.16 (-15.92 to 3.60)		

Statistical analyses

Statistical analysis title	HPES - Symptom - Cognitive Domain Score

Statistical analysis description:

ANCOVA model with unequal variance was used to analyze the key secondary Endpoints. The change from baseline is variable of interest at week 26 and was included in the model as response variables. Treatment assignment and etiology of hypoparathyroidism were entered as fixed effects and baseline value of the variable of interest was entered as a covariate.

Comparison groups	Double Blind: Placebo v Double Blind: TransCon PTH
Number of subjects included in analysis	78
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.0055
Method	t-test, 2-sided

Secondary: Change From Baseline to Week 26 in HPES Impact - Physical Functioning Domain Score

End point title	Change From Baseline to Week 26 in HPES Impact - Physical Functioning Domain Score

End point description:

Change from baseline in Hypoparathyroidism Patient Experience Scale (HPES) Impact - Physical Functioning Domain score, a disease-specific patient reported outcome, at 26 weeks of treatment. The measure uses a scale of 0-100 and values represent the change in scores from baseline. A decrease in HPES score denotes an improvement in physical functioning health-related quality of life.

End point type	Secondary

End point timeframe:

Week 26

End point values	Double Blind: TransCon PTH	Double Blind: Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	59	19		
Units: units on a scale				
least squares mean (confidence interval 95%)	-18.29 (-23.59 to -12.99)	-1.01 (-12.40 to 10.38)		

Statistical analyses

Statistical analysis title	HPES - Impact - Physical Functioning Domain Score

Statistical analysis description:

ANCOVA model with unequal variance was used to analyze the key secondary Endpoints. The change from baseline is variable of interest at week 26 and was included in the model as response variables. Treatment assignment and etiology of hypoparathyroidism were entered as fixed effects and baseline value of the variable of interest was entered as a covariate.

Comparison groups	Double Blind: TransCon PTH v Double Blind: Placebo
Number of subjects included in analysis	78
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.0046
Method	t-test, 2-sided

Secondary: Change From Baseline to Week 26 in HPES Impact - Daily Life Domain Score

End point title	Change From Baseline to Week 26 in HPES Impact - Daily Life Domain Score

End point description:

Change from baseline in Hypoparathyroidism Patient Experience Scale (HPES) Impact - Daily Life Domain score, a disease-specific patient reported outcome, at 26 weeks of treatment. The measure uses a scale of 0-100 and values represent the change in scores from baseline. A decrease in HPES score denotes an improvement in daily health-related quality of life.

End point type	Secondary

End point timeframe:

Week 26

End point values	Double Blind: TransCon PTH	Double Blind: Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	59	19		
Units: units on a scale				
least squares mean (confidence interval 95%)	-17.65 (-22.39 to -12.91)	-0.36 (-12.19 to 11.46)		

Statistical analyses

Statistical analysis title	HPES - Impact - Daily Life Domain Score

Statistical analysis description:

ANCOVA model with unequal variance was used to analyze the key secondary Endpoints. The change from baseline is variable of interest at week 26 and was included in the model as response variables. Treatment assignment and etiology of hypoparathyroidism were entered as fixed effects and baseline value of the variable of interest was entered as a covariate.

Comparison groups	Double Blind: TransCon PTH v Double Blind: Placebo
Number of subjects included in analysis	78
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.0061
Method	t-test, 2-sided

Secondary: Change From Baseline to Week 26 in SF-36 Physical Functioning Subscale Score

End point title	Change From Baseline to Week 26 in SF-36 Physical Functioning Subscale Score

End point description:

Change from baseline in the 36-item Short Form Survey (SF-36) Physical Functioning subscale score, a generic health survey, at 26 weeks of treatment. The Physical Functioning subscale uses a range of 19-57.6 and values represent the change in scores from baseline. An increase in SF-36 score denotes an improvement in physical functioning health-related quality of life.

End point type	Secondary

End point timeframe:

Week 26

End point values	Double Blind: TransCon PTH	Double Blind: Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	59	19		
Units: units on a scale				
least squares mean (confidence interval 95%)	5.29 (3.47 to 7.10)	0.12 (-4.64 to 4.89)		

Statistical analyses

Statistical analysis title	SF-36 – Physical Functioning Subscale Score

Statistical analysis description:

ANCOVA model with unequal variance was used to analyze the key secondary Endpoints. The change from baseline is variable of interest at week 26 and was included in the model as response variables. Treatment assignment and etiology of hypoparathyroidism were entered as fixed effects and baseline value of the variable of interest was entered as a covariate.

Comparison groups	Double Blind: TransCon PTH v Double Blind: Placebo
Number of subjects included in analysis	78
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.0347
Method	t-test, 2-sided

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From Week 0 to Week 26 for double-blind treatment period and up to Week 182 for open label extension (OLE) period

Adverse event reporting additional description:

Analysed on safety analysis set that included all randomised subjects who received at least one dose of trial drug and were analysed according to actual study treatment received.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	27.0

Reporting groups

Reporting group title	Double Blind: TransCon PTH

Reporting group description:

TransCon PTH at a starting dose of 18 mcg delivered once daily by subcutaneous injection and titrated to an optimal dose during the blinded period.

Reporting group title	Double Blind: Placebo

Reporting group description:

Placebo for TransCon PTH delivered once daily by subcutaneous injection during the blinded period.

Reporting group title	Total TransCon PTH Period

Reporting group description:

Subjects who completed the 26-week double blind treatment period in placebo and TransCon PTH groups, continued into the open-label extension (OLE) period and received treatment with TransCon PTH up to Week 182. This period refers to total period of exposure to TransCon PTH. For subjects randomised to TransCon PTH at enrollment, the "TransCon PTH Period" was the time from first dose of blinded TransCon PTH until final analysis in OLE period. The TransCon PTH Period for subjects randomised to placebo at enrollment was the time from first exposure to TransCon PTH at the time of cross-over from placebo, until final analysis in the OLE.

Serious adverse events	Double Blind: TransCon PTH	Double Blind: Placebo	Total TransCon PTH Period
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 61 (8.20%)	2 / 21 (9.52%)	20 / 80 (25.00%)
number of deaths (all causes)	1	0	1
number of deaths resulting from adverse events	1	0	1
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Invasive breast carcinoma			
subjects affected / exposed	0 / 61 (0.00%)	1 / 21 (4.76%)	0 / 80 (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
Prostate cancer			

subjects affected / exposed	0 / 61 (0.00%)	0 / 21 (0.00%)	1 / 80 (1.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tongue neoplasm malignant stage unspecified			
subjects affected / exposed	0 / 61 (0.00%)	0 / 21 (0.00%)	1 / 80 (1.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Hypertensive crisis			
subjects affected / exposed	0 / 61 (0.00%)	0 / 21 (0.00%)	1 / 80 (1.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Cardiac arrest			
subjects affected / exposed	1 / 61 (1.64%)	0 / 21 (0.00%)	1 / 80 (1.25%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 1
Cardiac failure			
subjects affected / exposed	0 / 61 (0.00%)	0 / 21 (0.00%)	1 / 80 (1.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear and labyrinth disorders			
Deafness neurosensory			
subjects affected / exposed	0 / 61 (0.00%)	0 / 21 (0.00%)	1 / 80 (1.25%)
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			
Colitis			
subjects affected / exposed	1 / 61 (1.64%)	0 / 21 (0.00%)	1 / 80 (1.25%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rectal haemorrhage			

subjects affected / exposed	1 / 61 (1.64%)	0 / 21 (0.00%)	2 / 80 (2.50%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Proctalgia			
subjects affected / exposed	0 / 61 (0.00%)	0 / 21 (0.00%)	1 / 80 (1.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Endometrial disorder			
subjects affected / exposed	0 / 61 (0.00%)	0 / 21 (0.00%)	1 / 80 (1.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Bipolar disorder			
subjects affected / exposed	0 / 61 (0.00%)	1 / 21 (4.76%)	0 / 80 (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
Post-traumatic stress disorder			
subjects affected / exposed	0 / 61 (0.00%)	0 / 21 (0.00%)	1 / 80 (1.25%)
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			
Neck pain			
subjects affected / exposed	0 / 61 (0.00%)	0 / 21 (0.00%)	1 / 80 (1.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Pneumonia			
subjects affected / exposed	0 / 61 (0.00%)	0 / 21 (0.00%)	2 / 80 (2.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enteritis infectious			

subjects affected / exposed	0 / 61 (0.00%)	0 / 21 (0.00%)	1 / 80 (1.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis			
subjects affected / exposed	0 / 61 (0.00%)	0 / 21 (0.00%)	1 / 80 (1.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	0 / 61 (0.00%)	0 / 21 (0.00%)	1 / 80 (1.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin infection			
subjects affected / exposed	0 / 61 (0.00%)	0 / 21 (0.00%)	1 / 80 (1.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Hypercalcaemia			
subjects affected / exposed	1 / 61 (1.64%)	0 / 21 (0.00%)	2 / 80 (2.50%)
occurrences causally related to treatment / all	1 / 1	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypocalcaemia			
subjects affected / exposed	1 / 61 (1.64%)	0 / 21 (0.00%)	5 / 80 (6.25%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 10
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	Double Blind: TransCon PTH	Double Blind: Placebo	Total TransCon PTH Period
Total subjects affected by non-serious adverse events			
subjects affected / exposed	50 / 61 (81.97%)	20 / 21 (95.24%)	72 / 80 (90.00%)
Vascular disorders			
Hypertension			
subjects affected / exposed	3 / 61 (4.92%)	3 / 21 (14.29%)	12 / 80 (15.00%)
occurrences (all)	3	3	13

Orthostatic hypotension			
subjects affected / exposed	1 / 61 (1.64%)	0 / 21 (0.00%)	10 / 80 (12.50%)
occurrences (all)	1	0	12
General disorders and administration site conditions			
Injection site reaction			
subjects affected / exposed	19 / 61 (31.15%)	0 / 21 (0.00%)	20 / 80 (25.00%)
occurrences (all)	20	0	22
Fatigue			
subjects affected / exposed	9 / 61 (14.75%)	5 / 21 (23.81%)	18 / 80 (22.50%)
occurrences (all)	10	5	23
Asthenia			
subjects affected / exposed	3 / 61 (4.92%)	1 / 21 (4.76%)	6 / 80 (7.50%)
occurrences (all)	3	1	6
Non-cardiac chest pain			
subjects affected / exposed	1 / 61 (1.64%)	0 / 21 (0.00%)	4 / 80 (5.00%)
occurrences (all)	1	0	4
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	4 / 61 (6.56%)	0 / 21 (0.00%)	5 / 80 (6.25%)
occurrences (all)	4	0	5
Psychiatric disorders			
Insomnia			
subjects affected / exposed	4 / 61 (6.56%)	1 / 21 (4.76%)	7 / 80 (8.75%)
occurrences (all)	4	1	7
Investigations			
Blood thyroid stimulating hormone decreased			
subjects affected / exposed	3 / 61 (4.92%)	3 / 21 (14.29%)	11 / 80 (13.75%)
occurrences (all)	3	3	11
Blood thyroid stimulating hormone increased			
subjects affected / exposed	1 / 61 (1.64%)	0 / 21 (0.00%)	8 / 80 (10.00%)
occurrences (all)	1	0	15
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	3 / 61 (4.92%)	1 / 21 (4.76%)	5 / 80 (6.25%)
occurrences (all)	5	1	9

Medication error			
subjects affected / exposed	2 / 61 (3.28%)	0 / 21 (0.00%)	4 / 80 (5.00%)
occurrences (all)	3	0	5
Cardiac disorders			
Palpitations			
subjects affected / exposed	3 / 61 (4.92%)	0 / 21 (0.00%)	9 / 80 (11.25%)
occurrences (all)	4	0	11
Postural orthostatic tachycardia syndrome			
subjects affected / exposed	2 / 61 (3.28%)	0 / 21 (0.00%)	7 / 80 (8.75%)
occurrences (all)	2	0	9
Nervous system disorders			
Headache			
subjects affected / exposed	13 / 61 (21.31%)	2 / 21 (9.52%)	19 / 80 (23.75%)
occurrences (all)	20	2	28
Paraesthesia			
subjects affected / exposed	12 / 61 (19.67%)	3 / 21 (14.29%)	21 / 80 (26.25%)
occurrences (all)	19	10	34
Dizziness			
subjects affected / exposed	4 / 61 (6.56%)	0 / 21 (0.00%)	7 / 80 (8.75%)
occurrences (all)	4	0	9
Brain fog			
subjects affected / exposed	1 / 61 (1.64%)	1 / 21 (4.76%)	6 / 80 (7.50%)
occurrences (all)	1	1	7
Dizziness postural			
subjects affected / exposed	3 / 61 (4.92%)	0 / 21 (0.00%)	4 / 80 (5.00%)
occurrences (all)	3	0	4
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	7 / 61 (11.48%)	2 / 21 (9.52%)	12 / 80 (15.00%)
occurrences (all)	11	3	19
Diarrhoea			
subjects affected / exposed	6 / 61 (9.84%)	1 / 21 (4.76%)	7 / 80 (8.75%)
occurrences (all)	6	1	12
Constipation			
subjects affected / exposed	4 / 61 (6.56%)	1 / 21 (4.76%)	5 / 80 (6.25%)
occurrences (all)	5	1	8

Vomiting			
subjects affected / exposed	3 / 61 (4.92%)	0 / 21 (0.00%)	5 / 80 (6.25%)
occurrences (all)	6	0	9
Dry mouth			
subjects affected / exposed	2 / 61 (3.28%)	1 / 21 (4.76%)	5 / 80 (6.25%)
occurrences (all)	2	1	5
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 61 (0.00%)	0 / 21 (0.00%)	5 / 80 (6.25%)
occurrences (all)	0	0	5
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	1 / 61 (1.64%)	0 / 21 (0.00%)	5 / 80 (6.25%)
occurrences (all)	1	0	5
Alopecia			
subjects affected / exposed	2 / 61 (3.28%)	0 / 21 (0.00%)	4 / 80 (5.00%)
occurrences (all)	2	0	4
Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	0 / 61 (0.00%)	1 / 21 (4.76%)	4 / 80 (5.00%)
occurrences (all)	0	1	4
Pollakiuria			
subjects affected / exposed	3 / 61 (4.92%)	0 / 21 (0.00%)	4 / 80 (5.00%)
occurrences (all)	3	0	4
Musculoskeletal and connective tissue disorders			
Muscle spasms			
subjects affected / exposed	7 / 61 (11.48%)	3 / 21 (14.29%)	17 / 80 (21.25%)
occurrences (all)	7	3	23
Arthralgia			
subjects affected / exposed	6 / 61 (9.84%)	2 / 21 (9.52%)	13 / 80 (16.25%)
occurrences (all)	7	2	17
Myalgia			
subjects affected / exposed	3 / 61 (4.92%)	1 / 21 (4.76%)	8 / 80 (10.00%)
occurrences (all)	3	1	9
Back pain			
subjects affected / exposed	3 / 61 (4.92%)	0 / 21 (0.00%)	7 / 80 (8.75%)
occurrences (all)	4	0	11

Osteoarthritis			
subjects affected / exposed	2 / 61 (3.28%)	0 / 21 (0.00%)	7 / 80 (8.75%)
occurrences (all)	3	0	8
Muscle twitching			
subjects affected / exposed	1 / 61 (1.64%)	1 / 21 (4.76%)	5 / 80 (6.25%)
occurrences (all)	1	1	5
Pain in extremity			
subjects affected / exposed	2 / 61 (3.28%)	0 / 21 (0.00%)	4 / 80 (5.00%)
occurrences (all)	2	0	5
Infections and infestations			
COVID-19			
subjects affected / exposed	1 / 61 (1.64%)	0 / 21 (0.00%)	40 / 80 (50.00%)
occurrences (all)	1	0	47
Influenza			
subjects affected / exposed	3 / 61 (4.92%)	0 / 21 (0.00%)	8 / 80 (10.00%)
occurrences (all)	3	0	11
Nasopharyngitis			
subjects affected / exposed	3 / 61 (4.92%)	1 / 21 (4.76%)	7 / 80 (8.75%)
occurrences (all)	3	1	7
Urinary tract infection			
subjects affected / exposed	1 / 61 (1.64%)	0 / 21 (0.00%)	6 / 80 (7.50%)
occurrences (all)	1	0	9
Upper respiratory tract infection			
subjects affected / exposed	1 / 61 (1.64%)	0 / 21 (0.00%)	5 / 80 (6.25%)
occurrences (all)	1	0	8
Pneumonia			
subjects affected / exposed	0 / 61 (0.00%)	0 / 21 (0.00%)	5 / 80 (6.25%)
occurrences (all)	0	0	5
Sinusitis			
subjects affected / exposed	2 / 61 (3.28%)	0 / 21 (0.00%)	4 / 80 (5.00%)
occurrences (all)	2	0	5
Gastroenteritis viral			
subjects affected / exposed	1 / 61 (1.64%)	0 / 21 (0.00%)	4 / 80 (5.00%)
occurrences (all)	1	0	4
Ear infection			

subjects affected / exposed	0 / 61 (0.00%)	0 / 21 (0.00%)	4 / 80 (5.00%)
occurrences (all)	0	0	4
Metabolism and nutrition disorders			
Hypocalcaemia			
subjects affected / exposed	5 / 61 (8.20%)	9 / 21 (42.86%)	15 / 80 (18.75%)
occurrences (all)	7	14	29
Hypercalcaemia			
subjects affected / exposed	5 / 61 (8.20%)	0 / 21 (0.00%)	9 / 80 (11.25%)
occurrences (all)	8	0	15

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
16 March 2021	The protocol amendment was to address comments and recommendations from Health Authorities and provide clarification on the trial.
10 June 2021	The protocol amendment provided clarification on the trial and addressed a Health Authority comment.
03 August 2021	The protocol amendment updated the primary and secondary efficacy endpoints based on FDA recommendation.
20 December 2021	The protocol amendment updated the primary and secondary efficacy endpoints based on FDA recommendation.
13 December 2022	The protocol amendment added an efficacy endpoint for the open-label extension period and provided clarification on the trial.
23 May 2023	The protocol amendment addressed a Health Authority comment.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/36271471