Clinical trial results:
A Phase 2, 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	2018-004815-33
Trial protocol	NO DE DK GB IT
Global end of trial date	

Results information

Result version number	v1 (current)
This version publication date	19 December 2022
First version publication date	19 December 2022

Trial information

Trial identification

Sponsor protocol code	TransCon PTH TCP-201

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04009291
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Ascendis Pharma A/S
Sponsor organisation address	Tuborg Boulevard 12, Hellerup, Denmark, DK 2900
Public contact	Clinical Trial Information Desk, Ascendis Pharma A/S, 0045 70222244, clinhelpdesk@ascendispharma.com
Scientific contact	Clinical Trial Information Desk, Ascendis Pharma A/S, 0045 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	Interim
Date of interim/final analysis	06 March 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	06 March 2020
Global end of trial reached?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the effectiveness of daily TransCon PTH on serum and urine calcium levels (FECa) and active vitamin D and calcium doses at 4 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	13 March 2019
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
Long term follow-up duration	4 Years
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United States: 18
Country: Number of subjects enrolled	Norway: 1
Country: Number of subjects enrolled	Denmark: 12
Country: Number of subjects enrolled	Germany: 2
Country: Number of subjects enrolled	Italy: 6
Country: Number of subjects enrolled	Canada: 20
Worldwide total number of subjects	59
EEA total number of subjects	21

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)	54
From 65 to 84 years	5
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Overall, 59 subjects were enrolled and dosed. Enrollment of subjects occurred in six countries: Canada, Denmark, Germany, Italy, Norway, and the United States.

Pre-assignment

Screening details:

A total of 104 subjects were screened and 59 of these met eligibility criteria and were enrolled into the study.

Period 1

Period 1 title	4 Week Blinded Period (overall period)
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	TransCon PTH 15 mcg/day

Arm description:

Once daily subcutaneous administration of 15 mcg of TransCon PTH

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.

Arm title	TransCon PTH 18 mcg/day

Arm description:

Once daily subcutaneous administration of 18 mcg of TransCon PTH

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.

Arm title	TransCon PTH 21 mcg/day

Arm description:

Once daily subcutaneous administration of 21 mcg of TransCon PTH

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.

Arm title	Placebo

Arm description:

Once daily subcutaneous administration of placebo for TransCon PTH to mimick administration of 15, 18, or 21 mcg 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	TransCon PTH 15 mcg/day	TransCon PTH 18 mcg/day	TransCon PTH 21 mcg/day
Started	14	15	15
Completed	14	15	15

Number of subjects in period 1	Placebo
Started	15
Completed	15

Baseline characteristics

Reporting groups	
Reporting group title	TransCon PTH 15 mcg/day
Reporting group description:	
Once daily subcutaneous administration of 15 mcg of TransCon PTH	
Reporting group title	TransCon PTH 18 mcg/day
Reporting group description:	
Once daily subcutaneous administration of 18 mcg of TransCon PTH	
Reporting group title	TransCon PTH 21 mcg/day
Reporting group description:	
Once daily subcutaneous administration of 21 mcg of TransCon PTH	
Reporting group title	Placebo
Reporting group description:	
Once daily subcutaneous administration of placebo for TransCon PTH to mimick administration of 15, 18, or 21 mcg of investigational product	

Reporting group values	TransCon PTH 15 mcg/day	TransCon PTH 18 mcg/day	TransCon PTH 21 mcg/day
Number of subjects	14	15	15
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	47.03	46.58	53.67
standard deviation	± 13.230	± 11.157	± 11.287
Gender categorical Units: Subjects			
Female	12	12	12
Male	2	3	3
Race Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	0	2
Black or African American	0	0	0
Pacific Islander	0	0	0
White	14	12	13
Other	0	3	0
Ethnicity Units: Subjects			
Hispanic or Latino	0	0	1
Not Hispanic or Latino	14	15	14
Unknown	0	0	0
Height Units: cm			
arithmetic mean	166.92	166.71	165.37
standard deviation	± 8.806	± 8.385	± 10.961
Weight Units: kg			

arithmetic mean	76.58	80.04	72.26
standard deviation	± 22.479	± 11.279	± 18.621
Body Mass Index			
Units: kg/m^2			
arithmetic mean	27.08	28.76	26.12
standard deviation	± 5.723	± 3.148	± 4.647

Reporting group values	Placebo	Total	
Number of subjects	15	59	
Age categorical			
Units: Subjects			
Age continuous			
Units: years			
arithmetic mean	51.80		
standard deviation	± 12.345	-	
Gender categorical			
Units: Subjects			
Female	12	48	
Male	3	11	
Race			
Units: Subjects			
American Indian or Alaska Native	0	0	
Asian	0	2	
Black or African American	0	0	
Pacific Islander	0	0	
White	15	54	
Other	0	3	
Ethnicity			
Units: Subjects			
Hispanic or Latino	0	1	
Not Hispanic or Latino	15	58	
Unknown	0	0	
Height			
Units: cm			
arithmetic mean	164.07		
standard deviation	± 10.368	-	
Weight			
Units: kg			
arithmetic mean	76.43		
standard deviation	± 14.256	-	
Body Mass Index			
Units: kg/m^2			
arithmetic mean	28.30		
standard deviation	± 3.775	-	

End points

End points reporting groups

Reporting group title	TransCon PTH 15 mcg/day
Reporting group description:	
Once daily subcutaneous administration of 15 mcg of TransCon PTH	
Reporting group title	TransCon PTH 18 mcg/day
Reporting group description:	
Once daily subcutaneous administration of 18 mcg of TransCon PTH	
Reporting group title	TransCon PTH 21 mcg/day
Reporting group description:	
Once daily subcutaneous administration of 21 mcg of TransCon PTH	
Reporting group title	Placebo
Reporting group description:	
Once daily subcutaneous administration of placebo for TransCon PTH to mimick administration of 15, 18, or 21 mcg of investigational product	

Primary: Efficacy - Primary Endpoint

End point title	Efficacy - Primary Endpoint
End point description:	
The proportion of subjects with albumin-adjusted or ionized serum calcium within the normal range, and spot morning fractional excretion of calcium (spot AM FECa) within normal range (≤2%) or a reduction by at least 50% from baseline, and not taking active vitamin D supplements, and taking ≤1000 mg/day of calcium supplements	
End point type	Primary
End point timeframe:	
4 weeks	

End point values	TransCon PTH 15 mcg/day	TransCon PTH 18 mcg/day	TransCon PTH 21 mcg/day	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	14	15	15	15
Units: percent				
number (confidence interval 95%)	50.0 (23.0 to 77.0)	40.0 (16.3 to 67.7)	60.0 (32.3 to 83.7)	26.7 (7.8 to 55.1)

Statistical analyses

Statistical analysis title	Primary efficacy endpoint
Statistical analysis description:	
Fisher's exact test is used to compare differences in the proportion of subjects meeting the composite primary endpoint in the TransCon PTH versus pooled placebo group	
Comparison groups	TransCon PTH 15 mcg/day v Placebo

Number of subjects included in analysis	29
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2635
Method	t-test, 2-sided

Statistical analysis title	Primary efficacy endpoint

Statistical analysis description:

Fisher's exact test is used to compare differences in the proportion of subjects meeting the composite primary endpoint in the TransCon PTH versus pooled placebo group

Comparison groups	TransCon PTH 18 mcg/day v Placebo
Number of subjects included in analysis	30
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6999
Method	t-test, 2-sided

Statistical analysis title	Primary efficacy endpoint

Statistical analysis description:

Fisher's exact test is used to compare differences in the proportion of subjects meeting the composite primary endpoint in the TransCon PTH versus pooled placebo group

Comparison groups	TransCon PTH 21 mcg/day v Placebo
Number of subjects included in analysis	30
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1394
Method	t-test, 2-sided

Secondary: Efficacy - Secondary Endpoint

End point title	Efficacy - Secondary Endpoint

End point description:

The proportion of subjects with albumin-adjusted or ionized serum calcium within the normal range, and spot morning fractional excretion of calcium (spot AM FECa) within normal range (≤2%) or a reduction by at least 50% from baseline, and not taking active vitamin D supplements, and taking ≤500 mg/day of calcium supplements

End point type	Secondary

End point timeframe:

4 weeks

End point values	TransCon PTH 15 mcg/day	TransCon PTH 18 mcg/day	TransCon PTH 21 mcg/day	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	14	15	15	15
Units: percent				
number (confidence interval 95%)	50.0 (23.0 to 77.0)	26.7 (7.8 to 55.1)	60 (32.3 to 83.7)	20.0 (4.3 to 48.1)

Statistical analyses

Statistical analysis title	Secondary efficacy endpoint

Statistical analysis description:

Fisher's exact test is used to compare differences in the proportion of subjects meeting the composite primary endpoint in the TransCon PTH versus pooled placebo group

Comparison groups	TransCon PTH 15 mcg/day v Placebo
Number of subjects included in analysis	29
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1281
Method	t-test, 2-sided

Statistical analysis title	Secondary efficacy endpoint

Statistical analysis description:

Fisher's exact test is used to compare differences in the proportion of subjects meeting the composite primary endpoint in the TransCon PTH versus pooled placebo group

Comparison groups	TransCon PTH 18 mcg/day v Placebo
Number of subjects included in analysis	30
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.9999
Method	t-test, 2-sided

Statistical analysis title	Secondary efficacy endpoint

Statistical analysis description:

Fisher's exact test is used to compare differences in the proportion of subjects meeting the composite primary endpoint in the TransCon PTH versus pooled placebo group

Comparison groups	TransCon PTH 21 mcg/day v Placebo
Number of subjects included in analysis	30
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0604
Method	t-test, 2-sided

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
4 Week Blinded Period	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	24

Reporting groups	
Reporting group title	TransCon PTH 15 mcg/day
Reporting group description:	
Once daily subcutaneous administration of 15 mcg of TransCon PTH	
Reporting group title	TransCon PTH 18 mcg/day
Reporting group description:	
Once daily subcutaneous administration of 18 mcg of TransCon PTH	
Reporting group title	TransCon PTH 21 mcg/day
Reporting group description:	
Once daily subcutaneous administration of 21 mcg of TransCon PTH	
Reporting group title	Placebo
Reporting group description:	
Once daily subcutaneous administration of placebo for TransCon PTH to mimick administration of 15, 18, or 21 mcg of investigational product	

Serious adverse events	TransCon PTH 15 mcg/day	TransCon PTH 18 mcg/day	TransCon PTH 21 mcg/day
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 14 (0.00%)	0 / 15 (0.00%)	0 / 15 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

Serious adverse events	Placebo		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 15 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

Frequency threshold for reporting non-serious adverse events: 3.4 %

Non-serious adverse events	TransCon PTH 15 mcg/day	TransCon PTH 18 mcg/day	TransCon PTH 21 mcg/day
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 14 (42.86%)	5 / 15 (33.33%)	7 / 15 (46.67%)
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 14 (7.14%)	1 / 15 (6.67%)	0 / 15 (0.00%)
occurrences (all)	1	1	0
Nervous system disorders			
Headache			
subjects affected / exposed	3 / 14 (21.43%)	1 / 15 (6.67%)	1 / 15 (6.67%)
occurrences (all)	3	1	1
Dizziness			
subjects affected / exposed	0 / 14 (0.00%)	2 / 15 (13.33%)	0 / 15 (0.00%)
occurrences (all)	0	2	0
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	0 / 14 (0.00%)	1 / 15 (6.67%)	1 / 15 (6.67%)
occurrences (all)	0	1	1
Injection site pain			
subjects affected / exposed	1 / 14 (7.14%)	0 / 15 (0.00%)	1 / 15 (6.67%)
occurrences (all)	1	0	1
Thirst			
subjects affected / exposed	0 / 14 (0.00%)	1 / 15 (6.67%)	1 / 15 (6.67%)
occurrences (all)	0	1	1
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	2 / 14 (14.29%)	1 / 15 (6.67%)	1 / 15 (6.67%)
occurrences (all)	2	1	1
Constipation			
subjects affected / exposed	0 / 14 (0.00%)	0 / 15 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 14 (0.00%)	0 / 15 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			

Urinary tract infection			
subjects affected / exposed	1 / 14 (7.14%)	0 / 15 (0.00%)	1 / 15 (6.67%)
occurrences (all)	1	0	1
Influenza			
subjects affected / exposed	0 / 14 (0.00%)	0 / 15 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Hypercalcemia			
subjects affected / exposed	0 / 14 (0.00%)	1 / 15 (6.67%)	2 / 15 (13.33%)
occurrences (all)	0	1	2
Hypocalcemia			
subjects affected / exposed	0 / 14 (0.00%)	0 / 15 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Placebo		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 15 (40.00%)		
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Dizziness			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Injection site pain			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Thirst			

subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0		
Gastrointestinal disorders Nausea subjects affected / exposed occurrences (all) Constipation subjects affected / exposed occurrences (all)	 1 / 15 (6.67%) 1 1 / 15 (6.67%) 1		
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all)	 1 / 15 (6.67%) 1		
Infections and infestations Urinary tract infection subjects affected / exposed occurrences (all) Influenza subjects affected / exposed occurrences (all)	 0 / 15 (0.00%) 0 1 / 15 (6.67%) 1		
Metabolism and nutrition disorders Hypercalcemia subjects affected / exposed occurrences (all) Hypocalcemia subjects affected / exposed occurrences (all)	 0 / 15 (0.00%) 0 1 / 15 (6.67%) 1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
08 May 2019	The TCP-201 protocol was amended to incorporate feedback from multiple Health Authorities and included changes to the trial design, secondary endpoints, and exclusion criteria.

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/34347093