Clinical trial results:
foresiGHt: A multicenter, randomized, parallel-arm, placebo- controlled (double- blind) and active-controlled (open-label) trial to compare the efficacy and safety of once-weekly lonapegsomatropin with placebo and a daily somatropin product in adults with growth hormone deficiency

Summary

EudraCT number	2020-000929-42
Trial protocol	DE SK FR DK BG ES NL GR IT
Global end of trial date	01 December 2023

Results information

Result version number	v1 (current)
This version publication date	26 February 2025
First version publication date	26 February 2025

Trial information

Trial identification

Sponsor protocol code	TCH-306

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04615273
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Ascendis Pharma
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	Final
Date of interim/final analysis	13 December 2023
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	01 December 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the efficacy of once-weekly lonapegsomatropin compared to placebo at 38 weeks in adults with growth hormone deficiency (GHD).

Protection of trial subjects:

This trial was conducted in accordance with the ethical principles of Good Clinical Practice, according to the International Conference on Harmonisation Harmonized Tripartite Guideline.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	03 December 2020
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	Poland: 38
Country: Number of subjects enrolled	Slovakia: 4
Country: Number of subjects enrolled	Spain: 13
Country: Number of subjects enrolled	United Kingdom: 1
Country: Number of subjects enrolled	France: 10
Country: Number of subjects enrolled	Germany: 1
Country: Number of subjects enrolled	Greece: 11
Country: Number of subjects enrolled	Italy: 5
Country: Number of subjects enrolled	United States: 48
Country: Number of subjects enrolled	Ukraine: 30
Country: Number of subjects enrolled	Georgia: 23
Country: Number of subjects enrolled	Japan: 17
Country: Number of subjects enrolled	Türkiye: 14
Country: Number of subjects enrolled	Australia: 12
Country: Number of subjects enrolled	Serbia: 7
Country: Number of subjects enrolled	Israel: 6
Country: Number of subjects enrolled	Armenia: 6
Country: Number of subjects enrolled	Malaysia: 4
Country: Number of subjects enrolled	Canada: 4
Country: Number of subjects enrolled	Korea, Republic of: 3
Country: Number of subjects enrolled	Romania: 2

Worldwide total number of subjects	259
EEA total number of subjects	84

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)	225
From 65 to 84 years	34
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Out of 264 subjects randomised in the study, 259 subjects were treated in the study. Five randomised subjects did not receive the treatment.

Period 1

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

Blinding implementation details:

Once-weekly lonapegsomatropin and once-weekly placebo treatment arms were double-blinded, daily somatropin product was open-label.

Arms

Are arms mutually exclusive?	Yes
Arm title	Lonapegsomatropin

Arm description:

Subjects received lonapegsomatropin administered once weekly by subcutaneous injection for a treatment period of up to 38 weeks.

Arm type	Experimental
Investigational medicinal product name	Lonapegsomatropin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate and solvent for solution for injection/infusion
Routes of administration	Subcutaneous use

Dosage and administration details:

Lonapegsomatropin administered once-weekly by subcutaneous injection.

Arm title	Placebo

Arm description:

Subjects received placebo matched to lonapegsomatropin administered once weekly by subcutaneous injection for a treatment period of up to 38 weeks.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate and solvent for solution for injection/infusion
Routes of administration	Subcutaneous use

Dosage and administration details:

Placebo for Lonapegsomatropin administered once-weekly by subcutaneous injection.

Arm title	Somatropin

Arm description:

Subjects received somatropin administered once daily by subcutaneous injection for a treatment period of up to 38 weeks.

Arm type	Active comparator

Investigational medicinal product name	Somatropin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled pen
Routes of administration	Subcutaneous use

Dosage and administration details:

Somatropin administered once-daily by subcutaneous injection.

Number of subjects in period 1	Lonapegsomatropin	Placebo	Somatropin
Started	89	84	86
Treated	89	84	86
Completed	85	81	82
Not completed	4	3	4
Consent withdrawn by subject	3	1	2
Physician decision	-	-	1
Adverse event, non-fatal	1	-	1
Unspecified	-	1	-
Lost to follow-up	-	1	-

Baseline characteristics

Reporting groups	
Reporting group title	Lonapegsomatropin
Reporting group description:	
Subjects received lonapegsomatropin administered once weekly by subcutaneous injection for a treatment period of up to 38 weeks.	
Reporting group title	Placebo
Reporting group description:	
Subjects received placebo matched to lonapegsomatropin administered once weekly by subcutaneous injection for a treatment period of up to 38 weeks.	
Reporting group title	Somatropin
Reporting group description:	
Subjects received somatropin administered once daily by subcutaneous injection for a treatment period of up to 38 weeks.	

Reporting group values	Lonapegsomatropin	Placebo	Somatropin
Number of subjects	89	84	86
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	43.0	44.1	41.3
standard deviation	± 13.40	± 14.74	± 14.34
Gender categorical Units: Subjects			
Female	42	39	38
Male	47	45	48
Ethnicity Units: Subjects			
Hispanic or Latino	3	4	5
Not Hispanic or Latino	82	79	78
Unknown or Not Reported	4	1	3
Race Units: Subjects			
American Indian or Alaska Native	0	1	0
Asian	11	8	9
Black or African American	0	0	1
Native Hawaiian or Other Pacific Islander	0	0	0
White	72	71	75
Other	6	4	1
Dose Group Units: Subjects			
Subgroup 1: Oral estrogen intake or <30 years old	32	29	30
Subgroup 2: >=30to<=60 years old; no oral estrogen	46	43	45
Subgroup 3: >60 years old; no oral estrogen intake	11	12	11

Reporting group values	Total		
Number of subjects	259		
Age categorical Units: Subjects			

Age continuous Units: years arithmetic mean standard deviation	- -		
Gender categorical Units: Subjects			
Female	119		
Male	140		
Ethnicity Units: Subjects			
Hispanic or Latino	12		
Not Hispanic or Latino	239		
Unknown or Not Reported	8		
Race Units: Subjects			
American Indian or Alaska Native	1		
Asian	28		
Black or African American	1		
Native Hawaiian or Other Pacific Islander	0		
White	218		
Other	11		
Dose Group Units: Subjects			
Subgroup 1: Oral estrogen intake or <30 years old	91		
Subgroup 2: >=30to<=60 years old; no oral estrogen	134		
Subgroup 3: >60 years old; no oral estrogen intake	34		

End points

End points reporting groups

Reporting group title	Lonapegsomatropin
Reporting group description:	
Subjects received lonapegsomatropin administered once weekly by subcutaneous injection for a treatment period of up to 38 weeks.	
Reporting group title	Placebo
Reporting group description:	
Subjects received placebo matched to lonapegsomatropin administered once weekly by subcutaneous injection for a treatment period of up to 38 weeks.	
Reporting group title	Somatropin
Reporting group description:	
Subjects received somatropin administered once daily by subcutaneous injection for a treatment period of up to 38 weeks.	

Primary: Change From Baseline in Trunk Percent Fat at Week 38

End point title	Change From Baseline in Trunk Percent Fat at Week 38[1]
End point description:	
Trunk percent fat was assessed by dual-energy X-ray absorptiometry. Analysis was performed on Intent-To-Treat population that consisted of all randomised subjects who received any amount of the trial drug and were analysed by the treatment arm as randomised. Here, "number of subjects analysed" = subjects with available data for this endpoint.	
End point type	Primary
End point timeframe:	
Baseline, Week 38	

Notes:

[1] - 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: Data for this endpoint was analysed for lonapegsomatropin and placebo groups.

End point values	Lonapegsomatropin	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	82	77		
Units: percent fat				
least squares mean (confidence interval 95%)	-1.68 (-2.44 to -0.91)	0.37 (-0.30 to 1.03)		

Statistical analyses

Statistical analysis title	Lonapegsomatropin versus Placebo
Statistical analysis description:	
Analysis included treatment arm, region, baseline age group, gender, concomitant oral estrogen, Adult Growth Hormone Deficiency (AGHD) onset as factors & baseline trunk percent fat as the covariates. Multiple imputation method was used to impute missing data.	
Comparison groups	Placebo v Lonapegsomatropin

Number of subjects included in analysis	159
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	ANCOVA
Parameter estimate	Estimate of Difference
Point estimate	-2.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.94
upper limit	-1.14
Variability estimate	Standard error of the mean
Dispersion value	0.46

Secondary: Change From Baseline in Total Body Lean Mass at Week 38

End point title	Change From Baseline in Total Body Lean Mass at Week 38[2]

End point description:

Total body lean mass was assessed by dual-energy X-ray absorptiometry. Analysis was performed on Intent-to-Treat population. Here, "number of subjects analysed" = subjects with available data for this endpoint.

End point type	Secondary

End point timeframe:

Baseline, Week 38

Notes:

[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: Data for this endpoint was analysed for lonapegsomatropin and placebo groups.

End point values	Lonapegsomatropin	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	82	77		
Units: kilograms				
least squares mean (confidence interval 95%)	1.60 (1.00 to 2.19)	-0.11 (-0.72 to 0.51)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Trunk Fat Mass at Week 38

End point title	Change From Baseline in Trunk Fat Mass at Week 38[3]

End point description:

Trunk fat mass was assessed by dual-energy X-ray absorptiometry. Analysis was performed on Intent-to-Treat population. Here, "number of subjects analysed" = subjects with available data for this endpoint.

End point type	Secondary

End point timeframe:

Baseline, Week 38

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: Data for this endpoint was analysed for lonapegsomatropin and placebo groups.

End point values	Lonapegsomatropin	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	82	77		
Units: kilograms				
least squares mean (confidence interval 95%)	-0.48 (-0.89 to -0.07)	0.22 (-0.15 to 0.60)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Treatment-Emergent Adverse Events (TEAEs), Serious TEAEs and TEAE Leading to Study Discontinuation

End point title	Number of Subjects With Treatment-Emergent Adverse Events (TEAEs), Serious TEAEs and TEAE Leading to Study Discontinuation

End point description:

An Adverse Event (AE) was defined as any untoward medical occurrence in a clinical investigation subject administered a pharmaceutical product and which does not necessarily have a causal relationship with the treatment. An AE was considered a TEAE if it occurred on or after the first dose of investigational product and was not present prior to the first dose, or it was present at the first dose but increased in severity during the trial. A serious AE is any untoward medical occurrence at any dose: resulted in death; was life threatening; required prolong inpatient hospitalisation; resulted in persistent or significant disability/incapacity; resulted in a congenital anomaly/birth defect or was considered a significant medical event by the investigator. Analysis was performed on safety population that included all randomised subjects who received any amount of trial drug and was analysed by the actual treatment received.

End point type	Secondary

End point timeframe:

Up to 38 weeks

End point values	Lonapegsomatropin	Placebo	Somatropin	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	89	84	86	
Units: subjects				
TEAEs	64	55	63	
Serious TEAEs	4	1	6	
TEAE Leading to Study Discontinuation	1	0	0	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From signing of the informed consent form (ICF) to up to 2 weeks after last dose of the study treatment (i.e., up to Week 40)

Adverse event reporting additional description:

Analysis was performed on safety population that included all randomised subjects who received any amount of trial drug and was analysed by the actual treatment received.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	26.0

Reporting groups

Reporting group title	Lonapegsomatropin

Reporting group description:

Subjects received lonapegsomatropin administered once weekly by subcutaneous injection for a treatment period of up to 38 weeks.

Reporting group title	Placebo

Reporting group description:

Subjects received placebo matched to lonapegsomatropin administered once weekly by subcutaneous injection for a treatment period of up to 38 weeks.

Reporting group title	Somatropin

Reporting group description:

Subjects received somatropin administered once daily by subcutaneous injection for a treatment period of up to 38 weeks.

Serious adverse events	Lonapegsomatropin	Placebo	Somatropin
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 89 (4.49%)	1 / 84 (1.19%)	6 / 86 (6.98%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Transitional cell carcinoma			
subjects affected / exposed	0 / 89 (0.00%)	0 / 84 (0.00%)	1 / 86 (1.16%)
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			
Hypertension			
subjects affected / exposed	0 / 89 (0.00%)	0 / 84 (0.00%)	1 / 86 (1.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			

Epilepsy			
subjects affected / exposed	1 / 89 (1.12%)	0 / 84 (0.00%)	0 / 86 (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
Seizure			
subjects affected / exposed	0 / 89 (0.00%)	0 / 84 (0.00%)	1 / 86 (1.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 89 (0.00%)	0 / 84 (0.00%)	1 / 86 (1.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Face oedema			
subjects affected / exposed	0 / 89 (0.00%)	0 / 84 (0.00%)	1 / 86 (1.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Non-cardiac chest pain			
subjects affected / exposed	1 / 89 (1.12%)	0 / 84 (0.00%)	0 / 86 (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
Oedema peripheral			
subjects affected / exposed	0 / 89 (0.00%)	0 / 84 (0.00%)	1 / 86 (1.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Drug eruption			
subjects affected / exposed	0 / 89 (0.00%)	0 / 84 (0.00%)	1 / 86 (1.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Acute kidney injury			

subjects affected / exposed	0 / 89 (0.00%)	1 / 84 (1.19%)	0 / 86 (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
Infections and infestations			
Coronavirus pneumonia			
subjects affected / exposed	1 / 89 (1.12%)	0 / 84 (0.00%)	0 / 86 (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
Metabolism and nutrition disorders			
Hyponatraemia			
subjects affected / exposed	1 / 89 (1.12%)	0 / 84 (0.00%)	0 / 86 (0.00%)
occurrences causally related to treatment / all	1 / 1	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	Lonapegsomatropin	Placebo	Somatropin
Total subjects affected by non-serious adverse events			
subjects affected / exposed	29 / 89 (32.58%)	47 / 84 (55.95%)	28 / 86 (32.56%)
Nervous system disorders			
Headache			
subjects affected / exposed	7 / 89 (7.87%)	9 / 84 (10.71%)	5 / 86 (5.81%)
occurrences (all)	13	11	5
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	8 / 89 (8.99%)	8 / 84 (9.52%)	7 / 86 (8.14%)
occurrences (all)	8	8	9
Infections and infestations			
COVID-19			
subjects affected / exposed	7 / 89 (7.87%)	11 / 84 (13.10%)	6 / 86 (6.98%)
occurrences (all)	7	11	7
Nasopharyngitis			
subjects affected / exposed	5 / 89 (5.62%)	11 / 84 (13.10%)	6 / 86 (6.98%)
occurrences (all)	6	16	7
Upper respiratory tract infection			

subjects affected / exposed occurrences (all)	2 / 89 (2.25%) 2	8 / 84 (9.52%) 10	4 / 86 (4.65%) 5

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
06 August 2020	The Protocol was amended in response to comments and recommendations toward clarification on aspects of the trial, from FDA, the Federal Institute for Drugs and Medical Devices (BfArM), Danish Medicines Agency (DKMA), and Pharmaceuticals and Medical Devices Agency (PMDA).
20 July 2021	The protocol was amended to include remarks from EU authorities, to facilitate patient recruitment and to provide a clearer trial overview.
02 June 2022	The protocol was amended to update safety including anaphylaxis precautions, prohibited medication, local German requirement and correction of typographic errors.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported