



## Clinical trial results:

**A follow-up study to examine the presence of anti-human growth hormone (anti-hGH) antibodies following a randomised, open-label, parallel-group, multi-centre trial (FE 999905 CS07) in which the efficacy and safety of 12 months' treatment with one daily dose of ZOMACTON were compared to one daily dose of GENOTROPIN.**

Due to the EudraCT – Results system being out of service between 31 July 2015 and 12 January 2016, these results have been published in compliance with revised timelines.

## Summary

EudraCT number	2014-000627-24
Trial protocol	HU PL
Global end of trial date	17 August 2015

## Results information

Result version number	v1 (current)
This version publication date	22 June 2016
First version publication date	22 June 2016

## Trial information

### Trial identification

Sponsor protocol code	000134
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### Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02173821
WHO universal trial number (UTN)	-

Notes:

## Sponsors

Sponsor organisation name	Ferring Pharmaceuticals A/S
Sponsor organisation address	Kay Fiskers Plads 11, Copenhagen S, Denmark, 2300
Public contact	Clinical Development Support, Ferring Pharmaceuticals, DK0-Disclosure@ferring.com
Scientific contact	Clinical Development Support, Ferring Pharmaceuticals, DK0-Disclosure@ferring.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	17 August 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	24 April 2015
Global end of trial reached?	Yes
Global end of trial date	17 August 2015
Was the trial ended prematurely?	No

Notes:

## General information about the trial

Main objective of the trial:

To investigate the presence of remaining immunogenicity among previously anti-hGH antibody positive children who participated in the clinical study FE 999905 CS07 and were treated with one daily dose of 0.03 mg/kg ZOMACTON (10 mg/mL) or one daily dose of 0.03 mg/kg GENOTROPIN (12 mg/mL).

Protection of trial subjects:

Before obtaining the consent from subject, parents(s)/legal representative, the Investigator appropriately explained the aims, methods, anticipated benefits, potential hazards, and any other aspects of the study which are relevant to the subjects' and parent(s)/ legal representatives' decision to participate. The Investigator explained to the subjects and their parent(s)/legal representatives about their right of freedom to refuse to enter the study or to withdraw from it at any time, without any consequences on subject's further care and without the need to justify their decision. The study was conducted in accordance with International Conference on Harmonization-Good Clinical Practice guidelines.

Background therapy:

The enrolled subjects were treated with either one daily dose of 0.03 mg/kg ZOMACTON (10 mg/mL) or one daily dose of 0.03 mg/kg GENOTROPIN (12 mg/mL) for 12 months prior to participation in this follow-up study.

Evidence for comparator: -

Actual start date of recruitment	23 October 2014
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: 6
Country: Number of subjects enrolled	Romania: 1
Country: Number of subjects enrolled	Hungary: 1
Country: Number of subjects enrolled	Israel: 7
Country: Number of subjects enrolled	Ukraine: 8
Worldwide total number of subjects	23
EEA total number of subjects	8

Notes:

### Subjects enrolled per age group

In utero	0
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Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	13
Adolescents (12-17 years)	10
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

## Subject disposition

### Recruitment

Recruitment details:

The study 000134 was a follow-up of subjects treated with one daily dose of 0.03 mg/kg ZOMACTON (10 mg/mL) or one daily dose of 0.03 mg/kg GENOTROPIN (12 mg) in the previously completed study FE 999905 CS07 who had confirmed positive formation of anti-hGH antibodies in at least one post-dose visit during the 12-month treatment period.

### Pre-assignment

Screening details:

The study was conducted to follow subjects who were anti-hGH antibody positive in at least one post-dosing sample in the study FE 999905 CS07.

### Period 1

Period 1 title	Visit 1 (Follow-up) (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

### Arms

Are arms mutually exclusive?	Yes
<b>Arm title</b>	ZOMACTON

Arm description:

One daily dose of 0.03 mg/kg ZOMACTON (10 mg/mL) administered for 12 months to subjects during their participation in the previous study FE 999905 CS07. No investigational medicinal product (IMP) was administered in the present follow-up study.

Arm type	Experimental
Investigational medicinal product name	Somatropin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solvent for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

No IMP was administered in the present follow-up study.

<b>Arm title</b>	GENOTROPIN
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Arm description:

One daily dose of 0.03 mg/kg GENOTROPIN (12 mg/mL) administered for 12 months to subjects during their participation in the previous study FE 999905 CS07. No IMP was administered in the present follow-up study.

Arm type	Active comparator
Investigational medicinal product name	Somatropin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solvent for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

No IMP was administered in the present follow-up study.

<b>Number of subjects in period 1</b>	ZOMACTON	GENOTROPIN
Started	22	1
Completed	22	1

## Baseline characteristics

### Reporting groups

Reporting group title	ZOMACTON
Reporting group description:	
One daily dose of 0.03 mg/kg ZOMACTON (10 mg/mL) administered for 12 months to subjects during their participation in the previous study FE 999905 CS07. No investigational medicinal product (IMP) was administered in the present follow-up study.	
Reporting group title	GENOTROPIN
Reporting group description:	
One daily dose of 0.03 mg/kg GENOTROPIN (12 mg/mL) administered for 12 months to subjects during their participation in the previous study FE 999905 CS07. No IMP was administered in the present follow-up study.	

Reporting group values	ZOMACTON	GENOTROPIN	Total
Number of subjects	22	1	23
Age categorical			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	13	0	13
Adolescents (12-17 years)	9	1	10
Adults (18-64 years)	0	0	0
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous			
Units: years			
arithmetic mean	11.5	14.9	
standard deviation	± 2.6	± 0	-
Gender categorical			
Units: Subjects			
Female	5	1	6
Male	17	0	17
Race			
Units: Subjects			
Black or African American	1	0	1
White	21	1	22
Ethnicity			
Units: Subjects			
Hispanic or Latino	0	0	0
Not Hispanic or Latino	22	1	23
Height			
Units: Centimeters (cm)			
arithmetic mean	138	160.5	
standard deviation	± 14.787	± 0	-
Weight			
Units: Kilograms (kg)			

arithmetic mean	35.7	48	
standard deviation	± 11.632	± 0	-
Body Mass Index (BMI)			
Units: Kg/m <sup>2</sup>			
arithmetic mean	18.23	18.6	
standard deviation	± 2.709	± 0	-
Duration from last visit of CS07 to follow-up visit			
Units: Years			
arithmetic mean	3.349	3.65	
standard deviation	± 0.454	± 0	-

### Subject analysis sets

Subject analysis set title	Full Analysis Set (FAS)
Subject analysis set type	Full analysis

Subject analysis set description:

The FAS comprised all enrolled subjects with an anti-hGH antibody measurement (and who were included in the FAS of the previous study FE 999905 CS07).

Reporting group values	Full Analysis Set (FAS)		
Number of subjects	23		
Age categorical			
Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	0		
Newborns (0-27 days)	0		
Infants and toddlers (28 days-23 months)	0		
Children (2-11 years)	13		
Adolescents (12-17 years)	10		
Adults (18-64 years)	0		
From 65-84 years	0		
85 years and over	0		
Age continuous			
Units: years			
arithmetic mean	11.7		
standard deviation	± 2.63		
Gender categorical			
Units: Subjects			
Female	6		
Male	17		
Race			
Units: Subjects			
Black or African American	1		
White	22		
Ethnicity			
Units: Subjects			
Hispanic or Latino	0		
Not Hispanic or Latino	23		

Height Units: Centimeters (cm) arithmetic mean standard deviation	138.97 ± 15.19		
Weight Units: Kilograms (kg) arithmetic mean standard deviation	36.23 ± 11.65		
Body Mass Index (BMI) Units: Kg/m <sup>2</sup> arithmetic mean standard deviation	18.24 ± 2.648		
Duration from last visit of CS07 to follow-up visit Units: Years arithmetic mean standard deviation	3.362 ± 0.447		

## End points

### End points reporting groups

Reporting group title	ZOMACTON
Reporting group description: One daily dose of 0.03 mg/kg ZOMACTON (10 mg/mL) administered for 12 months to subjects during their participation in the previous study FE 999905 CS07. No investigational medicinal product (IMP) was administered in the present follow-up study.	
Reporting group title	GENOTROPIN
Reporting group description: One daily dose of 0.03 mg/kg GENOTROPIN (12 mg/mL) administered for 12 months to subjects during their participation in the previous study FE 999905 CS07. No IMP was administered in the present follow-up study.	
Subject analysis set title	Full Analysis Set (FAS)
Subject analysis set type	Full analysis
Subject analysis set description: The FAS comprised all enrolled subjects with an anti-hGH antibody measurement (and who were included in the FAS of the previous study FE 999905 CS07).	

### Primary: Prevalence of anti-hGH antibodies

End point title	Prevalence of anti-hGH antibodies <sup>[1]</sup>
End point description: The prevalence of anti-hGH antibodies were estimated in the FAS by the percentage of subjects with positive anti-hGH antibodies and the exact 95% confidence interval (CI) (Clopper-Pearson) was provided.	
End point type	Primary
End point timeframe: At Visit 1	

#### 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: No hypothesis testing was conducted, and all statistics reported was descriptive. The data for immunogenicity was analysed and reported only for FAS, as FAS and Per Protocol analysis sets were identical.

End point values	ZOMACTON	GENOTROPIN	Full Analysis Set (FAS)	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	22	1	23	
Units: Percentage of subjects				
number (confidence interval 95%)	18.2 (5.2 to 40.3)	0 (0 to 97.5)	17.4 (5 to 38.8)	

### Statistical analyses

No statistical analyses for this end point

### Secondary: Prevalence of neutralising antibodies in confirmed positive anti-hGH antibody samples

End point title	Prevalence of neutralising antibodies in confirmed positive anti-hGH antibody samples
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End point description:

The prevalence of neutralising antibodies in confirmed anti-hGH antibody positive samples were estimated in the FAS by the percentage of subjects with neutralising antibodies in the subgroup of subjects with confirmed anti-hGH antibodies positive samples and the associated exact 95% CI (Clopper-Pearson) was provided.

End point type	Secondary
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End point timeframe:

At Visit 1

End point values	ZOMACTON	GENOTROPIN	Full Analysis Set (FAS)	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	4	0 <sup>[2]</sup>	4	
Units: Percentage of subjects				
number (confidence interval 95%)	0 (0 to 60.2)	( to )	0 (0 to 60.2)	

Notes:

[2] - No subject in this group was confirmed anti-hGH antibody positive.

### Statistical analyses

No statistical analyses for this end point

### Secondary: Binding capacity levels in confirmed anti-hGH antibody positive samples

End point title	Binding capacity levels in confirmed anti-hGH antibody positive samples
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End point description:

The binding capacity in confirmed anti-hGH antibody positive samples were described using descriptive summary statistics. The percentage of subjects with binding capacity  $\leq 2$  mg/L (i.e. below the threshold of clinical significance) in subjects with confirmed anti-hGH antibody positive samples were provided (including the exact 95% CI [Clopper-Pearson]).

End point type	Secondary
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End point timeframe:

At Visit 1

End point values	ZOMACTON	GENOTROPIN	Full Analysis Set (FAS)	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	4	0 <sup>[3]</sup>	4	
Units: Percentage of subjects				
number (confidence interval 95%)	100 (39.8 to 100)	( to )	100 (39.8 to 100)	

Notes:

[3] - No subject in this group was confirmed anti-hGH antibody positive.

### Statistical analyses

No statistical analyses for this end point

## Adverse events

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### Adverse events information<sup>[1]</sup>

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Timeframe for reporting adverse events:

No treatment-emergent adverse events were collected during the study period. Any adverse events that occurred were reported under medical history.

Assessment type	Systematic
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### Dictionary used

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Dictionary name	Unknown
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Dictionary version	0.0
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Frequency threshold for reporting non-serious adverse events: 0 %

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#### Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.

Justification: Since no IMP was administered in this follow-up study, no adverse event data were collected. However, the investigator monitored the condition of the subject throughout the study from the time of obtaining informed consent until completion of the study. Any adverse events that occurred during this period were to be recorded under medical history.

## **More information**

### **Substantial protocol amendments (globally)**

Were there any global substantial amendments to the protocol? No

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### **Interruptions (globally)**

Were there any global interruptions to the trial? No

### **Limitations and caveats**

None reported