Clinical trial results:
Pilot trial of recombinant human growth hormone for remyelination in multiple sclerosis

Summary

EudraCT number	2006-006465-16
Trial protocol	DE
Global end of trial date	15 March 2016

Results information

Result version number	v1 (current)
This version publication date	04 July 2020
First version publication date	04 July 2020

Trial information

Trial identification

Sponsor protocol code	rhGH in MS

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01541605
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	University of Leipzig
Sponsor organisation address	Ritterstr. 26, Leipzig, Germany, 04109
Public contact	Prof. Dr. F. Then Bergh , Klinik und Poliklinik für Neurologie Universität Leipzig , ThenBerF@medizin.uni-leipzig.de
Scientific contact	Prof. Dr. F. Then Bergh , Klinik und Poliklinik für Neurologie Universität Leipzig , ThenBerF@medizin.uni-leipzig.de

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 January 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	11 November 2015
Global end of trial reached?	Yes
Global end of trial date	15 March 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To rule out an increase in inflammatory disease activity by s.c. rhGH as detected by monthly contrast-enhanced MRI: Primary outcome measure is the cumulative number of active (new or gadolinium-enhancing) lesions during the 12-week baseline period and the first 12 weeks of the treatment period.

Protection of trial subjects:

There were two safety assessments earlon on in the trial:
1) Major increase in inflammatory disease activity by s.c. rhGH. An clinical safety assessment will be performed after four patients have completed week 12 of rhGH treatment. The study may be discontinued, if more than 2 out of the first four patients fulfill the following condition:
The cumulative number of new active lesions during the treatment phase exceeds the maximum of 12 and is more than twice the cumulative number of new active lesions during the baseline period.
2) Significant increase in clinical disease activity. A second clinical safety assessment is planned when 15 patients have completed 24 weeks of rhGH treatment. The study may be discontinued if more than 30% of these patients display a clinically significant increase of the relapse rate or neurological disability inconsistent with prior disease history and not explained by other intervening variables.
The patients were also closely watched for serious unexpected adverse drug reactions, serious unexpected interactions with immunomodulatory treatments for MS (interferon-beta, copolymer-1) / not justifiable toxicity

Background therapy:

-

Evidence for comparator:

Cross-over design; no active comparator.

Actual start date of recruitment	19 June 2009
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	Germany: 37
Worldwide total number of subjects	37
EEA total number of subjects	37

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)	37
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Only subjects who met all inclusion criteria, but none of the exclusion criteria specified for the screening phase were enrolled.

Period 1

Period 1 title	Screening
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	pre-treatment
Arm description: -	
Arm type	No intervention
No investigational medicinal product assigned in this arm	

Number of subjects in period 1	pre-treatment
Started	37
Completed	25
Not completed	12
exclusion criteria for treatment phase	12

Period 2

Period 2 title	Treatment
Is this the baseline period?	Yes[1]
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	recombinant growth factor
Arm description: -	
Arm type	Experimental

Investigational medicinal product name	Recombinant human growth hormone (rhGH)
Investigational medicinal product code	H01AC01
Other name	Genotropin®
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Then dosage was induividually adjusted to achieve an IGF-1 concentration in the upper quartile of the age-adjusted normal range.

Notes:

[1] - Period 1 is not the baseline period. It is expected that period 1 will be the baseline period.

Justification: Period 1 is the screening period. The screening period had a duration of 12 weeks, including regular visits and assessements. Data from the screening period was used as baseline data for the evaluation of trial endpoints. However, only patients eventually included into the treatment phase are analysed, and therefore baseline data is reported for patients who entered the second period only.

Number of subjects in period 2[2]	recombinant growth factor
Started	25
Completed	22
Not completed	3
Consent withdrawn by subject	1
Physician decision	1
Adverse event, non-fatal	1

Notes:

[2] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: Period 1 is the screening period. The screening period had a duration of 12 weeks, including regular visits and assessements. Data from the screening period was used as baseline data for the evaluation of trial endpoints. However, only patients eventually included into the treatment phase are analysed, and therefore baseline data is reported for patients who entered the second period only.

Baseline characteristics

Reporting groups	
Reporting group title	Treatment

Reporting group description: -

Reporting group values	Treatment	Total	
Number of subjects	25	25	
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)		0	
Adolescents (12-17 years)		0	
Adults (18-64 years)		0	
From 65-84 years		0	
85 years and over		0	
Age continuous Units: years			
arithmetic mean	45.2		
standard deviation	± 10.0	-	
Gender categorical Units: Subjects			
Female	10	10	
Male	15	15	
Type of MS Units: Subjects			
relapsing-remitting	23	23	
secondary progressive	2	2	
Number of MS episodes in the last two years Units: Subjects			
No episodes	9	9	
One episode	7	7	
Two episodes	1	1	
Three episodes	4	4	
Five episodes	2	2	
Seven episodes	1	1	
Not available	1	1	
Time since MS diagnosis Units: years			
median	5		
full range (min-max)	0.3 to 35.4	-	
EDSS score Units: number			
arithmetic mean	3.4		

standard deviation	± 1.5	-	

End points

End points reporting groups

Reporting group title	pre-treatment
Reporting group description: -	
Reporting group title	recombinant growth factor
Reporting group description: -	

Primary: Ratio pre/post of number of active lesions on brain MRI

End point title	Ratio pre/post of number of active lesions on brain MRI[1]
End point description:	
Cumulative number of active (i.e. new or gadolinium-enhancing) lesions on brain MRI performed every four weeks during the 12-week baseline period and the first 12 weeks of the treatment period. That is, numbers of active lesions from week –8, week –4 and baseline will be compared to numbers of active lesions from week 4, week 8 and week 12.	
End point type	Primary
End point timeframe:	
24 weeks	

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: This is a single arm trial. Reporting of statistical analyses in this database require at least two arms, otherwise an error message occurs.

End point values	recombinant growth factor			
Subject group type	Reporting group			
Number of subjects analysed	25			
Units: ratio				
number (confidence interval 95%)	1.82 (0.72 to 2.92)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change in VEP P100 latencies versus baseline

End point title	Change in VEP P100 latencies versus baseline
End point description:	
End point type	Secondary
End point timeframe:	
Pre / Post difference	

End point values	recombinant growth factor			
Subject group type	Reporting group			
Number of subjects analysed	24			
Units: ms				
number (confidence interval 95%)	-2.2 (-8.3 to 3.8)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were recorded at every visit from visit 2 (-8 weeks) until the follow-up visit (week 36).

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	18.0?

Reporting groups

Reporting group title	Safety set

Reporting group description: -

Serious adverse events	Safety set		
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 37 (8.11%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Hepatobiliary disorders			
Autoimmune hepatitis			
subjects affected / exposed	1 / 37 (2.70%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Non-alcoholic fatty liver			
subjects affected / exposed	1 / 37 (2.70%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Muscular weakness			
subjects affected / exposed	1 / 37 (2.70%)		
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	Safety set		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	29 / 37 (78.38%)		
Investigations			
Glycosylated haemoglobin increased			
subjects affected / exposed	8 / 37 (21.62%)		
occurrences (all)	8		
Blood potassium increased			
subjects affected / exposed	3 / 37 (8.11%)		
occurrences (all)	4		
Alanine aminotransferase increased			
subjects affected / exposed	3 / 37 (8.11%)		
occurrences (all)	3		
Gamma-glutamyltransferase increased			
subjects affected / exposed	3 / 37 (8.11%)		
occurrences (all)	3		
Hepatic enzyme increased			
subjects affected / exposed	3 / 37 (8.11%)		
occurrences (all)	3		
Platelet count increased			
subjects affected / exposed	2 / 37 (5.41%)		
occurrences (all)	2		
Injury, poisoning and procedural complications			
Ligament sprain			
subjects affected / exposed	2 / 37 (5.41%)		
occurrences (all)	2		
Vascular disorders			
Hypertension			
subjects affected / exposed	2 / 37 (5.41%)		
occurrences (all)	2		
Nervous system disorders			
Hypoaesthesia			
subjects affected / exposed	2 / 37 (5.41%)		
occurrences (all)	3		
General disorders and administration site conditions			

Injection site erythema subjects affected / exposed occurrences (all) Influenza like illness subjects affected / exposed occurrences (all) Oedema peripheral subjects affected / exposed occurrences (all)	4 / 37 (10.81%) 5 3 / 37 (8.11%) 3 3 / 37 (8.11%) 3		
Reproductive system and breast disorders Menorrhagia subjects affected / exposed occurrences (all)	2 / 37 (5.41%) 2		
Gastrointestinal disorders Vomiting subjects affected / exposed occurrences (all)	2 / 37 (5.41%) 2		
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) Epistaxis subjects affected / exposed occurrences (all) Pharyngeal erythema subjects affected / exposed occurrences (all)	4 / 37 (10.81%) 4 2 / 37 (5.41%) 6 2 / 37 (5.41%) 2		
Skin and subcutaneous tissue disorders Dry skin subjects affected / exposed occurrences (all) Erythema subjects affected / exposed occurrences (all)	3 / 37 (8.11%) 3 3 / 37 (8.11%) 3		
Renal and urinary disorders			

Leukocyturia			
subjects affected / exposed	3 / 37 (8.11%)		
occurrences (all)	5		
Proteinuria			
subjects affected / exposed	2 / 37 (5.41%)		
occurrences (all)	2		
Musculoskeletal and connective tissue disorders			
Pain in extremity			
subjects affected / exposed	3 / 37 (8.11%)		
occurrences (all)	3		
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	9 / 37 (24.32%)		
occurrences (all)	12		
Urinary tract infection			
subjects affected / exposed	4 / 37 (10.81%)		
occurrences (all)	4		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
24 September 2008	Change in trial product
31 March 2009	Change in an inclusion criterion
26 November 2009	Change in selection criteria
01 July 2010	Safety laboratory values added
16 November 2010	Extension of trial period
04 October 2011	Change in trial flow chart
10 December 2012	Extension of trial period
16 December 2014	Extension of trial period

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported