



Clinical trial results: Statin Treatment of Oxysterol Pathology in SPG5: a Randomized Controlled Trial -Proof of Principle

Summary

EudraCT number	2015-000978-35
Trial protocol	DE
Global end of trial date	01 March 2016

Results information

Result version number	v1 (current)
This version publication date	24 October 2021
First version publication date	24 October 2021

Trial information

Trial identification

Sponsor protocol code	STOP-SPG5
-----------------------	-----------

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	University Hospital Tuebingen
Sponsor organisation address	Hoppe - Seyler - Straße 3, Tuebingen, Germany, 72076
Public contact	PI, Prof. Dr. L. Schöls, University Hospital Tübingen, 0049 070712982057, ludger.schoels@uni-tuebingen.de
Scientific contact	PI, Prof. Dr. L. Schöls, University Hospital Tübingen, 0049 070712982057, ludger.schoels@uni-tuebingen.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	25 October 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	01 March 2016
Global end of trial reached?	Yes
Global end of trial date	01 March 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Change of biomarker 27-hydroxycholesterol (27-OHC) level in serum from baseline to day 56 after treatment with atorvastatin 20/40 mg/d for 8 weeks compared to placebo treatment

Protection of trial subjects:

The study was conducted in accordance with the Declaration of Helsinki and the ICH Guidelines in Good Clinical Practice. The study was not started before the competent ethics committee had given a favorable opinion. Written informed consent was obtained from all patients and the study was only conducted as approved by the Medical Ethic Boards of the University of Tübingen and the national regulatory institution (Bundesamt für Arzneimittel und Medizinprodukte - BfArM).

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	09 November 2015
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Germany: 14
Worldwide total number of subjects	14
EEA total number of subjects	14

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)	14
From 65 to 84 years	0

Subject disposition

Recruitment

Recruitment details:

A total of 34 subjects from 28 families with a clinical diagnosis of HSP and genetically confirmed SPG5 were recruited in clinical centres in Antwerp, Athens, Conegliano, Lecco, Milano, Munich, Naples, Tübingen, Porto Alegre and Sao Paulo. Additionally 11 unaffected family members, carrying heterozygous CYP7B1 mutations, were included.

Pre-assignment

Screening details:

A total of 34 subjects with a clinical diagnosis of HSP and genetically confirmed SPG5 were recruited . Additionally 11 unaffected family members, carrying heterozygous CYP7B1 mutations were included. Patients fulfilling the inclusion and exclusion criterias were enrolled into the study. Randomization was performed by www.randomization.com .

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Verum

Arm description:

7 patients received Atorvastatin.

Arm type	Experimental
Investigational medicinal product name	Atorvastatin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Atorvastatin was given at a dosage of 40mg/die for 8 weeks in adults and 20 mg/die in children under 18 years of age.

Arm title	Placebo
------------------	---------

Arm description:

7 patients received Placebo.

Arm type	Placebo
Investigational medicinal product name	Atorvastatin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Atorvastatin was given at a dosage of 40mg/die for 8 weeks in adults and 20 mg/die in children under 18 years of age.

Number of subjects in period 1	Verum	Placebo
Started	7	7
Completed	7	7

Baseline characteristics

Reporting groups

Reporting group title	Verum
Reporting group description: 7 patients received Atorvastatin.	
Reporting group title	Placebo
Reporting group description: 7 patients received Placebo.	

Reporting group values	Verum	Placebo	Total
Number of subjects	7	7	14
Age categorical			
According to protocol 7 patients received Atorvastatin and were compared to a second group of 7 patients receiving placebo.			
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)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	0	0	0
From 65-84 years	7	7	14
85 years and over	0	0	0
Subjects	0	0	0
Gender categorical			
Verum group: 4 males, 3 females Placebo group: 2 males, 5 females			
Units: Subjects			
Female	3	5	8
Male	4	2	6

End points

End points reporting groups

Reporting group title	Verum
Reporting group description:	
7 patients received Atorvastatin.	
Reporting group title	Placebo
Reporting group description:	
7 patients received Placebo.	

Primary: Biomarker 27 OHC

End point title	Biomarker 27 OHC ^[1]
End point description:	
End point type	Primary
End point timeframe:	
Change of biomarker 27-hydroxycholesterol (27-OHC) level in serum from baseline to day 56 after treatment with atorvastatin once daily for 8 weeks compared to placebo treatment.	

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: The statistical analysis can be found in the publication.

End point values	Verum	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7	7		
Units: ng/ml				
median (inter-quartile range (Q1-Q3))	-307 (-409 to -144)	-1 (-27 to 40)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information^[1]

Timeframe for reporting adverse events:

The side effects were monitored during the observation period by lab tests after and while treatment on visit 1 – 2 and in week 4 by the family doctor.

Adverse event reporting additional description:

Table of Adverse Events can be found in the publication

Assessment type	Non-systematic
-----------------	----------------

Dictionary used

Dictionary name	MedDRA
-----------------	--------

Dictionary version	20
--------------------	----

Reporting groups

Reporting group title	Verum
-----------------------	-------

Reporting group description:

a total of five adverse events were reported, including two adverse events in the verum group (n=1 GGT elevation from 109 to 119 U/l; n=1 prolonged menstrual bleeding)

Reporting group title	Placebo
-----------------------	---------

Reporting group description:

a total of five adverse events were reported, including three in the placebo group (n=2 post-dural-puncture; n=1 stomach flu)

Serious adverse events	Verum	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Verum	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	

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: The Adverse events can be found in the publication.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

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/29126212>