



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 |

| | |
|-------------------|---|
| 85 years and over | 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>