



Clinical trial results:

Evaluation of the effectiveness and tolerance of “on demand” sildenafil for Raynaud’s phenomenon - PROFIL

Summary

| | |
|--------------------------|----------------|
| EudraCT number | 2013-000014-38 |
| Trial protocol | FR |
| Global end of trial date | 04 July 2016 |

Results information

| | |
|-----------------------------------|--|
| Result version number | v1 (current) |
| This version publication date | 16 June 2022 |
| First version publication date | 16 June 2022 |
| Summary attachment (see zip file) | On-Demand Sildenafil as a Treatment for Raynaud Phenomenon (Roustit_On-demand sildenafil in Raynaud_Ann Intern Med 2018.pdf) |

Trial information

Trial identification

| | |
|-----------------------|-------|
| Sponsor protocol code | 12G01 |
|-----------------------|-------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT02050360 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | CHU Grenoble Alpes |
| Sponsor organisation address | La Tronche, Grenoble, France, |
| Public contact | Centre d'investigation clinique, University Hospital Grenoble, 33 476 76 92 60, MRoustit@chu-grenoble.fr |
| Scientific contact | Centre d'investigation clinique, University Hospital Grenoble, 33 476 76 92 60, MRoustit@chu-grenoble.fr |

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 | 28 April 2016 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 28 April 2016 |
| Global end of trial reached? | Yes |
| Global end of trial date | 04 July 2016 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

To determine the effectiveness of sildenafil (40 mg or 80 mg) "on demand" on the severity of Raynaud's phenomenon

Protection of trial subjects:

Any harmful manifestation occurring in an included patient whether or not related to the research or drug being evaluated will be considered an adverse event (AE).

Continuous blood pressure monitoring will be performed 3 times during the first treatment cycle, at the first dose of each treatment week (V1, V2, V3). The measurements will be performed at the Clinical Investigation Center in Grenoble, at the same time as the measurement of digital blood flow, by digital plethysmography (Nexfin®) (7).

The collection of AEs will be done during the interview and clinical examination at each visit (V1 to V6). In the event of 3 serious adverse events (SAEs) or an unexpected SAE, the independent monitoring committee (chaired by Dr. Sophie Logerot, hospital practitioner of the Grenoble Regional Pharmacovigilance Center) will meet. It can also be convened at any time at the request of the clinical trials pharmacovigilance team. . The protocol will only be continued after the committee has given its opinion.. This committee may propose to the sponsor and to the coordinating investigator the stopping of this research or a modification of the protocol if the safety of the subjects does not seem to be sufficient. Composition of the independent monitoring committee:

- Dr Sophie Logerot, Centre Régional de Pharmacovigilance, CHU de Grenoble
- Dr Bernadette Satger, Réseau GRANTED Ville-Hôpital, CHU de Grenoble
- Dr Olivier Ormezzano, Clinique de Cardiologie, CHU de Grenoble

Background therapy: -

Evidence for comparator: -

| | |
|---|------------------|
| Actual start date of recruitment | 01 November 2013 |
| 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 | France: 38 |
| Worldwide total number of subjects | 38 |
| EEA total number of subjects | 38 |

Notes:

Subjects enrolled per age group

| | |
|--|---|
| In utero | 0 |
| Preterm newborn - gestational age < 37 | 0 |

| | |
|--|----|
| wk | |
| 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) | 38 |
| From 65 to 84 years | 0 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

Patients were recruited through the vascular medicine department of Grenoble Alpes University Hospital and enrolled at the clinical pharmacology unit between November 2013 and April 2015.

Pre-assignment

Screening details:

All participants were at least 18 years of age and had primary or secondary RP diagnosed according to the criteria of LeRoy and Medsger (15), with at least 7 attacks per week on 5 or more days per week (assessed during the 2 weeks before inclusion). Color charts were used to confirm diagnosis and detail the topography of RP (16).

Period 1

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

Blinding implementation details:

Each trial consisted of a multiple crossover study in a single patient. Repeat blocks of 3 periods of on-demand treatment were evaluated: 1 week of placebo, 1 week of sildenafil at 40 mg per dose, and 1 week of sildenafil at 80 mg per dose, with a maximum of 2 doses daily. The sequence for each block was randomized by using a block size of 6 so that the same sequence could not be repeated in the same person.

Arms

| | |
|------------------------------|---------|
| Are arms mutually exclusive? | No |
| Arm title | Placebo |

Arm description: -

| | |
|--|----------|
| Arm type | Placebo |
| Investigational medicinal product name | PLACEBO |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

Placebo take on-demand before exposure to cold

| | |
|------------------|------------------|
| Arm title | Sildenafil 40 mg |
|------------------|------------------|

Arm description: -

| | |
|--|--------------|
| Arm type | Experimental |
| Investigational medicinal product name | sildenafil |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

40 mg and 80 mg, take on-demand before exposure to cold

| Number of subjects in period 1 | Placebo | Sildenafil 40 mg |
|---------------------------------------|---------|------------------|
| Started | 38 | 38 |
| Completed | 38 | 38 |

Baseline characteristics

Reporting groups

| | |
|-----------------------|--------|
| Reporting group title | run-in |
|-----------------------|--------|

Reporting group description: -

| Reporting group values | run-in | Total | |
|------------------------|--------|-------|--|
| Number of subjects | 38 | 38 | |
| Age categorical | | | |
| Units: Subjects | | | |
| Adults (18-64 years) | 38 | 38 | |
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | 0 | | |
| standard deviation | ± 0 | - | |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 28 | 28 | |
| Male | 10 | 10 | |

End points

End points reporting groups

| | |
|--------------------------------|------------------|
| Reporting group title | Placebo |
| Reporting group description: - | |
| Reporting group title | Sildenafil 40 mg |
| Reporting group description: - | |

Primary: Raynaud Condition Score

| | |
|------------------------|-------------------------|
| End point title | Raynaud Condition Score |
| End point description: | |
| End point type | Primary |
| End point timeframe: | |
| Daily | |

| End point values | Placebo | Sildenafil 40 mg | | |
|-----------------------------|-----------------|------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 38 | 38 | | |
| Units: 10-point scale | 38 | 38 | | |

Statistical analyses

| | |
|---|---------------------------------------|
| Statistical analysis title | Bayesian framework |
| Comparison groups | Placebo v Sildenafil 40 mg |
| Number of subjects included in analysis | 76 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0 ^[1] |
| Method | Bayesian framework |
| Parameter estimate | Data are expressed as individual aRVs |

Notes:

[1] - not applicable

Adverse events

Adverse events information

Timeframe for reporting adverse events:

9 weeks

| | |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

Dictionary used

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

| | |
|--------------------|----|
| Dictionary version | 18 |
|--------------------|----|

Reporting groups

| | |
|-----------------------|--------------|
| Reporting group title | experimental |
|-----------------------|--------------|

Reporting group description: -

| Serious adverse events | experimental | | |
|---|----------------|--|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 2 / 38 (5.26%) | | |
| number of deaths (all causes) | 0 | | |
| number of deaths resulting from adverse events | 0 | | |
| Vascular disorders | | | |
| Deep vein thrombosis | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pregnancy, puerperium and perinatal conditions | | | |
| Pregnancy | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

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

| Non-serious adverse events | experimental | | |
|---|----------------|--|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | | |
| Cardiac disorders | | | |
| Cyanosis | | | |

| | | | |
|-----------------------------|----------------|--|--|
| subjects affected / exposed | 1 / 38 (2.63%) | | |
| occurrences (all) | 1 | | |

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