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 Hospitaland 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 occurrences (all)	1 / 38 (2.63%) 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