Clinical trial results:
Effect of phosphodiesterase-5 inhibition with Tadalafil on SystEmic Right VEntricular size and function – a multi-center, double-blind, randomized, placebo-controlled clinical trial – SERVE Trial

Summary

EudraCT number	2016-004291-21
Trial protocol	AT
Global end of trial date	28 October 2021

Results information

Result version number	v1 (current)
This version publication date	15 December 2022
First version publication date	15 December 2022
Summary attachment (see zip file)	SERVE-Manuscript-Publication (Paper_SERVE_FINAL_Clean_20220811.pdf) SERVE Final Report Synopsis (SERVE_FINALREPORT-Synopsis.pdf) SERVE-SAPV1 (SERVE_SAP_v1.0.pdf)

Trial information

Trial identification

Sponsor protocol code	SERVE

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03049540
WHO universal trial number (UTN)	-
Other trial identifiers	Insel Nr: 3330, KOFAM: SNCTP000002130

Notes:

Sponsors

Sponsor organisation name	Insel Gruppe AG
Sponsor organisation address	Freiburgstrasse, Bern, Switzerland, 3010
Public contact	Prof. Dr. Markus Schwerzmann, Inselspital Zentrum für angeborene Herzfehler, +41 31632 00 99, markus.schwerzmann@insel.ch
Scientific contact	Prof. Dr. Markus Schwerzmann, Inselspital Zentrum für angeborene Herzfehler, +41 31632 00 99, markus.schwerzmann@insel.ch

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	18 October 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	28 October 2021
Global end of trial reached?	Yes
Global end of trial date	28 October 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

This study assesses in a double-blind, randomized, placebo-controlled multi-center pilot trial the effect of PDE-5 inhibition with Tadalafil on right ventricle (RV) size and functionin adults with a systemic RV over a 3-year follow-up period.

Protection of trial subjects:

Regular followup, Data Safety Monitoring Board (trial with approved drug / placebo but outside indication)

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 August 2017
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	Austria: 12
Country: Number of subjects enrolled	Switzerland: 88
Worldwide total number of subjects	100
EEA total number of subjects	12

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)	98

From 65 to 84 years	2
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Recruitment period: FPFV: 17/11/2017/ LPLV: 28/10/2021 CH and AU. For further details see main manuscript

Pre-assignment

Screening details:

See main manuscript

Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer, Assessor

Blinding implementation details:

Tadalafil 20 mg p.o. OD for 3 years vs. placebo p.o. OD . The study medication was provided in blinded manner.

Arms

Are arms mutually exclusive?	Yes
Arm title	Treatment Arm

Arm description:

Tadalafil 20 mg p.o. OD for 3 years

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

Dosage and administration details:

Tadalafil 20 mg p.o. OD for 3 years

Arm title	Placebo Arm

Arm description:

Placebo p.o. OD for 3 years

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

Dosage and administration details:

Placebo p.o. OD for 3 years

Number of subjects in period 1	Treatment Arm	Placebo Arm
Started	51	49
Completed	42	41
Not completed	9	8
Adverse event, serious fatal	1	1
Consent withdrawn by subject	8	4
Lost to follow-up	-	2
Protocol deviation	-	1

Baseline characteristics

End points

End points reporting groups

Reporting group title	Treatment Arm
Reporting group description: Tadalafil 20 mg p.o. OD for 3 years	
Reporting group title	Placebo Arm
Reporting group description: Placebo p.o. OD for 3 years	

Primary: mean RV-ESV change during follow-up

End point title	mean RV-ESV change during follow-up[1]
End point description:	
End point type	Primary
End point timeframe: 3 years	

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: See Statistical Analysis Plan and Manuscript attached for statistical analyses

End point values	Treatment Arm	Placebo Arm		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	45	46		
Units: ml				
RV-ESV change	3	1		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information[1]	
Timeframe for reporting adverse events:	
Events as defined per protocol needed to be reported from ICF signature until last follow-up visit	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	23

Frequency threshold for reporting non-serious adverse events: 1 %

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: See manuscript for Adverse Event listing as attached

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