Clinical trial results:
Effects of single dose tadalafil on urethral and anal closure function and on urinary flow in healthy females: A randomised, controlled, double-blinded, two-period cross-over study

Summary

EudraCT number	2020-005839-76
Trial protocol	DK
Global end of trial date	10 January 2022

Results information

Result version number	v1 (current)
This version publication date	27 July 2022
First version publication date	27 July 2022

Trial information

Trial identification

Sponsor protocol code	PDE5I-UPR-AAR-01

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05095077
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	University hospital Bispebjerg and Fred
Sponsor organisation address	Bispebjerg Bakke 23, indgang 20C, 2., Copenhagen, Denmark, 2400
Public contact	Information, Zelo phase 1 unit, +45 60770308, thea.christoffersen@regionh.dk
Scientific contact	Information, Zelo phase 1 unit, +45 60770308, thea.christoffersen@regionh.dk

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	01 April 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	10 January 2022
Global end of trial reached?	Yes
Global end of trial date	10 January 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

This study investigated the effect of tadalafil, a phosphodiesterase-type 5 (PDE-5) inhibitor, on urethral pressure, anal pressure and on urinary flow in healthy females.

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and in compliance with all International Conference on Harmonization (ICH) Good Clinical Practice (GCP) Guidelines. Written informed consent was obtained before any study related procedures. We performed minimally invasive measurements and used sterile technique where applicable.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	13 August 2021
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Denmark: 24
Worldwide total number of subjects	24
EEA total number of subjects	24

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)	24
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Healthy females were recruited by advertisement at the online research platform www.forsoegsperson.dk and via database with previous participants in similar trials.

Pre-assignment

Screening details:

Check of the in- and exclusion criteria, physical examination, vital signs

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, Assessor

Blinding implementation details:

Tadalafil and placebo were over-encapsultated in identical gelatine capsules

Arms

Are arms mutually exclusive?	No
Arm title	Tadalafil

Arm description:

Single oral dose of 40 mg tadalafil

Arm type	Experimental
Investigational medicinal product name	Tadalafil
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, soft + tablet
Routes of administration	Oral use

Dosage and administration details:

40 mg once

Arm title	Placebo

Arm description:

Single oral dose placebo

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, soft + tablet
Routes of administration	Oral use

Dosage and administration details:

major ingredients: Lactose monohydrate, Potato starch, Gelatine, Magnesium stearate, Talc, Gelatine capsule DB

Number of subjects in period 1	Tadalafil	Placebo
Started	24	24
Completed	24	24

Baseline characteristics

Reporting groups	
Reporting group title	Overall trial

Reporting group description: -

Reporting group values	Overall trial	Total	
Number of subjects	24	24	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	24	24	
From 65-84 years	0	0	
85 years and over	0	0	
Age continuous Units: years			
median	24.5		
full range (min-max)	20 to 43	-	
Gender categorical Units: Subjects			
Female	24	24	
Male	0	0	

End points

End points reporting groups	
Reporting group title	Tadalafil
Reporting group description: Single oral dose of 40 mg tadalafil	
Reporting group title	Placebo
Reporting group description: Single oral dose placebo	

Primary: Difference in mean resting opening urethral pressure (tadalafil vs placebo)	
End point title	Difference in mean resting opening urethral pressure (tadalafil vs placebo)
End point description:	
End point type	Primary
End point timeframe: Assessment 2 hours after administration of study medication on both placebo day and tadalafil day	

End point values	Tadalafil	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	24	24		
Units: cmH2O				
number (confidence interval 95%)	-6.8 (-11.8 to -1.9)	0 (0 to 0)		

Statistical analyses

Statistical analysis title	Statistical analysis
Comparison groups	Tadalafil v Placebo
Number of subjects included in analysis	48
Analysis specification	Pre-specified
Analysis type	other[1]
P-value	< 0.05
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-6.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-11.8
upper limit	-1.9

Notes:
[1] - Crossover analysis

Secondary: Difference in mean squeezing opening urethral pressure (tadalafil vs placebo)

End point title	Difference in mean squeezing opening urethral pressure (tadalafil vs placebo)

End point description:

End point type	Secondary

End point timeframe:
Assessment 2 hours after administration of study medication on both placebo day and tadalafil day

End point values	Tadalafil	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	24	24		
Units: cmH20				
number (confidence interval 95%)	-8.8 (-14.6 to -3.1)	0 (0 to 0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Difference in mean resting anal opening pressure (tadalafil vs placebo)

End point title	Difference in mean resting anal opening pressure (tadalafil vs placebo)

End point description:

End point type	Secondary

End point timeframe:
Assessment 2 hours after administration of study medication on both placebo day and tadalafil day

End point values	Tadalafil	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	24	24		
Units: cmH20				
number (confidence interval 95%)	-12.9 (-20.7 to -5.0)	0 (0 to 0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Difference in mean squeezing anal opening pressure (tadalafil vs placebo)

End point title	Difference in mean squeezing anal opening pressure (tadalafil vs placebo)

End point description:

End point type	Secondary

End point timeframe:

Assessment 2 hours after administration of study medication on both placebo day and tadalafil day

End point values	Tadalafil	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	24	24		
Units: cmH20				
number (confidence interval 95%)	-5.7 (-17.3 to 6.0)	0 (0 to 0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Difference in average uroflow (Qave) (tadalafil vs placebo)

End point title	Difference in average uroflow (Qave) (tadalafil vs placebo)

End point description:

End point type	Secondary

End point timeframe:

Assessment 2.5 hours after administration of study medication on both placebo day and tadalafil day

End point values	Tadalafil	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	24	24		
Units: ml/s				
number (confidence interval 95%)	-0.8 (-2.0 to 0.4)	0 (0 to 0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Difference in maximum uroflow (Qmax) (tadalafil vs placebo)

End point title	Difference in maximum uroflow (Qmax) (tadalafil vs placebo)

End point description:

End point type	Secondary

End point timeframe:

Assessment 2.5 hours after administration of study medication on both placebo day and tadalafil day

End point values	Tadalafil	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	24	24		
Units: ml/s				
number (confidence interval 95%)	-1.7 (-4.8 to 1.5)	0 (0 to 0)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: From dosing on Study Day 1 to six days after Study Day 2	
Assessment type	Systematic
Dictionary used	
Dictionary name	none
Dictionary version	0
Reporting groups	
Reporting group title	Tadalafil
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	

Serious adverse events	Tadalafil	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 24 (0.00%)	0 / 24 (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: 5 %

Non-serious adverse events	Tadalafil	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	18 / 24 (75.00%)	4 / 24 (16.67%)	
Vascular disorders			
Flushing			
subjects affected / exposed	8 / 24 (33.33%)	0 / 24 (0.00%)	
occurrences (all)	8	8	
Nervous system disorders			
Headache			
subjects affected / exposed	15 / 24 (62.50%)	3 / 24 (12.50%)	
occurrences (all)	18	18	
Fatigue			
subjects affected / exposed	2 / 24 (8.33%)	1 / 24 (4.17%)	
occurrences (all)	3	3	
Ear and labyrinth disorders			

Nasal congestion subjects affected / exposed occurrences (all)	2 / 24 (8.33%) 2	0 / 24 (0.00%) 2	

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