



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-encapsulated 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: cmH2O | | | | |
| 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: cmH2O | | | | |
| 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: cmH2O | | | | |
| 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