ISRCTN80655184 https://doi.org/10.1186/ISRCTN80655184

The intra-meatal application of Tadalafil cream (ErectoGel) versus oral administration efficacy and safety: results from a randomized, two-administration route, cross-over clinical trial

Submission date
29/09/2024

Recruitment status
No longer recruiting

Registration date
01/10/2024

Overall study status
Completed

Last Edited
11/11/2024

Condition category
Mental and Behavioural Disorders

[ ] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[X] Results
[ ] Individual participant data

Plain English summary of protocol

Background and study aims
Erectogel, a topically administered phosphodiesterase-5 inhibitor (PDE5) inhibitor, presents a potential alternative to oral PDE5 inhibitors like Cialis for the treatment of erectile dysfunction (ED). This study evaluates the noninferiority and potential superiority of Erectogel compared to Cialis. This study in which participants are randomly assigned to either a treatment group or a control group to compare the effects of the treatment employed a cross-over design with two treatment periods of two weeks each, separated by a one-week washout phase.

Who can participate?
Male participants aged 18-75 with diagnosed ED (International Index of Erectile Function – Erectile function: IIEF-EF score <26)

What does the study involve?
Participants were randomly allocated to receive either Erectogel or Cialis. Erectogel was applied topically, while Cialis was taken orally. The study will investigate the ability to achieve and maintain an erection sufficient for sexual intercourse, orgasmic function, sexual desire, intercourse satisfaction, and overall satisfaction. Adverse events and treatment preferences were also assessed.

What are the possible benefits and risks of participating?
Erectogel is a safe and effective treatment for erectile dysfunction, demonstrating noninferiority and potential superiority over Cialis, with a high patient preference. Its topical administration offers a promising alternative for patients, particularly those with cardiovascular diseases where oral PDE5 inhibitors are contraindicated or less well tolerated.

Where is the study run from?
Iuliu Hatieganul University of Medicine and Pharmacy PHD Research Projects

When is the study starting and how long is it expected to run for?
February 2022 to September 2024

Who is funding the study?
Iuliu Haţieganu University of Medicine and Pharmacy

Who is the main contact?
Trifu Dragos-Mihail, trifu.dragos.mihail@elearn.umfcluj.ro

Contact information

Type(s)
Public, Scientific, Principal investigator

Contact name
Dr Dragos Mihail Trifu

ORCID ID
https://orcid.org/0009-0004-9318-4036

Contact details
Iancu de Hunedoara st, no. 32, Cluj-Napoca
Cluj-Napoca
Romania
400535
+40219268
trifu.dragos.mihail@elearn.umfcluj.ro

Additional identifiers

Study information

Scientific Title
The intra-meatal application of Tadalafil cream (ErectoGel) versus oral administration efficacy and safety: results from a randomized, two-administration route, cross-over clinical trial

Study objectives
Intra-meatal Tadalafil eliminates systemic side effects of oral administration for PDE-5i

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 03/02/2022, Iuliu Hatieganu University of Medicine and Pharmacy Ethics Committee (Victor Babes no. 8, Cluj-Napoca, 400012, Romania; +40-264-597256; etica.cercetare@umfcluj.ro), ref: DEP48/24.11.2021

Primary study design
Interventional

Study design
Randomized controlled cross-over design study

Study type(s)
Treatment, Safety, Efficacy

Health condition(s) or problem(s) studied
Treatment for men with erectile dysfunction by using topical PDE-5i (Phosphodiesterase 5 Inhibitors)

Interventions
Erectogel, the investigational product, was administered locally. Participants applied the gel 10-15 min before intercourse for a minimum of 3 times in 2 weeks according to the following protocol: Application instructions: participants were instructed to apply one dose of Erectogel to the penile meatus area; Monitoring: participants were asked to maintain a diary documenting the time of application and any local adverse reactions such as irritation, redness, or itching, and any systemic side effects such as headache, dizziness, or gastrointestinal disturbances in their diaries. Each activation of the Pen delivers a dose equivalent to a 20 mg Tadalafil tablet. Cialis (Tadalafil), the comparator, was administered orally. Participants took the medication as follows: dosage: 20 mg 30-60 min before a sexual encounter, with or without food; adherence: participants recorded the time of intake and any systemic side effects such as headache, dizziness, or gastrointestinal disturbances in their diaries.

Randomization was performed using a computer-generated randomization schedule with a 1:1 allocation ratio, with blocks of 4, and 6 (Sealed Envelope Ltd. 2021. Create a blocked randomisation list. [Online] Available from: https://www.sealedenvelope.com/simple-randomiser/v1/lists [Accessed 7 Aug 2022].). Participants were randomly assigned to one of the two treatment sequences: sequence 1 (group A) - Erectogel for the first two-week period, followed by a week of washout period, and then Cialis for the second two-week period, and sequence 2 (group B): Cialis for the first two-week period, followed by a week of washout period, and then Erectogel for the second two-week period. The randomization list was accessible for a person not involved in the study. The participant was selected for the study after meeting the inclusion and exclusion criteria and signed the informed consent and the GDPR agreement. Then, the principal investigator requested the intervention of the person possessing the randomization list without conveying any data about the patient. Thus, allocation concealment was enacted in this study. Blinding of participants is not feasible due to the different modes of administration (local gel vs. oral tablet). The participants will complete the questionnaires on their own; thus, the outcome assessors were the participants.

The primary efficacy outcome was the International Index of Erectile Function (IIEF) Erectile Function domain score. The IIEF-EF is a validated questionnaire consisting of 6 questions (Q1, 2,3,4,5,15) with scores ranging from 0 to 30 (each question has a score ranging from 0 to 6). Higher scores indicate better erectile function. The Erectile Function Domain specifically assesses the ability to achieve and maintain an erection sufficient for sexual intercourse. This was used to compare the efficacy between oral administration (Cialis) and intra-meatal administration (ErectoGel).

The secondary efficacy outcomes were the other IIEF domain scores: orgasmic function, sexual desire, intercourse satisfaction, and overall satisfaction. A secondary exploratory outcome was the treatment preference; the patients were asked at the end of the trial which of the two interventions they preferred. Adverse events were categorized as local (e.g., skin irritation,

erythema) or systemic (e.g., headache, dizziness). These were documented throughout both study periods and assessed at each follow-up visit.

Sample Size
The sample size calculation was based on ensuring adequate power to detect noninferiority within a -3.22 margin for the IIEF Erectile Function Domain score, as used by Kim et al. 2017. Assuming a standard deviation of 6.23 for the difference between IIEF scores and a significance level of 0.05, a total of 21 participants was deemed sufficient to achieve 95% power. We increased the number of participants to 35 since the funding for the study allowed it. The sample size calculation was performed with an online calculator (Centre for Clinical Research and Biostatistics, The Chinese University of Hong Kong. Available from: https://www2.ccrb.cuhk.edu.hk/stat/mean/tsmc_sup.htm), that used the formulas provided by: Chow, Shao and Wang

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
ErectoGel (Tadalafil+Pentravan®), Cialis (Tadalafil)

Primary outcome(s)
Erectile function measured using the International Index of Erectile Function (IIEF) Erectile Function Domain score that specifically assesses the ability to achieve and maintain an erection sufficient for sexual intercourse at period one: beginning (day 1), 2 weeks (day 14); period two: beginning (day 1), 2 weeks (day 14) (the periods were separated by one-week wash-out)

Key secondary outcome(s)
1. Orgasmic function, sexual desire, intercourse satisfaction, and overall satisfaction measured using the other IIEF Domain scores at period one: beginning (day 1), 2 weeks (day 14); period two: beginning (day 1), 2 weeks (day 14) (the periods were separated by one week wash-out)
2. Treatment preference measured using data collected by asking patients which of the two interventions they preferred at the end of the trial
3. Adverse events measured as local (e.g., skin irritation, erythema) or systemic (e.g., headache, dizziness) and documented throughout both study periods and assessed at each follow-up visit

Completion date
01/09/2024

Eligibility

Key inclusion criteria
1. Males aged 18-75 years
2. Diagnosis of erectile dysfunction, confirmed by a score on the International Index of Erectile Function (IIEF)-EF<26
3. Willingness and ability to provide written informed consent, comply with the study procedures and agree with the GDPR terms
4. General good health as determined by medical history and a physical examination, ensuring participants could safely undergo both treatments

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
18 Years

Upper age limit
75 Years

Sex
Male

Total final enrolment
35

Key exclusion criteria
1. Endocrine dysregulation
2. The presence of severe cardiovascular, hepatic, renal, or hematological conditions that could interfere with the study treatments or outcomes
3. Radiotherapy, hormone therapy for prostate cancer
4. Known hypersensitivity to any components of Erectogel or Cialis
5. Use of other medications for erectile dysfunction during the study period to prevent potential drug interactions or confounding effects like beta-blockers, 5-α-reductase inhibitors etc
6. Psychological or psychiatric disorders that could influence the study results or participant compliance
7. History of alcohol or drug abuse within the past year
8. PSA was above 4 ng/mL

Date of first enrolment
05/02/2022

Date of final enrolment
15/08/2024

Locations

Countries of recruitment
Romania

Study participating centre
Prof. Dr. Ioan Puscas City Hospital, Simleu Silvaniei
Strada George Coșbuc no. 29
Simleu Silvaniei

Romania
455300

Study participating centre
REGINA MARIA - E. Grigorescu Clinic
Strada Iancu de Hunedoara no. 32
Cluj-Napoca
Romania
400535

Study participating centre
Medicover Clinic
Str. Republicii no. 75
Cluj-Napoca
Romania
400489

Sponsor information

Organisation
Iuliu Haţieganu University of Medicine and Pharmacy

ROR
https://ror.org/051h0cw83

Funder(s)

Funder type
University/education

Funder Name
Universitatea de Medicină şi Farmacie Iuliu Haţieganu Cluj-Napoca

Alternative Name(s)
University of Medicine and Pharmacy Cluj-Napoca, Iuliu Haţieganu University of Medicine and Pharmacy, University of Medicine and Pharmacy "Iuliu Haţieganu" Cluj-Napoca, “Iuliu Hatieganu” University of Medicine and Pharmacy Cluj-Napoca, Universitatea de Medicină și Farmacie “Iuliu Haţieganu”, UMF Iuliu Haţieganu Cluj-Napoca, UMF Cluj, UMF Cluj-Napoca, UMFCLUJ, UMF

Funding Body Type

Government organisation

Funding Body Subtype
Universities (academic only)

Location
Romania

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated and analysed during the study are not expected to be made available, but can be available upon request from Trifu Dragos-Mihail, trifu.dragos.mihail@elearn.umfcluj.ro

IPD sharing plan summary
Stored in non-publicly available repository, Not expected to be made available

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		31/10/2024	11/11/2024	Yes	No