PK of intra-vaginal oxybutynin

No registrations found.

Ethical review	Positive opinion
Status	Pending
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON20539

Source
Nationaal Trial Register

Brief title
CHDR2032

Health condition

N.A.

Sponsors and support

Primary sponsor: LiGalli BV
Source(s) of monetary or material Support: Sponsor

Intervention

Outcome measures

Primary outcome

PK parameters by non-compartmental analysis of the plasma concentration-time data:
• AUCinf, AUClast, Cmax, tmax, t1/2, tlag, CL/F, Vz/F
• Dose-normalized PK parameters: AUCinf, AUClast, Cmax

Secondary outcome

• Treatment-emergent (serious) adverse events ((S)AEs) throughout the study at every study

visit
• Anticholinergic side effect (pupil size, salivary flow, visual near point acuity and pulse rate) per assessment schedule
• Concomitant medication throughout the study at every study visit
• Vital signs (Pulse Rate (bpm), Systolic blood pressure (mmHg), Diastolic blood pressure (mmHg)) as per assessment schedule
• Physical examination including in speculum examination per assessment schedule

Study description

Background summary

Controlled release technologies, including sustained release of oral medication, implants and transdermal drug delivery, have been
developed to mimic physiological concentrations and endogenous substance profiles. However, there is still a need to develop novel
controlled release technologies. The intra-vaginal delivery route may facilitate such novel technology as it offers several advantages over more commonly used systemic drug delivery routes. It is a non-invasive route of administration, features a suitable residence
time for long-term treatment and could be used for placement of medical devices designed for pulsatile drug delivery.
Currently, no intravaginal controlled delivery method is available to achieve temporary peak concentration at pre-determined time intervals. Therefore, the vaginal MedRing was designed. The MedRing contains a drug formulation reservoir, a miniature peristaltic pump, a miniature electronic circuit board that controls the device, and a battery. The system can wirelessly connect to an external device (smartphone, tablet or laptop computer) from which drug delivery can be programmed and which receives data (volume delivered, temperature) from the ring.
The competitive muscarine receptor antagonist oxybutynin alleviates symptoms of an overactive bladder/urge incontinence, and is often administered orally. Oxybutynin is subject to an extensive first pass effect, resulting in the formation of the active metabolite N-desethyloxybutynin with systemic, anticholinergic side effects. An intravaginal route of administration of oxybutynin has potential advantages compared to oral administration. By this route it bypasses the first-pass effect and may have local efficacy. In contrast to intra-vaginal devices in which oxybutynin is released continuously[1], the MedRing is developed to administer the compound pulsatile and on-demand. Oxybutynin “on demand” could be of potential use in the treatment of overactive bladder/urge incontinence. Other potential indications are the treatment of post-menopausal or aromatase inhibitor-induced hot flashes.
In this study we will investigate the feasibility of pulsed intra-vaginal delivery via the LiGalli MedRing and explore systemic exposure
after a single dose of oxybutynin.

Study objective

Primary
• To evaluate the pharmacokinetics of oxybutynin and its main hepatic metabolite N-desethyloxybutynin after pulsed intra-vaginal
delivery of a single dose of oxybutynin

Secondary
• To assess the safety and tolerability of the intra-vaginal delivery of oxybutynin via the MedRing device in healthy females

Study design

Screening up to -28 days, study day and return day between day -15 and day 22, follow up by phone 7 days after drug administration

Intervention

single-dose oxybutynin intra-vaginally

Contacts

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Eligibility criteria

Inclusion criteria

1. Willing to give written informed consent and willing and able to comply with the study protocol;
2. Female subjects of child bearing potential (women of child bearing potential, WOCBP) aged between 18 and 45 years (inclusive)
OR
Female postmenopausal subjects aged between 50 and 69 years (inclusive); Postmenopausal

status is defined as age ≥ 50 years and having > 12 months amenorrhoea in the absence of hormonal therapy that may cause amenorrhoea.
3. Subject is in good general health, according to the investigator's judgement based on vital signs, medical history, physical examination, and laboratory tests performed.
4. Body mass index between 18-32 kg·m2 (inclusive) and with a minimum body weight of 50 kg at screening
5. Ability to communicate well with the investigator in the Dutch language and willing to comply with the study restrictions
6. Using contraceptives of second generation containing ethinylestradiol and progesterone derivate (WOCBP subjects only). This includes a hormone-containing IUD (e.g. Mirena), second generation oral contraceptive pill, hormonal contraception using parenteral medroxyprogesteron or subcutaneous etonogestrel.

Exclusion criteria

1. (A history of) any clinically significant medical condition or abnormalities, as judged by the investigator, in physical examination, laboratory test results (including chemistry panel with hepatic and renal panels, complete blood count, and urine dipstick) or electrocardiography (ECG). In the case of uncertain or questionable results,
tests performed during screening may be repeated to confirm eligibility or judged by the investigator to be clinically irrelevant for healthy subjects.
2. Being a virgin.
3. History of sexual abuse/violence.
4. First day of last withdrawal bleeding <10 days before Day 0
5. Plan to discontinue oral contraceptive during study period.
6. Positive pregnancy test at screening or at baseline prior to IMP administration and/or lactating.
7. Having given birth vaginally or by caesarean section 6 months prior to screening
8. Having had sexual intercourse or objects inserted vaginally that could potentially lacerate or damage the vaginal wall 24 hours prior to dosing.
9. Positive screening test for Hepatitis B/C and/or Human Immunodeficiency Virus (HIV) test at screening
10. Positive screening PCR test for Chlamydia trachomatis or gonorrhea at screening
11. Medical history of intra- and/or transvaginal operations that in the opinion of the investigator may interfere with placement or stability of the MedRing or absorption of the IMP. Exceptions may include endometrial curettage for e.g. miscarriage or abortion or LIS-excision of the cervix for CIN if performed > 3 months prior to screening.
12. High risk for sexual transmitted diseases (STD) (a. 3 or more different sexual contacts in last 6 months, and/or b. is a sex worker or visits them and/or c. has a partner with an STD risk as described (a. and/or b.), and/or d. partner is a male who has sex with male).
13. Any confirmed significant allergic reactions (urticaria or anaphylaxis) against oxybutynin, or multiple drug allergies (non-active hay fever is acceptable).
14. Participation in any marketed or investigational drug or device study within 3 months or 5 half-lives (whichever is longer) prior to first dosing.
15. Use of any prescription medication and any other substance that in the opinion of the

investigators may influence the outcome of the study within 21 days prior to study drug administrations, or less than five half-lives (whichever is longer, and during the course of the study). Exceptions are the incidental use of OTC medications paracetamol (up to 4 g/day) and ibuprofen (up to 1 g/day) which are allowed within two days of clinical Assessments.
16. Use of alcohol during the 24 hours prior to screening and/or an unwillingness to abstain from alcohol consumption during the stay at the clinical unit, and for at least 24 hours prior to each study visit;
17. Positive urine drug screen or alcohol test at screening and/or at study days.
18. Intake of grapefruit or grapefruit juice within 5 days of IMP administration, and/or unwillingness to abstain from the consumption of these products from 5 days prior to IMP administration until the last study visit;
19. Loss or donation of blood over 500 mL within four months prior to screening.
20. Any other condition that in the opinion of the investigator would complicate or compromise the study or the well-being of the subject.

Study design

Design

Study type:	Interventional
Intervention model:	Other
Allocation:	Non controlled trial
Masking:	Open (masking not used)
Control:	N/A , unknown

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-12-2020
Enrollment:	8
Type:	Anticipated

IPD sharing statement

Plan to share IPD: No

Plan description
N.A.

Ethics review

Positive opinion

Date:	26-01-2021
Application type:	First submission

Study registrations

Followed up by the following (possibly more current) registration

ID: 51105
Bron: ToetsingOnline
Titel:

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
NTR-new	NL9389
CCMO	NL75627.056.20
OMON	NL-OMON51105

Study results

Summary results
N.A.