An open-label, randomized, two-period, two-sequence crossover, single-center trial to assess the bioequivalence of a single dose of 600 IU of freeze-dried r-hLH (Luveris®) versus a single 600 IU dose of the liquid formulation of Luveris® in the Pre-Filled Pen, administered subcutaneously (SC) in pituitary suppressed healthy premenopausal female subjects.

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Primary: to assess the bioequivalence of LH after administration of the freeze-dried (FD) Luveris formulation (Reference) versus the liquid formulation of Luveris in the pre-filled pen (Test) based on the PK parameters AUC0-t and Cmax of serum LH....

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON37820

Source
ToetsingOnline

Brief title
BE study of freeze-dried Luveris vs Luveris in pre-filled pen

Condition

- Other condition

Synonym
female infertility; pituitary hormone deficiency

Health condition

vrouwelijke ovruchtbaarheid

Research involving
Human

Sponsors and support

Primary sponsor: Merck Sharp & Dohme (MSD)
Source(s) of monetary or material Support: farmaceutische industrie

Intervention

Keyword: luteinizing hormone, Luveris®, Marvelon®, pharmacokinetics, pregnancy

Outcome measures

Primary outcome

Pharmacokinetics: plasma LH concentrations, pharmacokinetic parameters

Safety: adverse events, vital signs, ECG-parameters, laboratory parameters,

physical examination, trans vaginal ultrasound, local tolerability

Secondary outcome

n/a

Study description

Background summary

Liquid Luveris® is a new formulation of the already registered Luveris®.
Luveris® is a genetic engineered and therefore named recombinant version of the natural hormone that stimulates ovulation in women (LH: luteinizing hormone)

and may be useful in helping women who have problems to get pregnant.
The formulation of Luveris® that is already registered is a freeze-dried (FD) form, a powder that has to be dissolved in water prior to injection. The liquid formulation of Luveris® does not require adding water and can be injected with a ready to use pen (Pre-Filled Pen).
The liquid Luveris® is not registered as a drug but has been administered to humans before.

Study objective

Primary:
to assess the bioequivalence of LH after administration of the freeze-dried (FD) Luveris formulation (Reference) versus the liquid formulation of Luveris in the pre-filled pen (Test) based on the PK parameters AUC0-t and Cmax of serum LH.

Secondary:
to assess the safety and tolerability of FD Luveris and liquid Luveris administered in the pre-filled pen
to compare the local tolerability of FD Luveris and liquid Luveris administered in the pre-filled pen

Study design

A phase I, open-label, randomized, two-period, two-sequence crossover, single center, bioequivalence study with 54 healthy premenopausal female subjects; subjects will be switched from their own combined oral contraceptive pill (COCP) to Marvelon®; eligibility will be checked after 17 days of Marvelon®; if eligibility is confirmed than subjects will be randomized to receive a single subcutaneous dose of FD Luveris® in one period and a dose with liquid Luveris® in the pre-filled pen in the other period, with a wash-out of fourteen days between dosing

Procedures and assessments:
Screening: Demographics, medical history, history of medication, physical examination (including gynecological exam), drug and alcohol screen, vital signs (including blood pressure, heart rate and temperature), 12-lead ECG, clinical laboratory, pregnancy test, LH/FSH/E2, testosterone, TVUS, adverse events and concomitant medication
Repeated at day of admission on each period: drug and alcohol screen, clinical laboratory, pregnancy test, LH/ E2, TVUS, adverse events and concomitant medication
Follow-up: physical examination (including gynecological exam), vital signs (including blood pressure, heart rate and temperature), 12-lead ECG, clinical laboratory, pregnancy test, LH/FSH/E2, TVUS, adverse events and concomitant medication

Blood sampling:
for pharmacokinetics of LH: pre-dose until144 h post-dose on Days 1 and 15.

Safety assessments:
adverse events and diary card check: throughout the study.
vital signs and 12-lead ECG: pre-dose on Days 1 and 15.
local tolerability: until 24 h post-dose on Days 1 and 15.

Intervention

Test treatment:
a single dose of four clicks with the fertility pen of 150 IU Luveris each, administered immediately after each other

Reference treatment:
a single dose of four subcutaneous injections of 150 IU Luveris each , administered immediately after each other

Study burden and risks

During the cervical smear and TVUS, subjects may experience discomfort from the pressure applied when the speculum (an instrument used to hold the vagina open) is inserted into the vagina or when the cervix is scraped to take a cervical smear. Subjects may experience temporary spotting or bleeding after a cervical smear is performed. The TVUS is usually painless and the level of discomfort is similar or less than a normal gynecological examination.

Luveris® has been well tolerated in previous clinical studies. Common possible side effects are injection site reactions (e.g. pain, redness, swelling, irritation) and headaches, nausea, vomiting, diarrhea, abdominal pain.
Very rarely there may be mild to severe allergic reactions seen.
The following more severe side-effects of Luveris may occur, however in particular when Luveris® is administered concurrently with Follicle Stimulating Hormone (FSH) in the treatment of infertility. In the present drug study in which no FSH will be administered and Marvelon will be taken these side-effects are unlikely: ovarian hyperstimulation (sometimes leading to ovarian enlargement), ovarian cysts. Ovarian hyperstimulation can further cause a potentially life threatening condition called ovarian hyperstimulation syndrome (OHSS). This condition is characterized by severe pelvic pain, swelling of the legs and hands, stomach swelling and dyspnea. Blood clots associated with ovarian hyperstimulation syndrome (when used with some hormonal therapies) have also been seen.

Common minor symptoms of Marvelon® include nausea, breast tenderness, fluid retention, and depression. Some women experience increases in blood pressure and thrombosis can occur.

Registration af adverse effects: During the entire investigation all adverse effects will be documented.

Blood draw, indwelling canula: During this study approximately 260 ml of blood will be drawn. On Day -1 and Day 14 an indwelling cannula will be inserted for blood sampling on Days 1, 2 and Days 15, 16. On the other days during this study, blood will be drawn by direct puncture of the vein.

Heart trace (ECG*s): ECG*s will be made regularly.

Gynecological examination: A gynecological examination including physical examination of the breast will be performed at screening and at the follow up visit.
Cervical Smear: At screening a cervical smear test will be performed.
Transvaginal Ultrasound (TVUS): This examination will take place at screening, at the follow-up visit and up to approximately 48 hours before dosing in each period.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

healthy female subjects
18-40 yrs, inclusive
BMI: 18.5-30.0 kg/m2, inclusive, and weigh more than 50 kg
non-smoking or smoking less then 5 cigarettes per day

Exclusion criteria

Suffering from hepatitis B, hepatitis C, cancer or HIV/AIDS. In case of participation in another drug study within 90 days before the start of this study or being a blood donor within 60 days from the start of the study. In case of donating more than 1.5 liters of blood in the 10 months prior the start of this study.

Study design

Design

Study type:	Interventional
Intervention model:	Crossover
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	01-10-2012
Enrollment:	54
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	FD Luveris
Generic name:	n/a
Product type:	Medicine
Brand name:	liquid Luveris
Generic name:	n/a
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	09-08-2012
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	24-08-2012
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

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

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2011-004778-27-NL
CCMO	NL40196.056.12