A dose finding study to assess contraceptive efficacy and the effect on liver function of estetrol contraception.

No registrations found.

Ethical review	Positive opinion
Status	Recruitment stopped
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON27454

Source
Nationaal Trial Register

Brief title
Protocol PR3095

Health condition

Hormonal contraceptive method

Sponsors and support

Primary sponsor: Estetra S.A.
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Source(s) of monetary or material Support: Estetra S.A.
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Intervention

Outcome measures

Primary outcome

1. Follicle development will be measured in both ovaries by transvaginal ultrasound during the pre-treatment cycle, cycle 1 and cycle 3 on frequent timepoints during each cycle;

2. Liver parameters (carrier proteins, lipids, haemostasis, liver function, bone, glucose metabolism) will be measured at pre-treatment cycle, at the day 3 and 24 of cycle 1 and cycle 3, and at follow up visit.

Secondary outcome

1. Cervical smear;

2. Endometrial thickness;

3. Vaginal bleeding;

4. Endocrinology;

5. Safety.

Study description

Background summary

This is an open, parallel dose finding study in young, healthy, female volunteers of reproductive age.

The first primary objective of the study is to investigate the effect of 3 dosages of estetrol (E4) combined with a progestogen on suppression of ovarian follicular activity and ovulation inhibition. The second primary objective of the study is to assess the pharmacodynamic effect of 3 doses of E4 in combination with a progestogen on a broad range of biochemical liver parameters, known to be affected by the use of a COC.

Women who want to participate and who are using hormonal contraception, stop using their hormonal contraceptive after completing their pill strip and wait for their first spontaneous menstruation (i.e. after a wash-out cycle). Women who do not use hormonal contraception wait for their next menstruation. From the 9th (± 1) day after start of the menstruation onwards follicle growth will be monitored by ultrasonography once every 3 days (± 1) until

ovulation occurs or until day 24 (± 1) after start of their menses (pre-treatment cycle). Women who ovulate within 24 (± 1) days after start of their menses will be eligible to participate. Treatment will start on the first day of their menses after the pre-treatment cycle. The women are randomized to one of six treatment groups. In each group approximately 18 subjects will be included. The subjects will be treated for 3 cycles of 24 days each followed by a 4 day pause.

During the pre-treatment and study period the activity of the hypothalamic-pituitary-ovarian (HPO) axis will be investigated by measuring follicular development using vaginal ultrasonography and by determining serum concentrations of Follicle Stimulating Hormone (FSH), Luteinising Hormone (LH), estradiol (E2), Progesterone (P), and testosterone (T).

Although the progestogen in COC inhibits ovulation when combined with EE, the effect on ovarian suppression and ovulation inhibition of the E4 COC regimen has not been studied before. Therefore volunteers have to use a barrier method (eg. condoms) of contraception during the study. The subjects will have to complete a daily diary to monitor study drug compliance and vaginal bleeding.

Study objective

N/A

Study design

3 treatment cycles; one cycle 28 days.

Intervention

Estetrol, in 3 different doses 5 mg E4, 10 mg E4 and 20 mg E4, each in combination with a progeston will be administered daily during three treatment cycles.

Contacts

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Eligibility criteria

Inclusion criteria

1. At least 18 years and not older than 35 years of age;

2. Willing to use a barrier method of contraception during wash-out;

3. Women who ovulate in the pre-treatment cycle between day 9 and day 24;

4. Body mass index between 18 and 30 kg/m2;

5. Good physical and mental health as judged by the Investigator determined by medical and gynaecological history, physical examination, clinical laboratory and vital signs;

6. Both ovaries visible upon vaginal ultrasonography;

7. Willing to give informed consent in writing.

Exclusion criteria

1. Clinically significant abnormal results of routine haematology, serum biocemistry, urinalysis and/or ECG;

2. Women with a washout cycle with a duration of more than 42 days;

3. Known or suspected pregnancy;

4. Lactation;

5. Pregnancy during accurate hormonal contraceptive use in the past;

6. Known or suspected breast cancer or a history of breast cancer;

7. Clinically significant abnormalities of the uterus and/or ovaries detected by examination and/or ultrasound;

8. A cervical smear with clinically relevant cytology with three years before study start;

9. Use of (hormonal) IUD within 2 months before screening;

10. Use of phytoestrogens;

11. Contraindications for contraceptive steroids;

12. Use of one or more of the following medications:

A. Antihypertensive drugs;

B. Present use or within 2 cycles before start study medication: phenytoin, barbiturates, primidone, carbamazepine, oxcarbazepine, topiramate, felbamate, rifampicin, nelfinavir, ritonavir, griseofulvin, ketoconazole, sex steroids and St. John¡¯s wort (Hypericum perforatum).

13. Status post-partum or post-abortion within a period of 2 months before study start;

14. Administration of investigational drugs within 2 months before screening;

15. A history of (within 12 months) alcohol and drug abuse.

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	02-11-2009
Enrollment:	100
Type:	Actual

Ethics review

Positive opinion

Date:	31-10-2009
Application type:	First submission

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
NTR-new	NL1985
NTR-old	NTR2102
Other	Estetra S.A. : PR3095
ISRCTN	ISRCTN wordt niet meer aangevraagd.

Study results

Summary results
N/A