Multi-center, open-label, randomized study to assess the safety and contraceptive efficacy of two doses (in vitro 12 µg/24 h and 16 µg/24 h) of the ultra low dose levonorgestrel contraceptive intrauterine systems (LCS) for a maximum of 3 years in women 18 to 35 years of age with an extension of the LCS16 treatment arm up to five years

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The objective of this study is to assess the safety, efficacy and pharmacokinetics of 2 doses of LNG, delivered locally by a new intrauterine contraceptive system suitable for use by women 18 to 35 years of age during 3 years and with an extension...

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

Summary

ID

NL-OMON36952

Source
ToetsingOnline

Brief title
LCS

Condition

- Other condition

Synonym
intrauterine contraceptive system

Health condition

intrauteriene anticonceptie

Research involving
Human

Sponsors and support

Primary sponsor: Bayer
Source(s) of monetary or material Support: Pharmaceutische industrie; Bayer Schering Pharma

Intervention

Keyword: contraceptive, intrauterine, levonorgestrel

Outcome measures

Primary outcome

The primary variable of this study is the pregnancy rate. The number of

pregnancies in both treatment arms will be recorded and PIs with 95 %, 2-sided

confidence intervals (CI) will be calculated.

Secondary outcome

Other variables include, number of IUS expulsions and discontinuations due to

(non-)bleeding problems, progestin-related side effects and overall

discontinuations will be recorded and their rate calculated.

In addition to the variables studied in the whole study population, a number of

variables will be studied in 4 subsets in (pre)selected centers in Finland.

Efficacy evaluations will be conducted in subsets 1 (Ovarian and cervical function studied in 40 subjects) and 2A (Endometrial histology studied in 60 subjects), pharmacokinetics in subset 3 and safety in subsets 2B (assessment of hemostatic factors) and 4 (Bone mineral density (BMD) studied in 200 subjects).

Note, that the subjects in subsets 2A and 2B are the same individuals.

Study description

Background summary

The experimental preparations of the ultra low dose levonorgestrel (LNG)contraceptive systems (LCSs) in this study are intrauterine systems (IUSs) initially releasing in vitro 12 and 16 µg of LNG per day. The study product is similar to the MIRENA IUS (a product that has been on the market for many years) initially releasing 20 µg of LNG per day (in vitro). In the experimental LCSs the drug reservoir is mounted on a smaller T-shape frame with diameters of 28 mm horizontal width and 30 mm vertical length and insertion tube diameter of 3,80 mm, while MIRENA's diameters are 32 x 32 mm and 4,75 mm, respectively. Therefore, the aim of this study is to search for a dose for a new contraceptive IUS which provides reliable contraception for 3 years (with an extension of the LCS16 treatment arm up to five years), but has a lower rate of progestin-related systemic side-effects and easier and less inconvenient insertion when compared to Mirena.

Study objective

The objective of this study is to assess the safety, efficacy and pharmacokinetics of 2 doses of LNG, delivered locally by a new intrauterine contraceptive system suitable for use by women 18 to 35 years of age during 3 years and with an extension of the LCS16 treatment arm up to 5 years.

Study design

This study is a multi-center, open, randomized, safety and efficacy phase III study. The number of pregnancies will be recorded and pregnancy rate will be calculated as the primary variable of this study. Transvaginal ultrasounds will be performed at each of the 10 scheduled visits. The ultrasound will be performed to ensure subject's safety including correct placement of the LCS. Bleeding pattern and information on dysmenorrhea will be collected on subject-kept diaries. LCS insertion and removal ease and pain will be evaluated

by the subject (pain) and the investigator (ease). Serum levels of LNG and sex hormone binding globulin (SHBG) will be monitored by means of sparse blood sampling and will be evaluated using a population pharmacokinetic approach (one sample per subject taken at different time-points during the 3 years of the study). All adverse events will be recorded as reported voluntarily by the subject or elicited. Progestin related adverse event will be collected from the adverse event data and reported separately. Adverse events specific to the use of intrauterine systems will receive special attention. General safety will be assured prior to entry and monitored during the study. Pregnancy testing will be done at entry, termination of trial and as necessary during the study. After one year from the cessation of treatment, if the subject discontinued prematurely for a wish to get pregnant, the return to fertility will be assessed by a questionnaire.

Intervention

Two different in vitro doses (daily release rates) of intrauterine LNG, designated as LCS, are studied in this study: Arm 1: 12 µg/day and arm 2: 16 µg/day. In the extension study only women can participate, who are in the LCS16 treatment arm yet.

Study burden and risks

Contraceptive failure is possible with all available contraceptive methods.

Expulsion of the LCS is possible in this study. Expulsion, especially when unnoticed, may be associated with an unwanted pregnancy.

Pelvic infection is possible in this study. Such infection is mainly associated with behavioral factors such as multiplicity of sexual partners.

Ectopic pregnancy is possible in this study.

Uterine perforation occurs in 1/1000 of insertions and at the same rate for all intrauterine devices and hormone releasing systems including Mirena.

LNG-releasing IUSs are associated with scanty bleeding and spotting especially during the first 3 months of use whether used for contraception or endometrial protection. The new LCS is expected to show a similar bleeding profile.

Other side-effects are possible in this study. The typical progestin-related side-effects are headache, nausea, bloating, edema, skin effects, breast pain and tension and weight gain. However, these side-effects are expected to occur less frequently with the new LCS compared to Mirena.

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

has signed informed consent.;is of age between 18 and 35 years (inclusive), in good general health and requesting contraception.;has, in the opinion of the investigator, suitable general and uterine conditions for inserting the LCS.;has clinically normal safety laboratory results (i.e., inside the specified range for inclusion). ;is willing and able to attend the scheduled visits and to comply with the study procedures.;has regular menstrual cycles (length of cycle 21-35 days) (i.e., endogenous cyclicity without hormonal contraceptive use).

Exclusion criteria

see also section 4.1.2 e.g.:;Known or suspected pregnancy or is lactating;History of ectopic pregnancies

Study design

Design

Study phase:	3
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	30-10-2007
Enrollment:	180
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	LCS
Generic name:	NVT

Ethics review

Approved WMO Date:	09-07-2007
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	24-08-2007
Application type:	First submission
Review commission:	METC Catharina Ziekenhuis (Eindhoven)
Approved WMO Date:	10-09-2007

Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	25-09-2007
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	11-02-2008
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	16-01-2009
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	20-01-2009
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	03-02-2010
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	12-02-2010
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	06-06-2011
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

Approved WMO Date:	15-06-2011
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

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	EUCTR2007-000420-40-NL
ClinicalTrials.gov	NCT00528112
CCMO	NL18188.003.07