



Clinical trial results:

Randomized, Open-Label Study to Evaluate the Influence on the Ovarian Activity, and the Cervix Score Over Two Treatment Cycles of 4.0 mg Drospirenone Daily for 24 Days as Compared to 0.075 mg Desogestrel Daily for 28 Days in 60 Healthy, Young Females

Summary

EudraCT number	2010-024546-30
Trial protocol	DE
Global end of trial date	24 September 2012

Results information

Result version number	v1 (current)
This version publication date	29 May 2020
First version publication date	29 May 2020

Trial information

Trial identification

Sponsor protocol code	CF111/202
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Laboratorios León Farma S.A.
Sponsor organisation address	La Vallina s/n, Polígono Industrial de Navatejera, León, Spain, 24008
Public contact	Directeur du Développement, CHEMO France, 0033 149662226, dominique.drouin@chemofrance.com
Scientific contact	Directeur du Développement, CHEMO France, 0033 149662226, dominique.drouin@chemofrance.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	01 July 2014
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	24 September 2012
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the ovulation inhibition potential as reflected by the ovarian activity (follicular growth, estradiol and progesterone serum concentrations) of Drospirenone (DRSP) in comparison to desogestrel, contained in the marketed progesterone only pill CERAZET®, in 60 healthy women

Protection of trial subjects:

N/A

Background therapy:

N/A

Evidence for comparator:

The present study was designed as an investigation of the known progestogen DRSP with respect to its ability to be used as a POP. To describe the ovarian function, the European Medicines Agency guideline's recommendation was to study at least two cycles in each woman. The ovulation inhibitory potential and the properties on the cervix score were assessed over two treatment cycles, which were completely monitored. The comparator in this parallel-group study was CERAZET®, a marketed product with similar features.

Actual start date of recruitment	01 January 2012
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Germany: 64
Worldwide total number of subjects	64
EEA total number of subjects	64

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0

Adults (18-64 years)	64
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Subjects had to meet of the inclusion criteria. Every subject had the right to refuse further participation in the study at any time and without providing reasons and without any personal disadvantage.

Pre-assignment

Screening details:

A total of 96 subjects were screened, of which 32 subjects were screening failures. Reasons for screening failure included withdrawal of consent: 5 subjects; persistent increase of blood pressure, headache with dizziness and vomiting, and intake of prohibited medication: 1 subject for each reason. The remaining 24 subjects had "other" reasons.

Period 1

Period 1 title	Treatment Period (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Blinding implementation details:

N/A

Arms

Are arms mutually exclusive?	Yes
Arm title	Test drug treatment group

Arm description:

Each subject will receive 3 blisters (2 blisters for two treatment cycles plus 1 reserve blister) of 28 coated tablets with 24 active tablets containing 4.0 mg drospirenone and 4 placebo tablets, each.

Arm type	Experimental
Investigational medicinal product name	Drospirenone (DRSP) 4.0 mg coated tablets
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Coated tablet
Routes of administration	Oral use

Dosage and administration details:

1 film-coated tablet with 4.0 mg drospirenone per day to be taken as close as possible to a 24 hour schedule ($\pm$ 3 hours) over 24 days, followed by four placebo tablets. Treatment starts on the 1st day or 2nd

day of menstruation following randomization (only if bleeding starts in the evening and the subject wants to take the study medication in the morning). The total amount of drospirenone will be 192 mg per subject.

Arm title	Reference drug treatment group
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Arm description:

Subjects will receive 3 packages (2 packages for two treatment cycles plus 1 reserve package) with 28 tablets containing 0.075 mg desogestrel

Arm type	Active comparator
Investigational medicinal product name	Cerazet (0.075 mg desogestrel)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

1 tablet with 0.075 mg desogestrel per day to be taken as close as possible to a 24 hour schedule ($\pm$ 3 hours) over 28 days. Treatment starts on the 1st day or 2nd day of menstruation following randomization (only if bleeding starts in the evening and the subject wants to take the study medication in the morning). The total amount of desogestrel will be 4.2 mg per subject.

Number of subjects in period 1	Test drug treatment group	Reference drug treatment group
Started	32	32
Completed	29	29
Not completed	3	3
Consent withdrawn by subject	1	1
Physician decision	1	-
Not specified	1	2

Baseline characteristics

Reporting groups

Reporting group title	Test drug treatment group
Reporting group description: Each subject will receive 3 blisters (2 blisters for two treatment cycles plus 1 reserve blister) of 28 coated tablets with 24 active tablets containing 4.0 mg drospirenone and 4 placebo tablets, each.	
Reporting group title	Reference drug treatment group
Reporting group description: Subjects will receive 3 packages (2 packages for two treatment cycles plus 1 reserve package) with 28 tablets containing 0.075 mg desogestrel	

Reporting group values	Test drug treatment group	Reference drug treatment group	Total
Number of subjects	32	32	64
Age categorical			
18 to 35 years of age			
Units: Subjects			
Adults (18-35 years)	32	32	64
Gender categorical			
Units: Subjects			
Female	32	32	64

Subject analysis sets

Subject analysis set title	Safety Set (SS)
Subject analysis set type	Safety analysis
Subject analysis set description: consists of all volunteers who have received at least one dose of study medication (test or reference)	
Subject analysis set title	Full Analysis Set (FAS)
Subject analysis set type	Full analysis
Subject analysis set description: consists of all subjects who received at least one dose of the study medication (test or reference), for whom CRF entries are available, and for whom at least one Hoogland-Score result is available after start of treatment, regardless of protocol deviations	
Subject analysis set title	Per Protocol Set (PP)
Subject analysis set type	Per protocol
Subject analysis set description: consists of all subjects from the FAS excluding volunteers with major protocol deviations.	

Reporting group values	Safety Set (SS)	Full Analysis Set (FAS)	Per Protocol Set (PP)
Number of subjects	64	63	56
Age categorical			
18 to 35 years of age			
Units: Subjects			
Adults (18-35 years)	64	63	56
Gender categorical			
Units: Subjects			
Female	64	63	56

End points

End points reporting groups

Reporting group title	Test drug treatment group
Reporting group description: Each subject will receive 3 blisters (2 blisters for two treatment cycles plus 1 reserve blister) of 28 coated tablets with 24 active tablets containing 4.0 mg drospirenone and 4 placebo tablets, each.	
Reporting group title	Reference drug treatment group
Reporting group description: Subjects will receive 3 packages (2 packages for two treatment cycles plus 1 reserve package) with 28 tablets containing 0.075 mg desogestrel	
Subject analysis set title	Safety Set (SS)
Subject analysis set type	Safety analysis
Subject analysis set description: consists of all volunteers who have received at least one dose of study medication (test or reference)	
Subject analysis set title	Full Analysis Set (FAS)
Subject analysis set type	Full analysis
Subject analysis set description: consists of all subjects who received at least one dose of the study medication (test or reference), for whom CRF entries are available, and for whom at least one Hoogland-Score result is available after start of treatment, regardless of protocol deviations	
Subject analysis set title	Per Protocol Set (PP)
Subject analysis set type	Per protocol
Subject analysis set description: consists of all subjects from the FAS excluding volunteers with major protocol deviations.	

Primary: Hoogland Score

End point title	Hoogland Score ^[1]
End point description: Multiple data of the leading follicle size and peripheral hormone levels of progesterone and estradiol were collected over two treatment cycles and condensed in a Hoogland-Score evaluation. In case of a suspected ovulation in any treatment cycle the Landgren Score was evaluated, in addition	
End point type	Primary
End point timeframe: cycle 1 and cycle 2	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: No statistical hypothesis tests for efficacy were performed in this exploratory study as the study was to generate first data

End point values	Test drug treatment group	Reference drug treatment group	Per Protocol Set (PP)	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	32	32	56	
Units: number	27	29	56	

Statistical analyses

No statistical analyses for this end point

Secondary: Follicle size

End point title Follicle size

End point description:

End point type Secondary

End point timeframe:

Follicle size was measured in the precycle every third day until ovulation, starting at Day 9 (± 1) up to Day 27 (± 1), as well as during both treatment cycles every third day starting at Day 3, and at final examination

End point values	Test drug treatment group	Reference drug treatment group	Per Protocol Set (PP)	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	32	32	56	
Units: mm	27	29	56	

Statistical analyses

No statistical analyses for this end point

Secondary: Serum progesterone levels

End point title Serum progesterone levels

End point description:

End point type Secondary

End point timeframe:

every third day during both treatment cycles, i.e. on Day 3, Day 6, Day 9 etc.

End point values	Test drug treatment group	Reference drug treatment group	Per Protocol Set (PP)	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	32	32	56	
Units: nmol/L	32	32	56	

Statistical analyses

No statistical analyses for this end point

Secondary: Serum estradiol levels

End point title	Serum estradiol levels
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End point description:

End point type	Secondary
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End point timeframe:

Serum estradiol (pmol/L) levels were measured every third day during both treatment cycles, i.e. on Day 3, Day 6, Day 9 etc

End point values	Test drug treatment group	Reference drug treatment group	Per Protocol Set (PP)	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	32	32	56	
Units: pmol/L	32	32	56	

Statistical analyses

No statistical analyses for this end point

Secondary: Insler score

End point title	Insler score
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End point description:

The cervix condition was evaluated by means of Insler Score in all cycles whenever the follicle size exceeded 13 mm. The Insler score reflects the cervical condition for a possible ascension of the sperms

End point type	Secondary
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End point timeframe:

precycle, cycle 1, cycle 2 and post-treatment cycle

End point values	Test drug treatment group	Reference drug treatment group	Per Protocol Set (PP)	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	32	32	56	
Units: points	27	29	56	

Statistical analyses

No statistical analyses for this end point

Secondary: Return of ovulation

End point title	Return of ovulation
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End point description:

End point type	Secondary
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End point timeframe:
post-treatment cycle

End point values	Test drug treatment group	Reference drug treatment group	Per Protocol Set (PP)	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	32	32	56	
Units: subjects	27	29	56	

Statistical analyses

No statistical analyses for this end point

Secondary: Serum LH levels

End point title	Serum LH levels
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End point description:

End point type	Secondary
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End point timeframe:

The subjects' serum LH levels were determined every third day during both treatment cycles

End point values	Test drug treatment group	Reference drug treatment group	Per Protocol Set (PP)	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	32	32	56	
Units: U/L	27	29	56	

Statistical analyses

No statistical analyses for this end point

Secondary: Serum FSH levels

End point title	Serum FSH levels
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End point description:

End point type	Secondary
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End point timeframe:

The subjects' serum FSH levels were determined every third day during both treatment cycles

End point values	Test drug treatment group	Reference drug treatment group	Per Protocol Set (PP)	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	32	32	56	
Units: U/L	27	29	56	

Statistical analyses

No statistical analyses for this end point

Secondary: Endometrial thickness

End point title	Endometrial thickness
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End point description:

End point type	Secondary
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End point timeframe:

all visits including precycle

End point values	Test drug treatment group	Reference drug treatment group	Per Protocol Set (PP)	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	32	32	56	
Units: mm	27	29	56	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

AE reported spontaneously by the subject or observed by the clinical investigator was monitored during the clinical trial or registered at each visit

Assessment type	Non-systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	14.1
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Reporting groups

Reporting group title	Test
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Reporting group description: -

Reporting group title	Reference
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Reporting group description: -

Serious adverse events	Test	Reference	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Test	Reference	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	29 / 32 (90.63%)	31 / 32 (96.88%)	
Nervous system disorders			
Headache			
subjects affected / exposed	8 / 32 (25.00%)	7 / 32 (21.88%)	
occurrences (all)	15	9	
Gastrointestinal disorders			
Abdominal pain lower			
subjects affected / exposed	4 / 32 (12.50%)	3 / 32 (9.38%)	
occurrences (all)	5	3	
toothache			
subjects affected / exposed	2 / 32 (6.25%)	0 / 32 (0.00%)	
occurrences (all)	4	0	

Reproductive system and breast disorders			
Ovarian cyst			
subjects affected / exposed	2 / 32 (6.25%)	4 / 32 (12.50%)	
occurrences (all)	2	6	
Dysmenorrhoea			
subjects affected / exposed	3 / 32 (9.38%)	2 / 32 (6.25%)	
occurrences (all)	4	4	
Breast discomfort			
subjects affected / exposed	1 / 32 (3.13%)	3 / 32 (9.38%)	
occurrences (all)	1	4	
Galactorrhoea			
subjects affected / exposed	2 / 32 (6.25%)	0 / 32 (0.00%)	
occurrences (all)	2	0	
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	0 / 32 (0.00%)	2 / 32 (6.25%)	
occurrences (all)	0	2	
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	3 / 32 (9.38%)	4 / 32 (12.50%)	
occurrences (all)	3	5	
Psychiatric disorders			
Affective disorder			
subjects affected / exposed	0 / 32 (0.00%)	2 / 32 (6.25%)	
occurrences (all)	0	2	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 32 (0.00%)	2 / 32 (6.25%)	
occurrences (all)	0	2	
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	14 / 32 (43.75%)	14 / 32 (43.75%)	
occurrences (all)	15	14	
Vulvovaginal candidiasis			
subjects affected / exposed	2 / 32 (6.25%)	3 / 32 (9.38%)	
occurrences (all)	2	4	

Cystitis			
subjects affected / exposed	1 / 32 (3.13%)	2 / 32 (6.25%)	
occurrences (all)	1	2	
Sinusitis			
subjects affected / exposed	0 / 32 (0.00%)	2 / 32 (6.25%)	
occurrences (all)	0	2	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported