Clinical trial results:
Phase II trial to evaluate the maintenance of ovulation inhibition with LF111 (drospirenone 4.0 mg 24/4 regimen) after scheduled 24-hour delays in pill intake.

Summary

EudraCT number	2013-001513-33
Trial protocol	DE
Global end of trial date	17 March 2014

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	CF111/204

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Laboratorios Leon Farma, S.A.
Sponsor organisation address	La Vallina s/n, Polígono Industrial de Navatejera, León, Spain, 28004
Public contact	Directeur du Dèveloppement, CHEMO France, 0033 149662226, dominique.drouin@chemofrance.com
Scientific contact	Directeur du Dèveloppement, 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	02 July 2014
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	17 March 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To demonstrate that ovulation inhibition with LF111 (drospirenone 4.0 mg 24/4 regimen) is maintained in spite of scheduled 24-hour delays in pill intake.

Protection of trial subjects:

N/A

Background therapy:

N/A

Evidence for comparator:

N/A

Actual start date of recruitment	21 May 2013
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: 130
Worldwide total number of subjects	130
EEA total number of subjects	130

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)	130
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Healthy premenopausal females of any ethnic origin without regular intake of medicine, 18 to 35 years of age, inclusive. Smokers not older than 30 years, inclusive (up to 10 cigarettes daily). Subjects had to be in good physical and mental health as determined by vital signs, medical history, physical examination,
gynaecological examination, etc.

Pre-assignment

Screening details:

Screening phase: During this period the information and informed consent procedure and screening examinations were performed:
• Medical, surgical and gynaecological history including demographic data
• Physical and gynaecological examinations including cervix smear and TVUS
• Standard laboratory examinations of blood and urine for safety

Period 1

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

Blinding implementation details:

Blinding was not applicable because this was an open-label trial.

Arms

Are arms mutually exclusive?	Yes
Arm title	Group A

Arm description:

Group A performed the following sequence:
• Cycle 1: DRSP 4.0 mg 24/4 regimen (regular intake scheme)
• Cycle 2: DRSP 4.0 mg 24/4 regimen (delayed intake scheme)

Arm type	Experimental
Investigational medicinal product name	Drospirenone 4 mg
Investigational medicinal product code	LF111
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

once daily. Drospirenone 4.0 mg was to be taken by all subjects enrolled in this trial for a duration of 2 x 28 days

Arm title	Group B

Arm description:

Group B performed the following sequence:
• Cycle 1: DRSP 4.0 mg 24/4 regimen (delayed intake scheme)
• Cycle 2: DRSP 4.0 mg 24/4 regimen (regular intake scheme)

Arm type	Experimental
Investigational medicinal product name	Drospirenone 4 mg
Investigational medicinal product code	LF111
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

once daily. Drospirenone 4.0 mg was to be taken by all subjects enrolled in this trial for a duration of 2 x

28 days

Number of subjects in period 1	Group A	Group B
Started	65	65
Completed	58	63
Not completed	7	2
private reasons	-	1
Consent withdrawn by subject	2	-
Adverse event, non-fatal	2	1
Pregnancy	2	-
subject missed visit at Cycle 2 Day 27 and follow-	1	-

Baseline characteristics

Reporting groups	
Reporting group title	Group A
Reporting group description:	
Group A performed the following sequence: • Cycle 1: DRSP 4.0 mg 24/4 regimen (regular intake scheme) • Cycle 2: DRSP 4.0 mg 24/4 regimen (delayed intake scheme)	
Reporting group title	Group B
Reporting group description:	
Group B performed the following sequence: • Cycle 1: DRSP 4.0 mg 24/4 regimen (delayed intake scheme) • Cycle 2: DRSP 4.0 mg 24/4 regimen (regular intake scheme)	

Reporting group values	Group A	Group B	Total
Number of subjects	65	65	130
Age categorical Units: Subjects			
Adults (18 to 35)	65	65	130
Gender categorical Units: Subjects			
Female	65	65	130

Subject analysis sets	
Subject analysis set title	Safety Saet
Subject analysis set type	Safety analysis
Subject analysis set description:	
The Safety Set consisted of all subjects who had been allocated to treatment and had at least one dose of IMP intake.	
Subject analysis set title	Allocated to Treatment Set
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
The Allocated to Treatment Set consisted of all subjects who signed the informed consent and had been allocated to treatment	
Subject analysis set title	Full Anaysis Set
Subject analysis set type	Full analysis
Subject analysis set description:	
The Full Analysis Set consisted of all subjects who were included in the Safety Set and had at least one study observation.	
Subject analysis set title	Per Protocol Set
Subject analysis set type	Per protocol
Subject analysis set description:	
The Per Protocol Set consisted of all subjects who were included in the Full Analysis Set and had no major protocol violation	

Reporting group values	Safety Saet	Allocated to Treatment Set	Full Anaysis Set
Number of subjects	127	130	127

Age categorical Units: Subjects			
Adults (18 to 35)	127	130	127
Gender categorical Units: Subjects			
Female	127	130	127

Reporting group values	Per Protocol Set		
Number of subjects	127		
Age categorical Units: Subjects			
Adults (18 to 35)	127		
Gender categorical Units: Subjects			
Female	127		

End points

End points reporting groups

Reporting group title	Group A

Reporting group description:

Group A performed the following sequence:
• Cycle 1: DRSP 4.0 mg 24/4 regimen (regular intake scheme)
• Cycle 2: DRSP 4.0 mg 24/4 regimen (delayed intake scheme)

Reporting group title	Group B

Reporting group description:

Group B performed the following sequence:
• Cycle 1: DRSP 4.0 mg 24/4 regimen (delayed intake scheme)
• Cycle 2: DRSP 4.0 mg 24/4 regimen (regular intake scheme)

Subject analysis set title	Safety Saet
Subject analysis set type	Safety analysis

Subject analysis set description:

The Safety Set consisted of all subjects who had been allocated to treatment and had at least one dose of IMP intake.

Subject analysis set title	Allocated to Treatment Set
Subject analysis set type	Intention-to-treat

Subject analysis set description:

The Allocated to Treatment Set consisted of all subjects who signed the informed consent and had been allocated to treatment

Subject analysis set title	Full Anaysis Set
Subject analysis set type	Full analysis

Subject analysis set description:

The Full Analysis Set consisted of all subjects who were included in the Safety Set and had at least one study observation.

Subject analysis set title	Per Protocol Set
Subject analysis set type	Per protocol

Subject analysis set description:

The Per Protocol Set consisted of all subjects who were included in the Full Analysis Set and had no major protocol violation

Primary: Ovulation rate

End point title	Ovulation rate[1]

End point description:

An ovulation was to be assumed if both of the following conditions were fulfilled:
• Ultrasound confirmation of a persisting or ruptured follicle > 13 mm
• Progesterone level > 16 nmol/L for at least five consecutive days

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: statistical analyses have not been performed

End point values	Group A	Group B	Full Anaysis Set	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	65	65	127	
Units: N/A	65	65	127	

Statistical analyses

No statistical analyses for this end point

Secondary: Adverse events

End point title	Adverse events

End point description:

End point type	Secondary

End point timeframe:

All AEs, including SAEs, occurring within the period of observation for the clinical trial had to be recorded. The period of observation for the collection of AEs extended from the time when the subject gave informed consent until the date of final visit

End point values	Group A	Group B	Safety Saet	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	62	65	127	
Units: number of adverse events	60	64	124	

Statistical analyses

No statistical analyses for this end point

Secondary: bleeding pattern

End point title	bleeding pattern

End point description:

Bleeding pattern was summarised based on the following defined tolerability endpoints:
• Number and rate of subjects with bleeding or spotting for each day of treatment, by cycle and by overall treatment period
• Number of days with bleeding or spotting per cycle
• Number of days with a certain spotting/bleeding intensity (spotting, slight, moderate, heavy) per cycle
• Number and length of bleeding/spotting episodes

End point type	Secondary

End point timeframe:

From Cycle 1 Day 1 (i.e. start of IMP intake) to final visit (or EDV), the subjects recorded daily any vaginal bleeding with bleeding intensity in their diary.

End point values	Group A	Group B	Safety Saet	Full Anaysis Set
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	65	65	127	127
Units: n/m (%)	62	65	127	127

Statistical analyses

No statistical analyses for this end point

Secondary: clinical laboratory evaluation

End point title	clinical laboratory evaluation

End point description:

safety laboratory values (haematology, biochemistry, liver function, clotting status, virology and urinalysis results)

End point type	Secondary

End point timeframe:

screening and final examination

End point values	Group A	Group B	Safety Saet	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	65	65	127	
Units: various units	62	65	127	

Statistical analyses

No statistical analyses for this end point

Secondary: Vital signs

End point title	Vital signs

End point description:

Blood pressure and pulse was measured in sitting position after the subject had rested for at least 5 minutes. The measurements were performed at screening visit, Cycle 1 Day 12 ±1, Cycle 2 Day 12 ±1 and final visit (or EDV). Height was measured at screening visit only. Body weight was measured at screening visit
and at final visit (or EDV), lightly dressed and without shoes.

End point type	Secondary

End point timeframe:

screening, cycle 1, cycle 2, Final visit

End point values	Group A	Group B	Safety Saet	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	65	65	127	
Units: various units	62	65	127	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

The period of observation for the collection of AEs extended from the time when the subject gave informed consent until the date of final visit.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	15.1

Reporting groups

Reporting group title	Group A
Reporting group description: -	
Reporting group title	Group B

Reporting group description: -

Serious adverse events	Group A	Group B	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 62 (0.00%)	0 / 65 (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	Group A	Group B	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	60 / 62 (96.77%)	64 / 65 (98.46%)	
Vascular disorders			
Hot flush			
subjects affected / exposed	1 / 62 (1.61%)	1 / 65 (1.54%)	
occurrences (all)	1	1	
Surgical and medical procedures			
Mole excision			
subjects affected / exposed	0 / 62 (0.00%)	1 / 65 (1.54%)	
occurrences (all)	0	1	
Tooth extraction			
subjects affected / exposed	0 / 62 (0.00%)	1 / 65 (1.54%)	
occurrences (all)	0	1	

Tooth repair			
subjects affected / exposed	1 / 62 (1.61%)	3 / 65 (4.62%)	
occurrences (all)	1	3	
General disorders and administration site conditions			
Chest discomfort			
subjects affected / exposed	0 / 62 (0.00%)	1 / 65 (1.54%)	
occurrences (all)	0	1	
Chest pain			
subjects affected / exposed	0 / 62 (0.00%)	1 / 65 (1.54%)	
occurrences (all)	0	1	
Fatigue			
subjects affected / exposed	2 / 62 (3.23%)	7 / 65 (10.77%)	
occurrences (all)	2	7	
Injection site haematoma			
subjects affected / exposed	0 / 62 (0.00%)	1 / 65 (1.54%)	
occurrences (all)	0	1	
Pyrexia			
subjects affected / exposed	2 / 62 (3.23%)	0 / 65 (0.00%)	
occurrences (all)	2	0	
Immune system disorders			
Mycotic allergy			
subjects affected / exposed	0 / 62 (0.00%)	1 / 65 (1.54%)	
occurrences (all)	0	1	
Social circumstances			
Tattoo			
subjects affected / exposed	0 / 62 (0.00%)	1 / 65 (1.54%)	
occurrences (all)	0	1	
Reproductive system and breast disorders			
Breast discomfort			
subjects affected / exposed	1 / 62 (1.61%)	3 / 65 (4.62%)	
occurrences (all)	1	3	
Breast enlargement			
subjects affected / exposed	2 / 62 (3.23%)	0 / 65 (0.00%)	
occurrences (all)	2	0	
Breast pain			

subjects affected / exposed	1 / 62 (1.61%)	1 / 65 (1.54%)	
occurrences (all)	1	1	
Dysmenorrhoea			
subjects affected / exposed	9 / 62 (14.52%)	11 / 65 (16.92%)	
occurrences (all)	11	11	
Hydrometra			
subjects affected / exposed	1 / 62 (1.61%)	0 / 65 (0.00%)	
occurrences (all)	1	0	
menorrhagia			
subjects affected / exposed	0 / 62 (0.00%)	1 / 65 (1.54%)	
occurrences (all)	0	1	
Ovarian cyst			
subjects affected / exposed	3 / 62 (4.84%)	3 / 65 (4.62%)	
occurrences (all)	3	3	
Vaginal discharge			
subjects affected / exposed	3 / 62 (4.84%)	0 / 65 (0.00%)	
occurrences (all)	3	0	
Vulvovaginal pruritus			
subjects affected / exposed	2 / 62 (3.23%)	2 / 65 (3.08%)	
occurrences (all)	2	2	
Respiratory, thoracic and mediastinal disorders			
cough			
subjects affected / exposed	1 / 62 (1.61%)	2 / 65 (3.08%)	
occurrences (all)	1	2	
Dysphonia			
subjects affected / exposed	0 / 62 (0.00%)	1 / 65 (1.54%)	
occurrences (all)	0	1	
Epistaxis			
subjects affected / exposed	1 / 62 (1.61%)	0 / 65 (0.00%)	
occurrences (all)	1	0	
Oropharyngeal pain			
subjects affected / exposed	4 / 62 (6.45%)	1 / 65 (1.54%)	
occurrences (all)	5	1	
Psychiatric disorders			

Affective disorder			
subjects affected / exposed	3 / 62 (4.84%)	2 / 65 (3.08%)	
occurrences (all)	3	2	
Agitation			
subjects affected / exposed	1 / 62 (1.61%)	0 / 65 (0.00%)	
occurrences (all)	1	0	
Depression			
subjects affected / exposed	1 / 62 (1.61%)	0 / 65 (0.00%)	
occurrences (all)	1	0	
Libido increased			
subjects affected / exposed	1 / 62 (1.61%)	0 / 65 (0.00%)	
occurrences (all)	1	0	
Loss of libido			
subjects affected / exposed	0 / 62 (0.00%)	1 / 65 (1.54%)	
occurrences (all)	0	1	
Mood altered			
subjects affected / exposed	2 / 62 (3.23%)	3 / 65 (4.62%)	
occurrences (all)	2	3	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 62 (0.00%)	1 / 65 (1.54%)	
occurrences (all)	0	1	
Blood bilirubin increased			
subjects affected / exposed	2 / 62 (3.23%)	2 / 65 (3.08%)	
occurrences (all)	2	2	
Blood cholesterol increased			
subjects affected / exposed	1 / 62 (1.61%)	0 / 65 (0.00%)	
occurrences (all)	1	0	
Blood potassium decreased			
subjects affected / exposed	1 / 62 (1.61%)	0 / 65 (0.00%)	
occurrences (all)	1	0	
Body temperature increased			
subjects affected / exposed	1 / 62 (1.61%)	0 / 65 (0.00%)	
occurrences (all)	1	0	
Glucose urine			

subjects affected / exposed	1 / 62 (1.61%)	0 / 65 (0.00%)	
occurrences (all)	1	0	
Hepatic enzyme increased			
subjects affected / exposed	0 / 62 (0.00%)	1 / 65 (1.54%)	
occurrences (all)	0	1	
Lymphocyte count increased			
subjects affected / exposed	0 / 62 (0.00%)	1 / 65 (1.54%)	
occurrences (all)	0	1	
Neutrophil count decreased			
subjects affected / exposed	0 / 62 (0.00%)	1 / 65 (1.54%)	
occurrences (all)	0	1	
Nitrite urine present			
subjects affected / exposed	1 / 62 (1.61%)	0 / 65 (0.00%)	
occurrences (all)	1	0	
Platelet count increased			
subjects affected / exposed	1 / 62 (1.61%)	0 / 65 (0.00%)	
occurrences (all)	1	0	
Weight decreased			
subjects affected / exposed	1 / 62 (1.61%)	1 / 65 (1.54%)	
occurrences (all)	1	1	
Weight increased			
subjects affected / exposed	1 / 62 (1.61%)	1 / 65 (1.54%)	
occurrences (all)	1	1	
Injury, poisoning and procedural complications			
Animal bite			
subjects affected / exposed	0 / 62 (0.00%)	1 / 65 (1.54%)	
occurrences (all)	0	1	
Arthropod bite			
subjects affected / exposed	1 / 62 (1.61%)	0 / 65 (0.00%)	
occurrences (all)	1	0	
Contusion			
subjects affected / exposed	1 / 62 (1.61%)	2 / 65 (3.08%)	
occurrences (all)	1	2	
Joint injection			

subjects affected / exposed	0 / 62 (0.00%)	1 / 65 (1.54%)	
occurrences (all)	0	1	
Limb injury			
subjects affected / exposed	1 / 62 (1.61%)	1 / 65 (1.54%)	
occurrences (all)	1	1	
Radius fracture			
subjects affected / exposed	1 / 62 (1.61%)	0 / 65 (0.00%)	
occurrences (all)	1	0	
Rib fracture			
subjects affected / exposed	0 / 62 (0.00%)	1 / 65 (1.54%)	
occurrences (all)	0	1	
Thermal burn			
subjects affected / exposed	0 / 62 (0.00%)	2 / 65 (3.08%)	
occurrences (all)	0	2	
Cardiac disorders			
Cardiovascular disorder			
subjects affected / exposed	0 / 62 (0.00%)	1 / 65 (1.54%)	
occurrences (all)	0	1	
Tachycardia			
subjects affected / exposed	0 / 62 (0.00%)	1 / 65 (1.54%)	
occurrences (all)	0	1	
Nervous system disorders			
Cervicogenic headache			
subjects affected / exposed	0 / 62 (0.00%)	1 / 65 (1.54%)	
occurrences (all)	0	1	
Disturbance in attention			
subjects affected / exposed	0 / 62 (0.00%)	1 / 65 (1.54%)	
occurrences (all)	0	1	
Dizziness			
subjects affected / exposed	0 / 62 (0.00%)	2 / 65 (3.08%)	
occurrences (all)	0	2	
Headache			
subjects affected / exposed	26 / 62 (41.94%)	32 / 65 (49.23%)	
occurrences (all)	45	52	
Hypoaesthesia			

subjects affected / exposed	0 / 62 (0.00%)	1 / 65 (1.54%)	
occurrences (all)	0	1	
Sciatica			
subjects affected / exposed	1 / 62 (1.61%)	0 / 65 (0.00%)	
occurrences (all)	1	0	
Blood and lymphatic system disorders			
leukopenia			
subjects affected / exposed	0 / 62 (0.00%)	1 / 65 (1.54%)	
occurrences (all)	0	1	
Lymphadenopathy			
subjects affected / exposed	1 / 62 (1.61%)	0 / 65 (0.00%)	
occurrences (all)	1	0	
Ear and labyrinth disorders			
Auricular swelling			
subjects affected / exposed	1 / 62 (1.61%)	0 / 65 (0.00%)	
occurrences (all)	1	0	
Vertigo			
subjects affected / exposed	2 / 62 (3.23%)	0 / 65 (0.00%)	
occurrences (all)	2	0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	3 / 62 (4.84%)	2 / 65 (3.08%)	
occurrences (all)	3	2	
Abdominal pain lower			
subjects affected / exposed	9 / 62 (14.52%)	8 / 65 (12.31%)	
occurrences (all)	11	10	
Abdominal pain upper			
subjects affected / exposed	1 / 62 (1.61%)	1 / 65 (1.54%)	
occurrences (all)	1	1	
Stomatitis			
subjects affected / exposed	1 / 62 (1.61%)	0 / 65 (0.00%)	
occurrences (all)	1	0	
Constipation			
subjects affected / exposed	1 / 62 (1.61%)	1 / 65 (1.54%)	
occurrences (all)	1	1	
Diarrhoea			

subjects affected / exposed	1 / 62 (1.61%)	2 / 65 (3.08%)	
occurrences (all)	1	2	
Gastritis			
subjects affected / exposed	0 / 62 (0.00%)	1 / 65 (1.54%)	
occurrences (all)	0	1	
Haematochezia			
subjects affected / exposed	0 / 62 (0.00%)	1 / 65 (1.54%)	
occurrences (all)	0	1	
Nausea			
subjects affected / exposed	4 / 62 (6.45%)	7 / 65 (10.77%)	
occurrences (all)	4	7	
Toothache			
subjects affected / exposed	1 / 62 (1.61%)	1 / 65 (1.54%)	
occurrences (all)	1	1	
Vomiting			
subjects affected / exposed	2 / 62 (3.23%)	4 / 65 (6.15%)	
occurrences (all)	2	4	
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	8 / 62 (12.90%)	7 / 65 (10.77%)	
occurrences (all)	9	7	
Alopecia			
subjects affected / exposed	1 / 62 (1.61%)	1 / 65 (1.54%)	
occurrences (all)	1	1	
Dry skin			
subjects affected / exposed	1 / 62 (1.61%)	0 / 65 (0.00%)	
occurrences (all)	1	0	
Eczema			
subjects affected / exposed	1 / 62 (1.61%)	1 / 65 (1.54%)	
occurrences (all)	1	1	
Paronychia			
subjects affected / exposed	0 / 62 (0.00%)	1 / 65 (1.54%)	
occurrences (all)	0	1	
Rash			
subjects affected / exposed	1 / 62 (1.61%)	0 / 65 (0.00%)	
occurrences (all)	1	0	

Renal and urinary disorders			
Albuminuria			
subjects affected / exposed	1 / 62 (1.61%)	2 / 65 (3.08%)	
occurrences (all)	1	2	
Bilirubinuria			
subjects affected / exposed	0 / 62 (0.00%)	1 / 65 (1.54%)	
occurrences (all)	0	1	
Haematuria			
subjects affected / exposed	1 / 62 (1.61%)	1 / 65 (1.54%)	
occurrences (all)	1	1	
Leukocyturia			
subjects affected / exposed	2 / 62 (3.23%)	1 / 65 (1.54%)	
occurrences (all)	2	1	
Pollakiuria			
subjects affected / exposed	0 / 62 (0.00%)	1 / 65 (1.54%)	
occurrences (all)	0	1	
Polyuria			
subjects affected / exposed	0 / 62 (0.00%)	1 / 65 (1.54%)	
occurrences (all)	0	1	
Proteinuria			
subjects affected / exposed	0 / 62 (0.00%)	1 / 65 (1.54%)	
occurrences (all)	0	1	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	5 / 62 (8.06%)	1 / 65 (1.54%)	
occurrences (all)	5	1	
Muscle spasms			
subjects affected / exposed	0 / 62 (0.00%)	1 / 65 (1.54%)	
occurrences (all)	0	1	
Neck pain			
subjects affected / exposed	0 / 62 (0.00%)	1 / 65 (1.54%)	
occurrences (all)	0	1	
Pain in extremity			
subjects affected / exposed	0 / 62 (0.00%)	1 / 65 (1.54%)	
occurrences (all)	0	1	
Spinal deformity			

subjects affected / exposed	0 / 62 (0.00%)	1 / 65 (1.54%)	
occurrences (all)	0	1	
Tenosynovitis			
subjects affected / exposed	0 / 62 (0.00%)	1 / 65 (1.54%)	
occurrences (all)	0	1	
Infections and infestations			
Abscess limb			
subjects affected / exposed	1 / 62 (1.61%)	0 / 65 (0.00%)	
occurrences (all)	1	0	
Tonsillitis			
subjects affected / exposed	0 / 62 (0.00%)	2 / 65 (3.08%)	
occurrences (all)	0	2	
Cystitis			
subjects affected / exposed	1 / 62 (1.61%)	5 / 65 (7.69%)	
occurrences (all)	1	5	
Echinococciasis			
subjects affected / exposed	0 / 62 (0.00%)	1 / 65 (1.54%)	
occurrences (all)	0	1	
Gastrointestinal infection			
subjects affected / exposed	1 / 62 (1.61%)	1 / 65 (1.54%)	
occurrences (all)	1	1	
Nasopharyngitis			
subjects affected / exposed	27 / 62 (43.55%)	34 / 65 (52.31%)	
occurrences (all)	31	39	
Oral herpes			
subjects affected / exposed	4 / 62 (6.45%)	4 / 65 (6.15%)	
occurrences (all)	4	4	
Otitis externa			
subjects affected / exposed	1 / 62 (1.61%)	0 / 65 (0.00%)	
occurrences (all)	1	0	
Sinusitis			
subjects affected / exposed	0 / 62 (0.00%)	1 / 65 (1.54%)	
occurrences (all)	0	1	
Urethritis			
subjects affected / exposed	1 / 62 (1.61%)	0 / 65 (0.00%)	
occurrences (all)	1	0	

Metabolism and nutrition disorders Increased appetite subjects affected / exposed occurrences (all)	 3 / 62 (4.84%) 3	 1 / 65 (1.54%) 1	

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