



## Clinical trial results:

**An investigator-blinded, active controlled, randomized, two parallel group, multi-dose clinical trial to prove the non-inferior efficacy of Lactobacillus plantarum P 17630 100.000.000 CFU soft vaginal capsules (Proge Farm s.r.l.) versus miconazole nitrate 400 mg vaginal soft capsules in vaginal candidiasis.**

## Summary

EudraCT number	2018-003095-12
Trial protocol	BG
Global end of trial date	05 May 2020

## Results information

Result version number	v1 (current)
This version publication date	13 December 2021
First version publication date	13 December 2021

## Trial information

### Trial identification

Sponsor protocol code	LPP17630-C-018
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### Additional study identifiers

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

Notes:

## Sponsors

Sponsor organisation name	Proge Farm s.r.l.
Sponsor organisation address	Largo Guido Donegani 4/A, Novara, Italy, 28100
Public contact	Clinical Trials Information, R&D Solutions srl, info@rdsolutions.it
Scientific contact	Clinical Trials Information, R&D Solutions srl, info@rdsolutions.it

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	05 May 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	14 April 2020
Global end of trial reached?	Yes
Global end of trial date	05 May 2020
Was the trial ended prematurely?	No

Notes:

## General information about the trial

Main objective of the trial:

To demonstrate the non-inferiority efficacy of LJ LACTO - Lactobacillus plantarum P 17630 100.000.000 CFU (Test) versus DAKTARIN - miconazole nitrate 400 mg soft capsules in patients with clinically symptomatic vulvovaginal candidiasis. The evaluation of the following symptoms: pruritus, discharge, pain, dryness will be done using a daily VAS scale.

Protection of trial subjects:

No protections were established in the study protocol

Background therapy:

No treatments were used across all arm/groups in the trial

Evidence for comparator:

Daktarin 400 mg soft gelatine capsules is indicated for the local treatment of vulvovaginal candidosis and superinfections due to Gram-positive bacteria. Furthermore the comparator present the same pharmaceutical form as the Test and it present a comparable treatment period to the studied product.

Actual start date of recruitment	11 September 2019
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

## Population of trial subjects

### Subjects enrolled per country

Country: Number of subjects enrolled	Bulgaria: 200
Worldwide total number of subjects	200
EEA total number of subjects	200

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)	200

From 65 to 84 years	0
85 years and over	0

## Subject disposition

### Recruitment

Recruitment details:

Start date: 11th September 2019

End date: 26th February 2020

MC Comac Medical, 3 Urvich str, 1612 Sofia-Bulgaria; MC-1-Sevlievo EOOD, 60

Nikola Petkov Str., 5402 Sevlievo-Bulgaria; MBAL Trakia, boulevard Patriarh Evtimiy 84, 6004 Stara Zagora-Yugoiztochen-Bulgaria; Deva Maria University Hosp., Al. Stamboliiski str., 8000 Burgas, Vetre-Bulgaria

### Pre-assignment

Screening details:

The present study was carried-out in 200 female patients with a medical history, physical and neurological examinations that support a clinical diagnosis of clinically symptomatic vulvovaginal candidiasis.

### Pre-assignment period milestones

Number of subjects started	200
Number of subjects completed	200

### Period 1

Period 1 title	overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Single blind
Roles blinded	Subject

### Arms

Are arms mutually exclusive?	Yes
<b>Arm title</b>	Experimental arm Reference

Arm description: -

Arm type	Active comparator
Investigational medicinal product name	DAKTARIN® - miconazole nitrate 400 mg soft vaginal capsules
Investigational medicinal product code	Reference
Other name	
Pharmaceutical forms	Vaginal capsule, soft
Routes of administration	Vaginal use

Dosage and administration details:

DAKTARIN® - miconazole nitrate 400 mg soft vaginal capsules (Reference) by vaginal route each day, for a period of 3 consecutive days starting from the evening of Visit 1. During Visit 2, if the physician judged their complete recovery the patients stopped the therapy, otherwise they continue the assigned treatment for other 3 days

<b>Arm title</b>	Experimental arm Test
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Arm description: -

Arm type	Experimental
Investigational medicinal product name	LJ LACTO - Lactobacillus plantarum P 17630 100.000.000 CFU soft vaginal capsules
Investigational medicinal product code	Test
Other name	
Pharmaceutical forms	Vaginal capsule, soft
Routes of administration	Vaginal use

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**Dosage and administration details:**

LJ LACTO - Lactobacillus plantarum P 17630 100.000.000 CFU soft vaginal capsules (Test) by vaginal route each day, for a period of 3 consecutive days starting from the evening of Visit 1. During Visit 2, if the physician judged their complete recovery the patients stopped the therapy, otherwise their continue the assigned treatment for other 3 days

<b>Number of subjects in period 1</b>	Experimental arm Reference	Experimental arm Test
Started	100	100
Completed	97	99
Not completed	3	1
Lost to follow-up	3	1

## Baseline characteristics

### Reporting groups

Reporting group title	overall trial
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Reporting group description: -

Reporting group values	overall trial	Total	
Number of subjects	200	200	
Age categorical			
Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	200	200	
From 65-84 years	0	0	
85 years and over	0	0	
Age continuous			
Units: years			
arithmetic mean	33.31		
standard deviation	± 6.39	-	
Gender categorical			
Female patients with a medical history, physical and neurological examinations that support a clinical diagnosis of clinically symptomatic Vulvovaginal candidiasis were selected for the study.			
Units: Subjects			
Female	200	200	

### Subject analysis sets

Subject analysis set title	Visit 1
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Subject analysis set type	Full analysis
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Subject analysis set description:

Eligibility criteria for diagnosis of VVC: clinical symptoms (pruritus, discharge, pain, dryness)

Subject analysis set title	Visit 2
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Subject analysis set type	Full analysis
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Subject analysis set description:

pruritus, discharge, pain, dryness

Subject analysis set title	Visit 3
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Subject analysis set type	Full analysis
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Subject analysis set description:

pruritus, discharge, pain, dryness

Subject analysis set title	Visit 4
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Subject analysis set type	Full analysis
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Reporting group values	Visit 1	Visit 2	Visit 3
Number of subjects	200	198	152
Age categorical			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	200	198	152
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous			
Units: years			
arithmetic mean	33.31	33.38	33.08
standard deviation	± 6.39	± 6.37	± 6.43
Gender categorical			
Female patients with a medical history, physical and neurological examinations that support a clinical diagnosis of clinically symptomatic Vulvovaginal candidiasis were selected for the study.			
Units: Subjects			
Female	200	198	152

Reporting group values	Visit 4		
Number of subjects	196		
Age categorical			
Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	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)	196		
From 65-84 years	0		
85 years and over	0		
Age continuous			
Units: years			
arithmetic mean	33.37		
standard deviation	± 6.41		
Gender categorical			
Female patients with a medical history, physical and neurological examinations that support a clinical diagnosis of clinically symptomatic Vulvovaginal candidiasis were selected for the study.			
Units: Subjects			
Female	196		





## End points

### End points reporting groups

Reporting group title	Experimental arm Reference
Reporting group description: -	
Reporting group title	Experimental arm Test
Reporting group description: -	
Subject analysis set title	Visit 1
Subject analysis set type	Full analysis
Subject analysis set description: Eligibility criteria for diagnosis of VVC: clinical symptoms (pruritus, discharge, pain, dryness)	
Subject analysis set title	Visit 2
Subject analysis set type	Full analysis
Subject analysis set description: pruritus, discharge, pain, dryness	
Subject analysis set title	Visit 3
Subject analysis set type	Full analysis
Subject analysis set description: pruritus, discharge, pain, dryness	
Subject analysis set title	Visit 4
Subject analysis set type	Full analysis
Subject analysis set description: pruritus, discharge, pain, dryness	

### Primary: Pruritus comparison V1

End point title	Pruritus comparison V1
End point description:	
End point type	Primary
End point timeframe:	
Visit 1	

End point values	Experimental arm Reference	Experimental arm Test	Visit 1	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	100	100	200	
Units: VAS scale				
number (not applicable)	100	100	200	

### Statistical analyses

Statistical analysis title	Pruritus Statistical significant difference V1
Comparison groups	Experimental arm Reference v Experimental arm Test

Number of subjects included in analysis	200
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.05
Method	t-test, 2-sided
Parameter estimate	Mean difference (net)
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.058
upper limit	0.5184
Variability estimate	Standard error of the mean

### Primary: Pruritus comparison V2

End point title	Pruritus comparison V2
End point description:	
End point type	Primary
End point timeframe:	
V2	

End point values	Experimental arm Reference	Experimental arm Test	Visit 2	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	99	99	198	
Units: VAS scale				
number (not applicable)	99	99	198	

### Statistical analyses

<b>Statistical analysis title</b>	Pruritus Statistical significant difference V2
Comparison groups	Experimental arm Test v Experimental arm Reference
Number of subjects included in analysis	198
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.05
Method	t-test, 2-sided
Parameter estimate	Mean difference (net)
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.9816
upper limit	0.2341

Variability estimate	Standard error of the mean
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### Primary: Pruritus comparison V3

End point title	Pruritus comparison V3
End point description:	
End point type	Primary
End point timeframe: V3	

End point values	Experimental arm Reference	Experimental arm Test	Visit 3	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	73	79	152	
Units: VAS scale				
number (not applicable)	73	79	152	

### Statistical analyses

<b>Statistical analysis title</b>	Pruritus Statistical significant difference V3
Comparison groups	Experimental arm Reference v Experimental arm Test
Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.05
Method	t-test, 2-sided
Parameter estimate	Mean difference (net)
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.8069
upper limit	0.0421
Variability estimate	Standard error of the mean

### Primary: Pruritus comparison V4

End point title	Pruritus comparison V4
End point description:	
End point type	Primary
End point timeframe: V4	

<b>End point values</b>	Experimental arm Reference	Experimental arm Test	Visit 4	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	97	99	196	
Units: VAS Scale				
number (not applicable)	97	99	196	

### Statistical analyses

<b>Statistical analysis title</b>	Pruritus Statistical significant difference V4
Comparison groups	Experimental arm Reference v Experimental arm Test
Number of subjects included in analysis	196
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.05
Method	t-test, 2-sided
Parameter estimate	Mean difference (net)
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.5194
upper limit	0.1526
Variability estimate	Standard error of the mean

### Primary: Discharge comparison V1

End point title	Discharge comparison V1
End point description:	
End point type	Primary
End point timeframe:	
V1	

<b>End point values</b>	Experimental arm Reference	Experimental arm Test	Visit 2	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	100	100	200	
Units: VAS scale				
number (not applicable)	100	100	200	

### Statistical analyses

<b>Statistical analysis title</b>	Discharge Statistical significant difference V1
Comparison groups	Experimental arm Reference v Experimental arm Test
Number of subjects included in analysis	200
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.05
Method	t-test, 2-sided
Parameter estimate	Mean difference (net)
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.6169
upper limit	0.7369
Variability estimate	Standard error of the mean

### Primary: Discharge comparison V2

End point title	Discharge comparison V2
End point description:	
End point type	Primary
End point timeframe:	
V2	

<b>End point values</b>	Experimental arm Reference	Experimental arm Test	Visit 2	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	99	99	198	
Units: VAS scale				
number (not applicable)	99	99	198	

### Statistical analyses

<b>Statistical analysis title</b>	Discharge Statistical significant difference V2
Comparison groups	Experimental arm Reference v Experimental arm Test

Number of subjects included in analysis	198
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.05
Method	t-test, 2-sided
Parameter estimate	Mean difference (net)
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.8185
upper limit	0.3034
Variability estimate	Standard error of the mean

### Primary: Discharge comparison V3

End point title	Discharge comparison V3
End point description:	
End point type	Primary
End point timeframe:	
V3	

End point values	Experimental arm Reference	Experimental arm Test	Visit 3	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	73	79	152	
Units: VAS Scale				
number (not applicable)	73	79	152	

### Statistical analyses

<b>Statistical analysis title</b>	Discharge Statistical significant difference V3
Comparison groups	Experimental arm Reference v Experimental arm Test
Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.05
Method	t-test, 2-sided
Parameter estimate	Mean difference (net)
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.6891
upper limit	0.145

Variability estimate	Standard error of the mean
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### Primary: Dscharge comparison V4

End point title	Dscharge comparison V4
End point description:	
End point type	Primary
End point timeframe:	V4

End point values	Experimental arm Reference	Experimental arm Test	Visit 4	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	97	99	196	
Units: VAS Scale				
number (not applicable)	97	99	196	

### Statistical analyses

Statistical analysis title	Discharge Statistical significant difference V4
Comparison groups	Experimental arm Reference v Experimental arm Test
Number of subjects included in analysis	196
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.05
Method	t-test, 2-sided
Parameter estimate	Mean difference (net)
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.4041
upper limit	0.1446
Variability estimate	Standard error of the mean

### Primary: Pain comparison V1

End point title	Pain comparison V1
End point description:	
End point type	Primary
End point timeframe:	V1

<b>End point values</b>	Experimental arm Reference	Experimental arm Test	Visit 1	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	100	100	200	
Units: VAS Scale				
number (not applicable)	100	100	200	

### Statistical analyses

<b>Statistical analysis title</b>	Pain Statistical significant difference V1
Comparison groups	Experimental arm Reference v Experimental arm Test
Number of subjects included in analysis	200
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.05
Method	t-test, 2-sided
Parameter estimate	Mean difference (net)
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.855
upper limit	0.795
Variability estimate	Standard error of the mean

### Primary: Pain comparison V2

End point title	Pain comparison V2
End point description:	
End point type	Primary
End point timeframe:	
V2	

<b>End point values</b>	Experimental arm Reference	Experimental arm Test	Visit 2	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	99	99	198	
Units: VAS Scale				
number (not applicable)	99	99	198	



### Statistical analyses

<b>Statistical analysis title</b>	Pain Statistical significant difference V2
Comparison groups	Experimental arm Reference v Experimental arm Test
Number of subjects included in analysis	198
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.05
Method	t-test, 2-sided
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.7865
upper limit	0.1401
Variability estimate	Standard error of the mean

### Primary: Pain comparison V3

End point title	Pain comparison V3
End point description:	
End point type	Primary
End point timeframe:	
V3	

<b>End point values</b>	Experimental arm Reference	Experimental arm Test	Visit 3	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	73	79	152	
Units: VAS Scale				
number (not applicable)	73	79	152	

### Statistical analyses

<b>Statistical analysis title</b>	Pain Statistical significant difference V3
Comparison groups	Experimental arm Reference v Experimental arm Test

Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.05
Method	t-test, 2-sided
Parameter estimate	Mean difference (net)
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.1669
upper limit	0.7814
Variability estimate	Standard error of the mean

### Primary: Pain comparison V4

End point title	Pain comparison V4
End point description:	
End point type	Primary
End point timeframe:	
V4	

End point values	Experimental arm Reference	Experimental arm Test	Visit 4	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	97	99	196	
Units: VAS scale				
number (not applicable)	97	99	196	

### Statistical analyses

<b>Statistical analysis title</b>	Pain Statistical significant difference V4
Comparison groups	Experimental arm Test v Experimental arm Reference
Number of subjects included in analysis	196
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.05
Method	t-test, 2-sided
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.3912
upper limit	0.1024
Variability estimate	Standard error of the mean

**Primary: Dryness comparison V1**

End point title	Dryness comparison V1
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End point description:
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End point type	Primary
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End point timeframe:
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V1
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End point values	Experimental arm Reference	Experimental arm Test	Visit 1	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	100	100	200	
Units: VAS Scale				
number (not applicable)	100	100	200	

**Statistical analyses**

<b>Statistical analysis title</b>	Dryness Statistical significant difference V1
Comparison groups	Experimental arm Reference v Experimental arm Test
Number of subjects included in analysis	200
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.05
Method	t-test, 2-sided
Parameter estimate	Mean difference (net)
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.5895
upper limit	1.35
Variability estimate	Standard error of the mean

**Primary: Dryness comparison V2**

End point title	Dryness comparison V2
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End point description:
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End point type	Primary
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End point timeframe:
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V2
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<b>End point values</b>	Experimental arm Reference	Experimental arm Test	Visit 2	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	99	99	198	
Units: VAS Scale				
number (not applicable)	99	99	198	

### Statistical analyses

<b>Statistical analysis title</b>	Dryness Statistical significant difference V2
Comparison groups	Experimental arm Reference v Experimental arm Test
Number of subjects included in analysis	198
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.05
Method	t-test, 2-sided
Parameter estimate	Mean difference (net)
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.5992
upper limit	0.3567
Variability estimate	Standard error of the mean

### Primary: Dryness comparison V3

End point title	Dryness comparison V3
End point description:	
End point type	Primary
End point timeframe:	
V3	

<b>End point values</b>	Experimental arm Reference	Experimental arm Test	Visit 3	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	73	79	152	
Units: VAS Scale				
number (not applicable)	73	79	152	

### Statistical analyses

<b>Statistical analysis title</b>	Dryness Statistical significant difference V3
Comparison groups	Experimental arm Reference v Experimental arm Test
Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.05
Method	t-test, 2-sided
Parameter estimate	Mean difference (net)
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.2207
upper limit	0.0959
Variability estimate	Standard error of the mean

### Primary: Dryness comparison V4

End point title	Dryness comparison V4
End point description:	
End point type	Primary
End point timeframe:	
V4	

<b>End point values</b>	Experimental arm Reference	Experimental arm Test	Visit 4	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	97	99	198	
Units: VAS Scale				
number (not applicable)	97	99	198	

### Statistical analyses

<b>Statistical analysis title</b>	Dryness Statistical significant difference V4
Comparison groups	Experimental arm Reference v Experimental arm Test

Number of subjects included in analysis	196
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.05
Method	t-test, 2-sided
Parameter estimate	Mean difference (net)
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.327
upper limit	0.0063
Variability estimate	Standard error of the mean

## Secondary: Interleukin IL6 comparison V1

End point title	Interleukin IL6 comparison V1
End point description:	
End point type	Secondary
End point timeframe:	
V1	

End point values	Experimental arm Reference	Experimental arm Test	Visit 1	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	99	100	199	
Units: pg/mL	99	100	199	

## Statistical analyses

<b>Statistical analysis title</b>	IL6 Statistical significant difference V1
Comparison groups	Experimental arm Reference v Experimental arm Test
Number of subjects included in analysis	199
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.05
Method	t-test, 2-sided
Parameter estimate	Mean difference (net)
Confidence interval	
level	95 %
sides	2-sided
lower limit	-10.38
upper limit	17.05
Variability estimate	Standard error of the mean

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**Secondary: Interleukin IL6 comparison V2**

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End point title	Interleukin IL6 comparison V2
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End point description:

End point type	Secondary
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End point timeframe:

V2

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End point values	Experimental arm Reference	Experimental arm Test	Visit 2	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	96	90	186	
Units: pg/mL	96	90	186	

**Statistical analyses**

<b>Statistical analysis title</b>	IL6 Statistical significant difference V2
Comparison groups	Experimental arm Reference v Experimental arm Test
Number of subjects included in analysis	186
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.05
Method	t-test, 2-sided
Parameter estimate	Mean difference (net)
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.825
upper limit	6.281
Variability estimate	Standard error of the mean

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**Secondary: Interleukin IL6 comparison V3**

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End point title	Interleukin IL6 comparison V3
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End point description:

End point type	Secondary
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End point timeframe:

V3

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<b>End point values</b>	Experimental arm Reference	Experimental arm Test	Visit 3	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	68	70	138	
Units: pg/mL	68	70	138	

### Statistical analyses

<b>Statistical analysis title</b>	IL6 Statistical significant difference V3
Comparison groups	Experimental arm Reference v Experimental arm Test
Number of subjects included in analysis	138
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.05
Method	t-test, 2-sided
Parameter estimate	Mean difference (net)
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.386
upper limit	3.17
Variability estimate	Standard error of the mean



## Adverse events

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### Adverse events information<sup>[1]</sup>

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Timeframe for reporting adverse events:

Adverse events were evaluated on Visit 1, Visit2, Visit 3 and Follow-up.

Assessment type	Non-systematic
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	21.0
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Frequency threshold for reporting non-serious adverse events: 0 %

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### Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.

Justification: No non-serious and/or serious adverse events were recorded through the entire study period neither by the investigator neither by the patients.

## **More information**

### **Substantial protocol amendments (globally)**

Were there any global substantial amendments to the protocol? No

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### **Interruptions (globally)**

Were there any global interruptions to the trial? No

### **Limitations and caveats**

None reported