Clinical trial results:
A phase 3, double-blind, multicentre, randomised, placebo-controlled study to determine the efficacy and safety of SPL7013 Gel (VivaGel®) to prevent the recurrence of bacterial vaginosis

Summary

EudraCT number	2014-000694-39
Trial protocol	CZ GB HU BG
Global end of trial date	04 October 2016

Results information

Result version number	v1 (current)
This version publication date	07 August 2021
First version publication date	07 August 2021

Trial information

Trial identification

Sponsor protocol code	SPL7013-018

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02236156
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Starpharma Pty Ltd
Sponsor organisation address	4-6 Southampton Crescent, Abbotsford, Australia, 3067
Public contact	VP Development and Regulatory Affairs, Starpharma Pty Ltd, jeremy.paull@starpharma.com
Scientific contact	VP Development and Regulatory Affairs, Starpharma Pty Ltd, jeremy.paull@starpharma.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	07 August 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	04 July 2016
Global end of trial reached?	Yes
Global end of trial date	04 October 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To determine the efficacy of 1% SPL7013 Gel in reducing recurrent bacterial vaginosis (BV) in women with a history of recurrent BV.

Protection of trial subjects:

The study was conducted in accordance with Good Clinical Practice (GCP) as required by the International Council for Harmonisation guidelines and in accordance with country-specific laws and regulations governing clinical studies of investigational products (IPs). Compliance with these requirements also constitutes conformity with the ethical principles of the Declaration of Helsinki. An informed consent document approved by each study centre's IRB/IEC was signed by the subject or legal representative and the investigator before any study-related procedures were performed. The investigator provided copies of the signed informed consent to the subject or legal representative, and the original was retained by the investigator.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 August 2014
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	Romania: 119
Country: Number of subjects enrolled	United Kingdom: 22
Country: Number of subjects enrolled	Bulgaria: 145
Country: Number of subjects enrolled	Czechia: 60
Country: Number of subjects enrolled	Hungary: 130
Country: Number of subjects enrolled	Ukraine: 113
Country: Number of subjects enrolled	Thailand: 6
Country: Number of subjects enrolled	United States: 42
Worldwide total number of subjects	637
EEA total number of subjects	454

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)	637
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Subjects aged 18-45 years with current BV (3/4 Amsel criteria, Nugent score 4-10 and symptoms of vaginal discharge and/or unpleasant vaginal odour), and history of recurrent BV (3 episodes in last 12 months, including current), and after metronidazole therapy, BV had to be resolved (no symptoms and negative for discharge, whiff test, clue cells)

Period 1

Period 1 title	Double-blind treatment phase (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	SPL7013 Gel

Arm description: -

Arm type	Experimental
Investigational medicinal product name	1% SPL7013 Gel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Gel
Routes of administration	Vaginal use

Dosage and administration details:

5 g every second day for 16 weeks

Arm title	Placebo Gel

Arm description: -

Arm type	Placebo
Investigational medicinal product name	Placebo Gel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Gel
Routes of administration	Vaginal use

Dosage and administration details:

5 g every second day for 16 weeks

Number of subjects in period 1	SPL7013 Gel	Placebo Gel
Started	319	318
Completed	294	298
Not completed	25	20
Consent withdrawn by subject	12	11
Adverse event, non-fatal	-	2

Not specified/missing	6	-
Not specified	-	2
Pregnancy	3	1
Lost to follow-up	4	4

Baseline characteristics

Reporting groups

Reporting group title	Double-blind treatment phase

Reporting group description: -

Reporting group values	Double-blind treatment phase	Total	
Number of subjects	637	637	
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)		0	
From 65-84 years		0	
85 years and over		0	
Age continuous Units: years			
arithmetic mean	31.6		
standard deviation	± 7.26	-	
Gender categorical Units: Subjects			
Female	637	637	
Male	0	0	

End points

End points reporting groups	
Reporting group title	SPL7013 Gel
Reporting group description: -	
Reporting group title	Placebo Gel
Reporting group description: -	

Primary: Recurrence of BV	
End point title	Recurrence of BV
End point description:	
Number of participants with a recurrence of BV, where a diagnosis of BV is defined as the presence of at least 3 clinical findings (Amsel criteria)	
End point type	Primary
End point timeframe:	
At or by the Week 16 visit	

End point values	SPL7013 Gel	Placebo Gel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	318	318		
Units: Subjects	50	72		

Statistical analyses

Statistical analysis title	Recurrence of BV at or by Week 16
Comparison groups	SPL7013 Gel v Placebo Gel
Number of subjects included in analysis	636
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.027
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.64
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.43
upper limit	0.95

Secondary: Time to recurrence of BV

End point title	Time to recurrence of BV

End point description:

Time to recurrence of BV (days), where a diagnosis of BV is defined as the presence of at least 3 clinical findings (Amsel criteria)

End point type	Secondary

End point timeframe:

At or by the Week 16 visit

End point values	SPL7013 Gel	Placebo Gel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	318	318		
Units: Days				
median (confidence interval 95%)	114 (113 to 115)	112 (112 to 113)		

Statistical analyses

Statistical analysis title	Time to recurrence
Comparison groups	Placebo Gel v SPL7013 Gel
Number of subjects included in analysis	636
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.009
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.56
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.4
upper limit	0.9

Secondary: Recurrence of patient-reported BV symptoms

End point title	Recurrence of patient-reported BV symptoms

End point description:

Number of participants with self-reported BV symptoms (vaginal discharge and/or odor)

End point type	Secondary

End point timeframe:

At or by the Week 16 visit

End point values	SPL7013 Gel	Placebo Gel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	312	309		
Units: Subjects	32	49		

Statistical analyses

Statistical analysis title	Recurrence of BV Symptoms
Comparison groups	SPL7013 Gel v Placebo Gel
Number of subjects included in analysis	621
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.012
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.59
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.39
upper limit	0.89

Secondary: Recurrence of individual Amsel criteria

End point title	Recurrence of individual Amsel criteria
End point description:	
Number of participants with positive individual Amsel criterion - Clue cells representing at least 20% of total epithelial cells	
End point type	Secondary
End point timeframe:	
At or by the Week 16 visit	

End point values	SPL7013 Gel	Placebo Gel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	312	305		
Units: Participants	33	61		

Statistical analyses

Statistical analysis title	Amsel criterion - Clue cells
Comparison groups	SPL7013 Gel v Placebo Gel

Number of subjects included in analysis	617
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.47
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.3
upper limit	0.75

Secondary: Recurrence of BV as determined by Nugent score 7-10

End point title	Recurrence of BV as determined by Nugent score 7-10

End point description:

Number of participants with a recurrence of BV as determined by presence of a Nugent score of 7-10 (BV), where 0-3 is normal, and 4-6 is intermediate.

End point type	Secondary

End point timeframe:

At or by the Week 16 visit

End point values	SPL7013 Gel	Placebo Gel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	299	305		
Units: Participants	43	75		

Statistical analyses

Statistical analysis title	Recurrence of Nugent score 7-10
Comparison groups	SPL7013 Gel v Placebo Gel
Number of subjects included in analysis	604
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.002
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.52
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.34
upper limit	0.78

Secondary: Recurrence of BV

End point title	Recurrence of BV
End point description:	
Number of participants with a recurrence of BV, where a diagnosis of BV is defined as the presence of at least 3 clinical findings (Amsel criteria)	
End point type	Secondary
End point timeframe:	
At or by the Week 24 visit	

End point values	SPL7013 Gel	Placebo Gel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	318	318		
Units: Particpants	100	122		

Statistical analyses

Statistical analysis title	Recurrence of BV at or by Week 24
Comparison groups	SPL7013 Gel v Placebo Gel
Number of subjects included in analysis	636
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.068
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.74
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.53
upper limit	1.02

Secondary: Recurrence of BV according to composite of Amsel criteria and Nugent score

End point title	Recurrence of BV according to composite of Amsel criteria and Nugent score
End point description:	
Number of participants with a recurrence of BV according to the composite definition of at least 3 clinical findings (Amsel criteria) and a Nugent score of 4-10 (intermediate to BV), where 0-3 is normal.	
End point type	Secondary
End point timeframe:	
At or by the Week 16 visit	

End point values	SPL7013 Gel	Placebo Gel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	312	306		
Units: Participants	30	50		

Statistical analyses

Statistical analysis title	Recurrence of BV according to composite definition
Comparison groups	SPL7013 Gel v Placebo Gel
Number of subjects included in analysis	618
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.014
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.54
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.34
upper limit	0.88

Secondary: Adverse events (AEs)

End point title	Adverse events (AEs)
End point description:	
Number of participants with genitourinary AEs considered potentially related to study treatment	
End point type	Secondary
End point timeframe:	
From Baseline to end of Week 28	

End point values	SPL7013 Gel	Placebo Gel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	318	318		
Units: Participants	7	6		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Baseline to end of study	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	17

Reporting groups	
Reporting group title	SPL7013 Gel
Reporting group description: -	
Reporting group title	Placebo Gel
Reporting group description: -	

Serious adverse events	SPL7013 Gel	Placebo Gel	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 318 (0.31%)	2 / 318 (0.63%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Immune system disorders			
Drug hypersensitivity			
subjects affected / exposed	1 / 318 (0.31%)	0 / 318 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Epistaxis			
subjects affected / exposed	0 / 318 (0.00%)	1 / 318 (0.31%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Meningitis aseptic			
subjects affected / exposed	0 / 318 (0.00%)	1 / 318 (0.31%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	SPL7013 Gel	Placebo Gel	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	32 / 318 (10.06%)	38 / 318 (11.95%)	
Nervous system disorders			
Headache			
alternative assessment type: Non-systematic			
subjects affected / exposed	19 / 318 (5.97%)	16 / 318 (5.03%)	
occurrences (all)	19	16	
Infections and infestations			
Vulvovaginal candidiasis			
subjects affected / exposed	13 / 318 (4.09%)	22 / 318 (6.92%)	
occurrences (all)	13	22	

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