Clinical trial results:
A Phase 3, Multicenter, Randomized, Double-Blind, Placebo-Controlled Study to Evaluate the Efficacy and Safety of Oral Ibrexafungerp (SCY-078) vs. Placebo in Subjects with Acute Vulvovaginal Candidiasis

Summary

EudraCT number	2018-004492-12
Trial protocol	BG
Global end of trial date	07 February 2020

Results information

Result version number	v1 (current)
This version publication date	26 February 2021
First version publication date	26 February 2021

Trial information

Trial identification

Sponsor protocol code	SCY-078-306

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-
Other trial identifiers	IND: 107521

Notes:

Sponsors

Sponsor organisation name	SCYNEXIS, Inc.
Sponsor organisation address	1 Evertrust Plaza, 13th Floor, Jersey City, United States, NJ 07302
Public contact	VANISH Study Team, SCYNEXIS, Inc., +1 201884 5485, info@scynexis.com
Scientific contact	VANISH Study Team, SCYNEXIS, Inc., +1 201884 5485, info@scynexis.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	08 July 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	07 February 2020
Global end of trial reached?	Yes
Global end of trial date	07 February 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the efficacy of oral ibrexafungerp versus placebo in subjects with acute vulvovaginal candidiasis (AVVC) by comparing the clinical outcomes of ibrexafungerp and placebo. Efficacy was defined as the percentage of subjects with clinical cure (complete resolution of signs and symptoms) at the TOC visit.

Protection of trial subjects:

The ICH issued guidelines to provide protection for human subjects in clinical investigations. The ICH E6 GCP guideline establishes the general requirements for informed consent. Each subject was provided with oral and written information in a language they could understand that described the nature and duration of the study. Before undergoing screening, each subject must have consented in writing to study participation. In case of a minor and according to the local definition (eg, below 16 or 18 years of age), the parent or legal representative should have also signed and dated the ICF.

Background therapy:

All prior and concomitant medications including Rescue Antifungal medication were coded using the World Health Organization (WHO) Drug Dictionary (WHODrug) Global Sept 2018 B3 and summarized by treatment group for all subjects in the ITT and mITT sets.

Evidence for comparator:

No active comparator, placebo controlled study

Actual start date of recruitment	07 June 2019
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	United States: 171
Country: Number of subjects enrolled	Bulgaria: 278
Worldwide total number of subjects	449
EEA total number of subjects	278

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)	445
From 65 to 84 years	4
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Subjects who met all of the inclusion criteria and none of the exclusion criteria were enrolled into the study and were randomly assigned in a 2:1 ratio to
- Ibrexafungerp: oral 300-mg dose BID for 1 day
- Placebo: oral ibrexafungerp matching placebo BID for 1 day

Pre-assignment

Screening details:

Screening and baseline visits may have occurred on the same day. A total number of 449 subjects were enrolled in the study: 298 subjects to ibrexafungerp and 151 subjects to placebo.

Period 1

Period 1 title	Treatment period (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

Blinding implementation details:

This was a double-blind, double-dummy study. The study drugs were identical in number and appearance. Blinding was maintained throughout the study by use of active or placebo dosage forms of similar appearance.

Arms

Are arms mutually exclusive?	Yes
Arm title	Ibrexafungerp

Arm description:

The study consisted of a screening visit, a baseline visit on Day 1 (the screening and baseline visits may have occurred on the same day), a TOC visit on Day 11 (± 3 days or Day 8 to Day 14), and a FU visit on Day 25 (± 4 days).

Arm type	Experimental
Investigational medicinal product name	Ibrexafungerp
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Ibrexafungerp 150-mg tablets administered orally as 2 tablets (300 mg) BID for 1 day.

Arm title	Placebo

Arm description:

The placebo product matching ibrexafungerp was supplied as a tablet matching the size and appearance of the active tablet. The tablet formulation contained silicified microcrystalline cellulose, crospovidone, mannitol, colloidal silicon dioxide, magnesium stearate (nonbovine), and butylated hydroxyanisole.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Oral ibrexafungerp matching placebo BID for 1 day.

Number of subjects in period 1	Ibrexafungerp	Placebo
Started	298	151
Completed	246	102
Not completed	52	49
Adverse event, non-fatal	3	-
Other	48	47
Lost to follow-up	1	2

Baseline characteristics

Reporting groups	
Reporting group title	Ibrexafungerp
Reporting group description:	
The study consisted of a screening visit, a baseline visit on Day 1 (the screening and baseline visits may have occurred on the same day), a TOC visit on Day 11 (± 3 days or Day 8 to Day 14), and a FU visit on Day 25 (± 4 days).	
Reporting group title	Placebo
Reporting group description:	
The placebo product matching ibrexafungerp was supplied as a tablet matching the size and appearance of the active tablet. The tablet formulation contained silicified microcrystalline cellulose, crospovidone, mannitol, colloidal silicon dioxide, magnesium stearate (nonbovine), and butylated hydroxyanisole.	

Reporting group values	Ibrexafungerp	Placebo	Total
Number of subjects	298	151	449
Age categorical Units: Subjects			
Adults (18-64 years)	296	149	445
From 65-84 years	2	2	4
Age continuous Units: years			
median	33	32	
full range (min-max)	18 to 67	18 to 66	-
Gender categorical Units: Subjects			
Female	298	151	449
Male	0	0	0

Subject analysis sets	
Subject analysis set title	Intent-to-treat (ITT) set
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
All randomized subjects who signed the ICF and received at least 1 dose of study drug.	
Subject analysis set title	Safety set
Subject analysis set type	Safety analysis
Subject analysis set description:	
All randomized subjects who received at least 1 dose of study drug and who had at least 1 postbaseline evaluation.	
Subject analysis set title	Modified intent-to-treat (mITT) set
Subject analysis set type	Modified intention-to-treat
Subject analysis set description:	
All randomized subjects who had a positive culture for Candida species at baseline, a diagnosis of symptomatic AVVC at baseline and received at least 1 dose of study drug.	

Reporting group values	Intent-to-treat (ITT) set	Safety set	Modified intent-to-treat (mITT) set
Number of subjects	449	449	272

Age categorical Units: Subjects			
Adults (18-64 years)	445	445	270
From 65-84 years	4	4	2
Age continuous Units: years median full range (min-max)			
Gender categorical Units: Subjects			
Female	449	449	272
Male	0	0	0

End points

End points reporting groups

Reporting group title	Ibrexafungerp

Reporting group description:

The study consisted of a screening visit, a baseline visit on Day 1 (the screening and baseline visits may have occurred on the same day), a TOC visit on Day 11 (± 3 days or Day 8 to Day 14), and a FU visit on Day 25 (± 4 days).

Reporting group title	Placebo

Reporting group description:

The placebo product matching ibrexafungerp was supplied as a tablet matching the size and appearance of the active tablet. The tablet formulation contained silicified microcrystalline cellulose, crospovidone, mannitol, colloidal silicon dioxide, magnesium stearate (nonbovine), and butylated hydroxyanisole.

Subject analysis set title	Intent-to-treat (ITT) set
Subject analysis set type	Intention-to-treat

Subject analysis set description:

All randomized subjects who signed the ICF and received at least 1 dose of study drug.

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

Subject analysis set description:

All randomized subjects who received at least 1 dose of study drug and who had at least 1 postbaseline evaluation.

Subject analysis set title	Modified intent-to-treat (mITT) set
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

All randomized subjects who had a positive culture for Candida species at baseline, a diagnosis of symptomatic AVVC at baseline and received at least 1 dose of study drug.

Primary: Clinical Outcome at the TOC Visit (mITT)

End point title	Clinical Outcome at the TOC Visit (mITT)

End point description:

The percentage of subjects with clinical cure (complete resolution of signs and symptoms) at the TOC visit, was conducted on the mITT set using a CMH test for ibrexafungerp versus placebo.

End point type	Primary

End point timeframe:

At TOC visit

End point values	Ibrexafungerp	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	188	84		
Units: percent				
number (not applicable)				
Clinical cure, n (%)	63.3	44		
Clinical failure, n (%)	36.7	56		

Statistical analyses

Statistical analysis title	Statistical analysis
Statistical analysis description: Cochran-Mantel-Haenszel (CMH) test has been used for the statistical analysis.	
Comparison groups	Ibrexafungerp v Placebo
Number of subjects included in analysis	272
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.007
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk ratio (RR)
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.073
upper limit	1.783

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events have been recorded at baseline visit on Day 1, a TOC visit on Day 11 (± 3 days or Day 8 to Day 14), and a FU visit on Day 25 (± 4 days).

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	21.1

Reporting groups

Reporting group title	Ibrexafungerp

Reporting group description:

The study consisted of a screening visit, a baseline visit on Day 1 (the screening and baseline visits may have occurred on the same day), a TOC visit on Day 11 (± 3 days or Day 8 to Day 14), and a FU visit on Day 25 (± 4 days).

Reporting group title	Placebo

Reporting group description:

The placebo product matching ibrexafungerp was supplied as a tablet matching the size and appearance of the active tablet. The tablet formulation contained silicified microcrystalline cellulose, crospovidone, mannitol, colloidal silicon dioxide, magnesium stearate (nonbovine), and butylated hydroxyanisole.

Serious adverse events	Ibrexafungerp	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 298 (0.34%)	1 / 151 (0.66%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Infections and infestations			
Gastrointestinal bacterial infection			
subjects affected / exposed	1 / 298 (0.34%)	0 / 151 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Diabetic ketoacidosis			
subjects affected / exposed	0 / 298 (0.00%)	1 / 151 (0.66%)	
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	Ibrexafungerp	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	58 / 298 (19.46%)	14 / 151 (9.27%)	
Nervous system disorders			
Headache			
subjects affected / exposed	22 / 298 (7.38%)	11 / 151 (7.28%)	
occurrences (all)	22	11	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	28 / 298 (9.40%)	1 / 151 (0.66%)	
occurrences (all)	28	1	
Nausea			
subjects affected / exposed	25 / 298 (8.39%)	4 / 151 (2.65%)	
occurrences (all)	25	4	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
23 October 2019	The total number of subjects randomized was increased (to an estimated maximum of 470 subjects) to achieve the required 282 evaluable subjects due to higher than anticipated rate of "no growth" samples at baseline (above 20%).

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported