Efficacy and Safety of Oral Ibrexafungerp in the Treatment of Vulvovaginal Candidiasis: A Phase 3 Study (VANISH-306)

R. Sobel[1], N. Azie[2], D. Angulo[2]

[1]Sidney Kimmel Medical College at Thomas Jefferson University; [2]SCYNEXIS, Inc.

ACOG VIRTUAL Annual Clinical and Scientific Meeting April 30–May 2, 2021

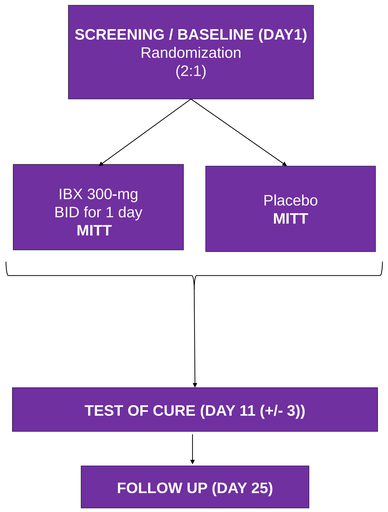
BACKGROUND

Vulvovaginal candidiasis (VVC) affects 75% of women at least once in their lifetime. Current approved therapies are all azoles with several topical and only one oral treatment option available. There has been no new therapies approved for treatment in over 25 year. Ibrexafungerp (IBX) is a novel oral triterpenoid antifungal in development for the treatment of vulvovaginal candidiasis. IBX is fungicidal with broad activity against *Candida* spp., including fluconazole-resistant strains. IBX is currently in regulatory review with the FDA. We present the second of two phase 3 studies evaluating the safety and efficacy of oral IBX in VVC, VANISH-306

METHODS

VANISH-306, a multicenter, randomized, double-blind study was conducted in the U.S. and Bulgaria, with patients randomized to oral IBX 300 mg BID for one day or matching placebo in a 2:1 ratio. Eligible patients had to present with an episode of VVC with vaginal signs and symptoms (VSS) score ≥4 (moderate to severe VVC). Primary efficacy population was the modified-intent-to-treat (mITT), patients with culture confirmed *Candida* spp. infection at baseline who received at least one dose of study treatment. The primary endpoint was Clinical Cure, defined as complete resolution (score of 0) of all VSS at the Day-10 test-of-cure (TOC) visit. This endpoint is more stringent than previous studies of VVC where a VSS of ≤2 has been the primary endpoint for determining clinical cure of VVC.

Figure 1: Oral Ibrexafungerp Study Design



Primary Objectives:

To evaluate the efficacy of oral IBX versus placebo in subjects with VVC by comparing the clinical outcomes of ibrexafungerp and placebo

Secondary Objectives:

To evaluate the efficacy of oral IBX versus placebo in subjects with VVC based on mycological and clinical outcomes

- To evaluate the safety and tolerability of oral IBX versus placebo in subjects with VVC

CONCLUSIONS

These results show that IBX achieved the primary endpoint and was statistically superior to placebo. If approved, IBX will be the first new treatment approved for VVC in over 20 years, providing the first non-azole option of women with VVC.

RESULTS

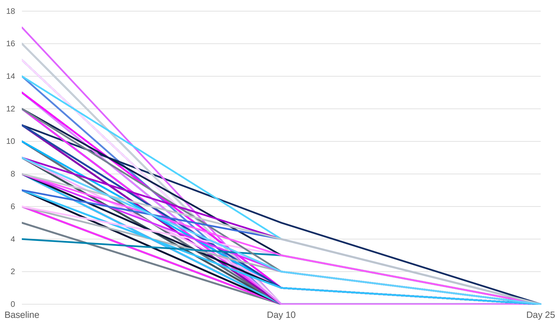
VANISH-306 study included 272 subjects in the mITT population. Most of the patients (91.9%) had severe VVC (VSS≥7). The demographic of the study are shown in Table 1.

Table 1: VANISH-306 Study Demographics

MITT	IBX 300mg BID (N=188) n (%)	PLACEBO (N=84) n (%)
Age , median (Min,Max)	32 (18, 65)	32 (18, 65)
Race % White | % Black or African American	81.4 | 18.1	82.1 | 17.9
Percent enrolled in USA | Bulgaria	35.1 | 64.9	42.9 |57.1
Body Mass Index (kg/m^2) Median (Min, Max) Percent BMI > 35	24.14 (15.43, 58.85) 11.2	24.46 (17.44, 55.08) 17.9
Baseline pathogen (more than 1 baseline isolate was reported in some cases)		
Candida albicans	165 (87.8)	76 (90.5)
Candida glabrata	20 (10.6)	8 (9.5)
Candida tropicalis	3 (1.6)	3 (3.6)

The majority of IBX patients achieved a VSS score of 0 at day 10, but there were additional patients who achieved a Symptom score of 0 at day 25 as illustrated in Figure 2. The mean reduction in VSS for subjects who didn't achieve a VSS=0 by day 10 was 7.3. (9.2 at baseline to 1.9 at day 10). Previous VVC studies have used a VSS score ≤2 as the clinical cure endpoint.

Figure 2: Individual IBX Patient VSS Scores: All Patients with Resolution of Symptoms at Day 25



A total of 139 IBX subjects (73.9%) achieved Symptom Resolution on Day 25

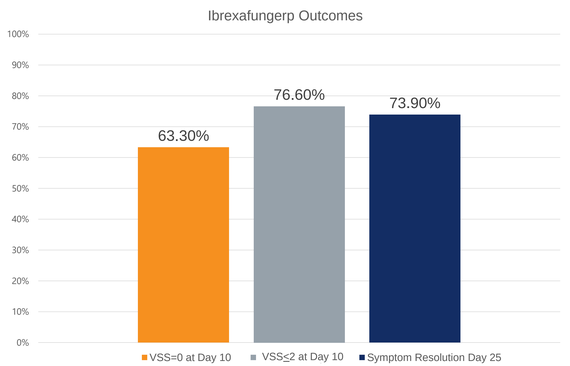
IBX was statistically superior to placebo in the primary endpoint of clinical cure at the TOC visit on Day 10, along with clinical improvement and mycological eradication at TOC.

Table 2. : Outcomes at TOC (Day 10)

MITT	IBX 300mg BID (N=188) n (%)	PLACEBO (N=84) n (%)	RR (95 % CI) P value
Clinical Cure (Complete resolution of signs and symptoms [VSS scale =0])	119 (63.3)	37 (44.0)	1.38 (1.07, 1.78) 0.007
Clinical Improvement (VSS≤1)	136 (72.3)	46 (54.8)	1.28 (1.04, 1.57) 0.010
Mycological Eradication	110 (58.5)	25 (29.8)	1.85 (1.33, 2.58) <0.001

IBX demonstrated sustained efficacy with a higher # of subjects with Symptom Resolution at Day 25, 73.9% compared to Day 10 outcomes,63.3%. Additionally, subjects with a VSS ≤2 at Day 10 was 76.6%.

Figure 3: Ibrexafungerp outcomes at Day 10 and Day 25



In the Safety population the # of Treatment-Emergent Adverse Events were similar with IBX (33.2%) and PBO (29.1%). No Serious adverse events (SAE) were related to drug.

Table 3: Overall Adverse Events

Safety Population Number of Subjects with:	IBX 300mg BID (N=298) n (%)	PLACEBO (N=151) n (%)
Treatment-Emergent Adverse Event (TEAE)	99 (33.2)	44 (29.1)
Serious Adverse Event (SAE)	1 (0.3) (bacterial GI infection)	1 (0.7) (DKA) display full name
Related – SAE	0	0
TEAE leading to study discontinuation	0	0

Gastrointestinal (GI) adverse events(AEs) were the most common treatment related AEs and they were more frequently reported in the IBX group. The majority of the GI AEs were mild to moderate with most lasting 1 day, only one subject in each group (IBX and PBO) reported a severe GI adverse event (nausea).

Table 4: Gastrointestinal Adverse Events

SAFETY Population	IBX 300mg BID (N=298) n (%)	PLACEBO (N=151) n (%)
GI Adverse Events	65 (21.8)	11 (7.3)
Diarrhea	28 (9.4)	1 (0.7)
Mild | Moderate | Severe	24 | 4 | 0	1 | 0 | 0
Nausea	25 (8.4)	5 (3.3)
Mild | Moderate | Severe	22 | 2 | 1	2 | 2 | 1
Abdominal pain	8 (2.7)	2 (1.3)
Mild | Moderate | Severe	8 | 0 | 0	2 | 0 | 0

For additional information contact SCYNEXIS at info@scynexis.com.