



# A Phase 2b, Dose-Finding Study Evaluating Oral Ibrexafungerp in Moderate to Severe Acute Vulvovaginal Candidiasis (DOVE)

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SCYNEXIS

# Forward-Looking Statements

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# Disclosures

- Nkechi Azie, MD is an employee and shareholder of SCYNEXIS, Inc

# Ibexafungerp (formerly SCY-078)

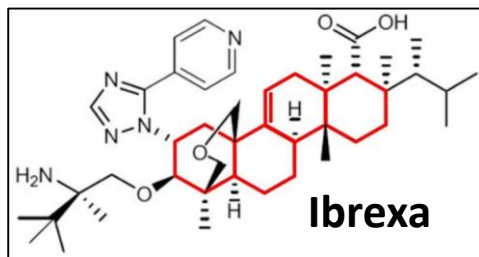
- New WHO INN designation
  - SCY-078, Triterpenoid class provided new stem
    - **Fungal Triterpenoid**

“fungerp”

# Ibrexafungerp

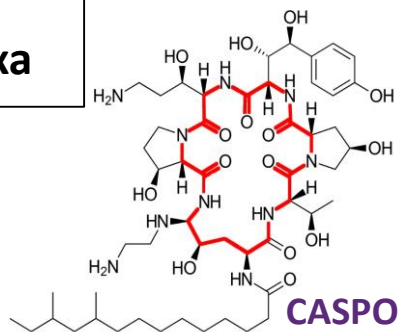
## A Novel Triterpenoid Antifungal

Novel Glucan Synthase Inhibitor (GSI)



Structurally distinct  
from other GSIs  
(echinocandins)

- Different enzyme-drug interaction  
→ lower impact of common FKS mutations
- Oral bioavailability



Key Attributes

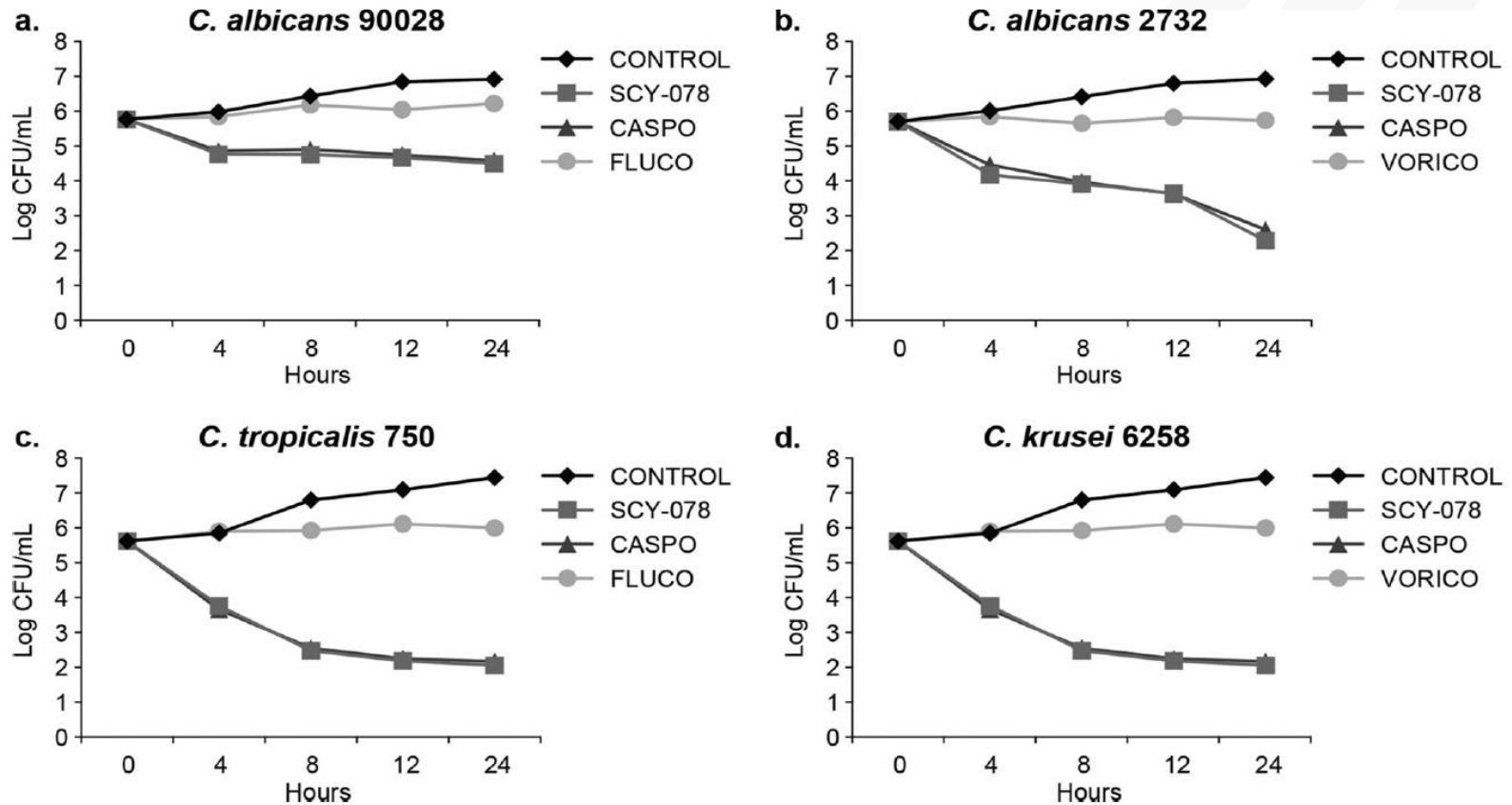
- Activity against: *Candida* spp.; *Aspergillus* spp.; *Pneumocystis* spp.; Endemic fungi
- Active against azole-R and Candin-R strains
- Oral formulations
- Enhanced activity at low PH
- Large tissue distribution (Human  $V_{dss} > 8$  L/kg)
- No Preclinical fetal Toxicity
- Favorable safety profile > 700 exposed
- Low risk of drug-drug Interactions

# *In Vitro* Activity of Ibrexafungerp vs. Fluconazole-Resistant Strains

Ibrexafungerp displayed activity against fluconazole resistant *Candida spp.* similar to that observed against Wild-Type

<i>Candida glabrata</i> (N) UAB study	Ibrexafungerp (mcg/mL) [MIC <sub>50</sub> (MIC <sub>90</sub> )]
Fluconazole susceptible (N=137)	0.5 (0.5)
Fluconazole resistant (N=162)	0.5 (0.5)

# Ibrexafungerp is Fungicidal vs. *Candida* spp.



**FIG 2** Time-kill curves for SCY-078, caspofungin (CASPO), fluconazole (FLUCO), and voriconazole (VORICO) at 4 times the MIC<sub>80</sub> against the indicated *Candida* species and a control. 2732, MYA-2732.

- Fluconazole is fungistatic against *Candida* spp. = inhibits the growth but doesn't kill the fungi

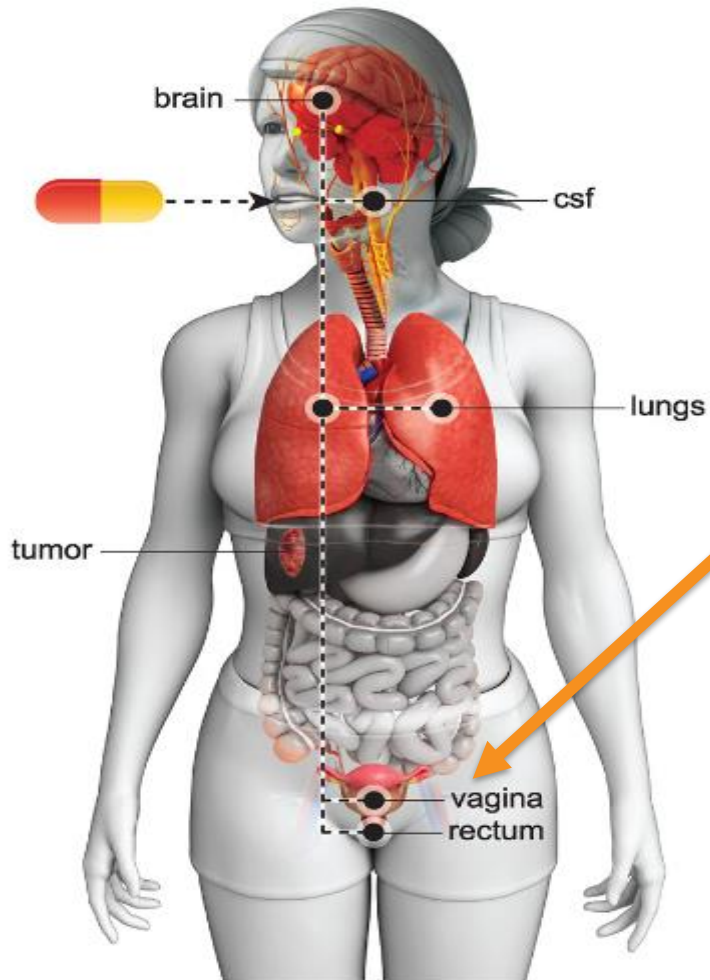
# *In Vitro* Activity is Enhanced at Low (Vaginal) pH

	pH level		
	7.0	5.72	4.5
<i>C.glabrata</i> MIC <sub>50</sub> (mg/L)			
<b>Ibexafungerp</b>	0.5 - 1	0.5	<b>0.031 - 0.063</b>
<b>Fluconazole</b>	0.5 - 2	2 - 16	<b>1 - 16</b>
<i>C.albicans</i> MIC <sub>50</sub> (mg/L)			
<b>Ibexafungerp</b>	0.125 - 0.5	0.125-0.25	0.16-0.031
<b>Fluconazole</b>	<0.125 - 1	<0.125-1	0.25 - 8

Ten strains each of vaginal *Candida* isolates from a recent clinical trial were tested



# Vaginal Tissue Concentration



## Plasma to Genital Tissue Ratio:

Fluconazole – 1:1

Ibrexafungerp – **1:9**

**Highest Tissue Concentration among antifungals reported.**

**Figure 1** Schematic of relevant sites of action for assessing drug exposure, including the brain, cerebrospinal fluid (csf), lung, solid tumor, cervicovaginal fluid, and colorectal tissue.

# Completed Studies

Over 500 subjects received at least one dose of ibrexafungerp in Phase 1 studies and Phase 2 studies.

- Sixteen Phase I studies completed including
  - SAD; MAD studies
  - Food effect
  - Age and Gender studies
  - DDI
- Three phase 2 studies completed
  - 2 in **VVC**
  - 1 in Invasive Candidiasis

**A Phase 2, Multicenter, Randomized, Double-Blind, Double-Dummy, Active-Controlled, Dose-Finding Study to Compare the Safety and Efficacy of Oral Ibrexafungerp vs. Oral Fluconazole in Subjects with Acute Vulvovaginal Candidiasis (DOVE)**

# Ibrexafungerp- 204 (DOVE): Study Objectives

- **Primary Objectives:**
  - To identify the recommended dose of oral ibrexafungerp in subjects with moderate to severe acute vulvovaginal candidiasis (aVVC) by comparing the efficacy of different dose levels and dosing regimens of oral ibrexafungerp
- **Secondary Objectives:**
  - To evaluate the efficacy of oral ibrexafungerp in subjects with aVVC based on mycological and clinical outcomes
  - To evaluate the safety and tolerability of different dose levels and dosing regimens of oral ibrexafungerp in subjects with aVVC

# DOVE Study Design

## Key Inclusions:

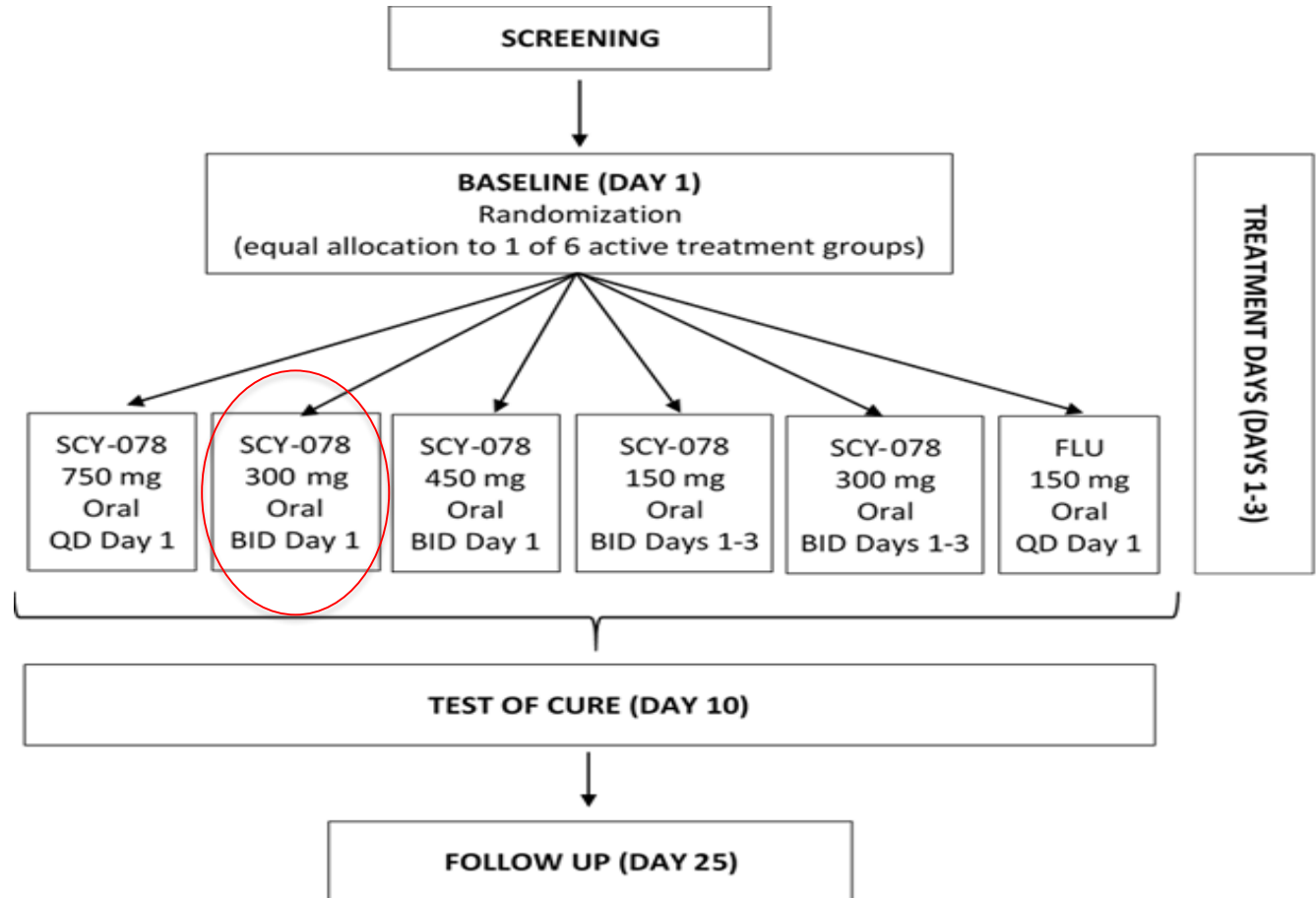
✓ Moderate to severe VVC (signs and symptoms of  $\geq 7$ )

✓ KOH +

✓ pH  $\leq 4.5$

~30 patients per arm

Primary population for analysis mITT = Culture-confirmed VVC



# DOVE Study Design / Demographics

- **Key Endpoints:**

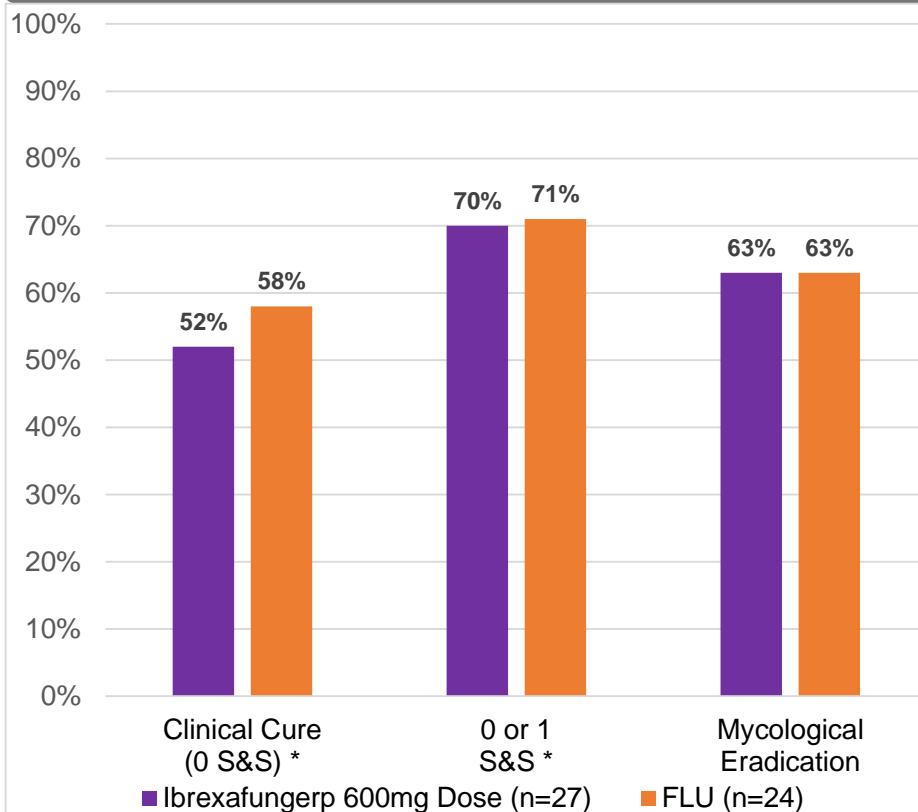
- At Test-of-Cure (T.O.C.) and Follow-up visit (F.U.)
  - Clinical Cure (Signs and Symptoms = 0)
  - Significant improvement (Signs and Symptoms = 0 or 1)
  - Mycological eradication (negative culture for yeast)
- Use of rescue antifungal treatment
- Safety and tolerability

- **186 subjects enrolled**

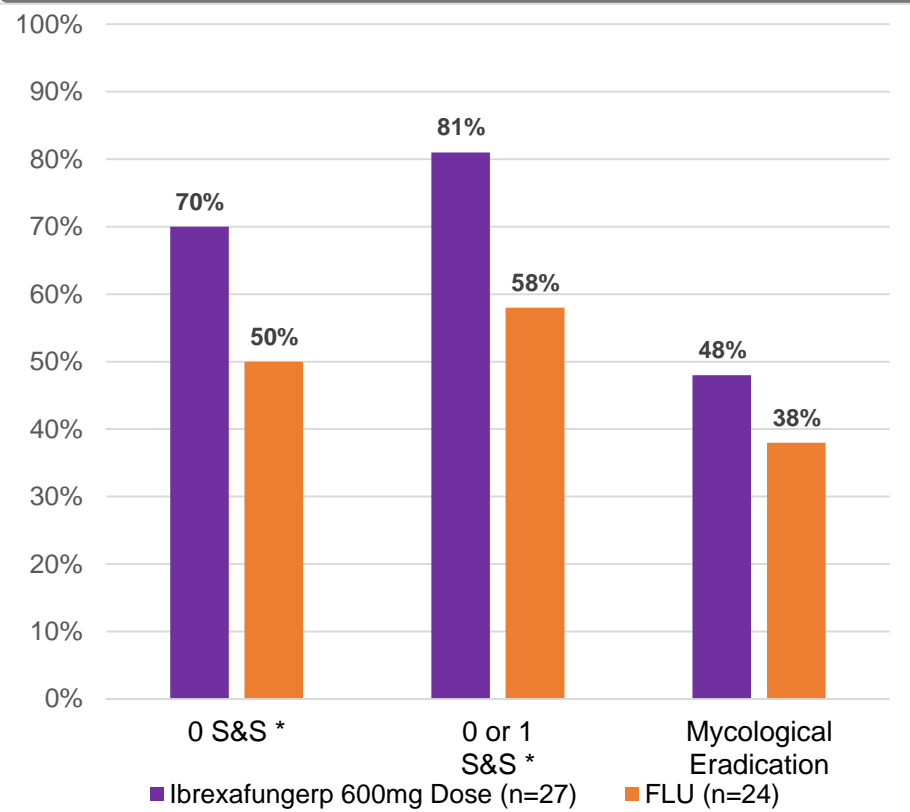
- 153 with culture-confirmed VVC, (mITT)
- Median age 32 years
- Race: White 59%, Black or African American 39%, Other 2%

# DOVE Study Key Efficacy Results Ibrexafungerp 600mg Dose (mITT)

Day 10 (Test-of-Cure)



Day 25 (Follow-up)

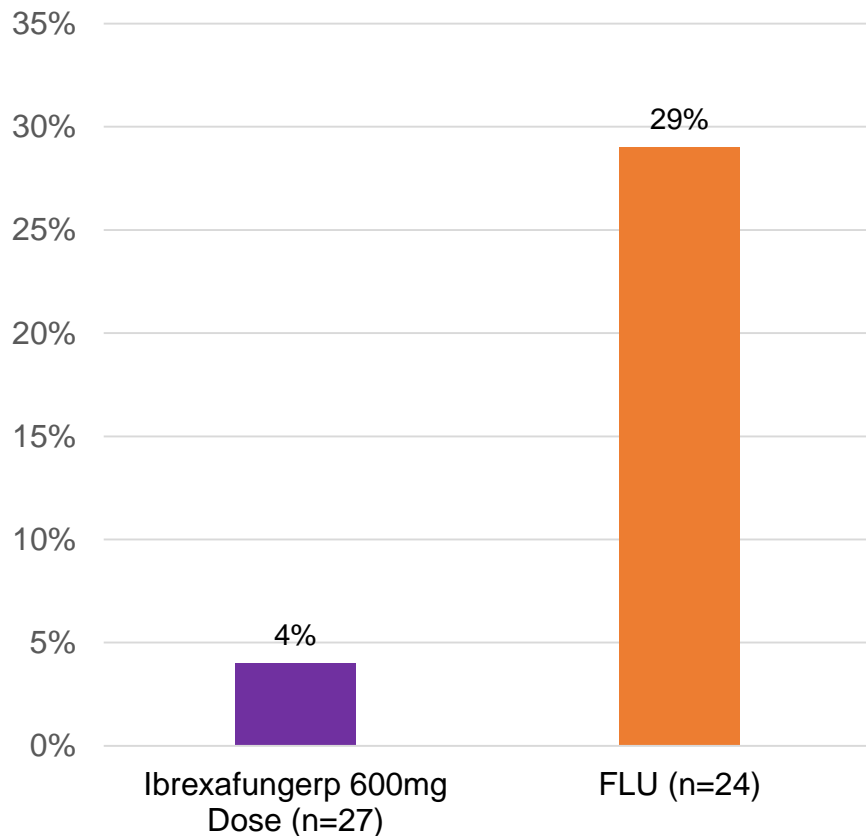


Results based on mITT population | \* No rescue antifungal use.

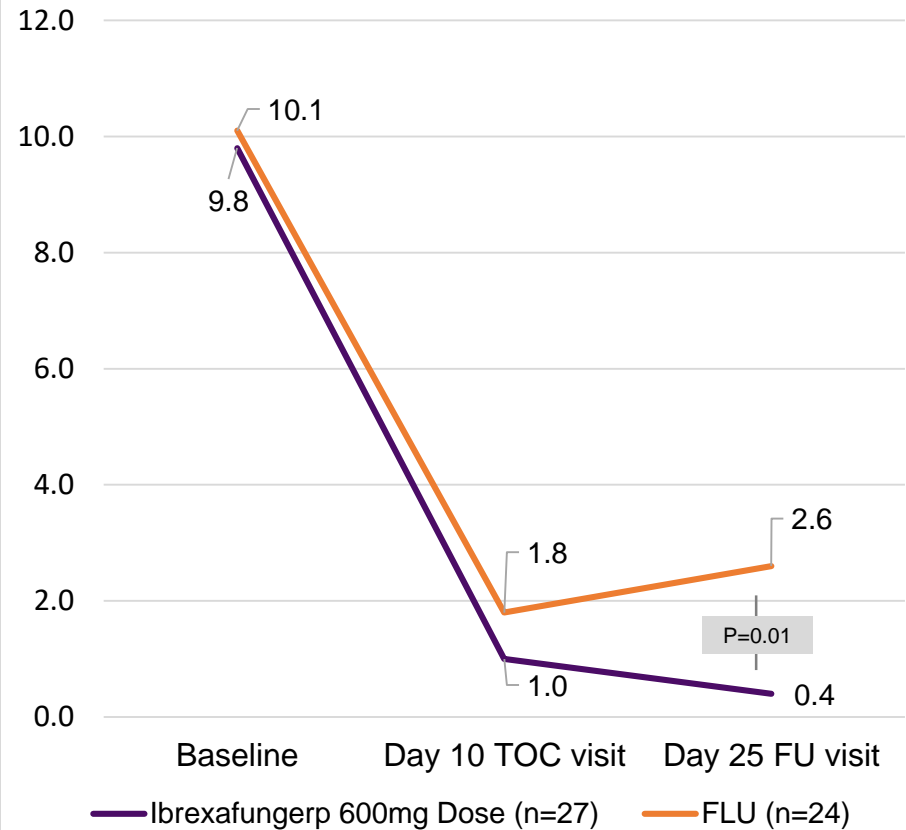
Signs and Symptoms [S&S] score is a composite endpoint of the subject's reported symptoms (burning, itching and irritation) and the investigator's assessed signs (swelling, redness and excoriations). Each sign and symptom can be absent (0), mild (1), moderate (2) or severe (3).

# DOVE Study Additional Efficacy Results Ibrexafungerp 600mg Dose (mITT)

DOVE - % of Required Rescue Therapy (mITT)



DOVE- Mean Signs and Symptoms Score



*P* value based on change from baseline score mean difference between Ibrexafungerp 600mg and FLU.

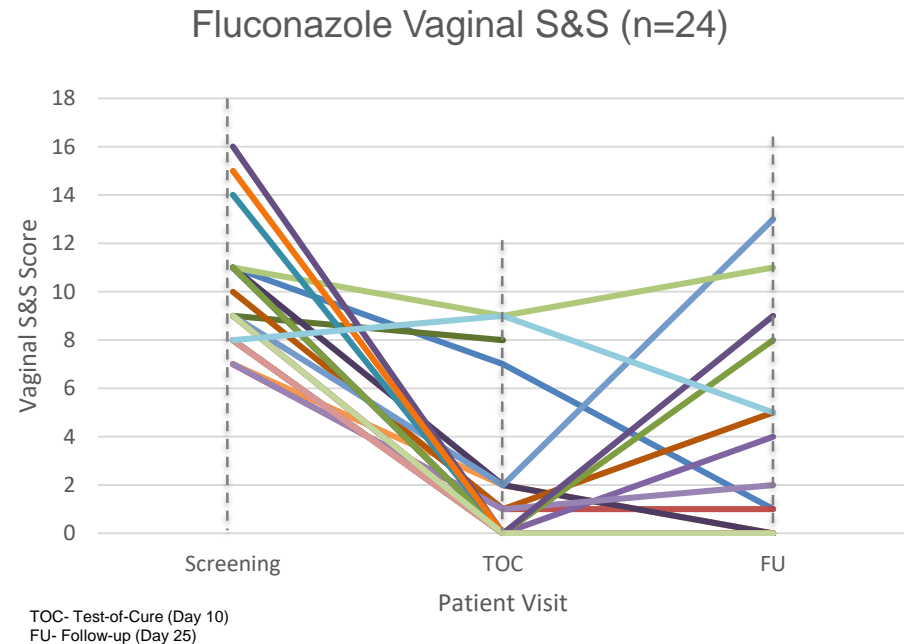
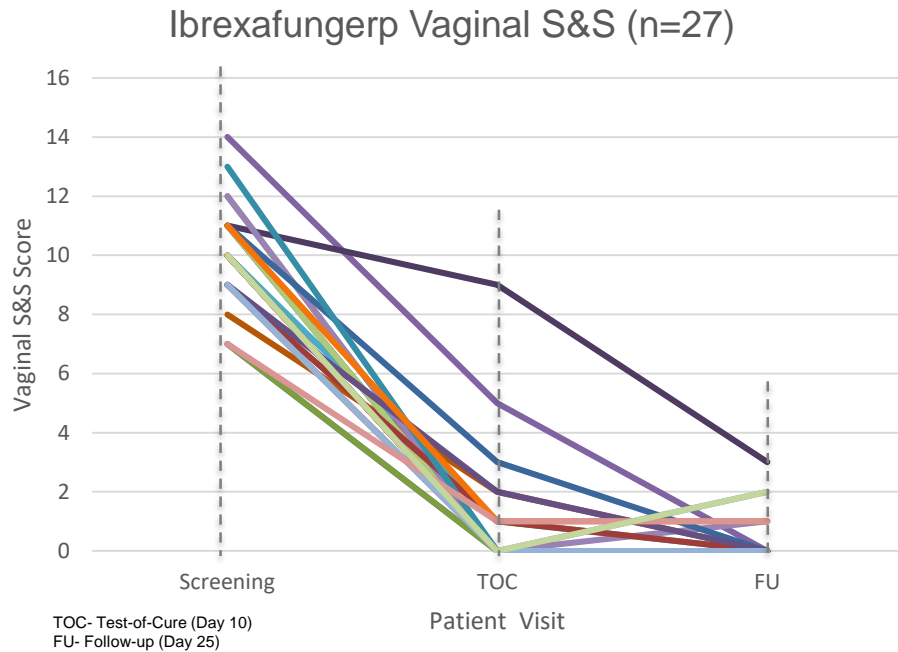


# Profile of Patients Requiring Rescue Therapy in DOVE Study

	Patient	<i>Candida spp.</i>	Timing of Rescue Medication	Rescue Antifungal Therapy
Ibrexafungerp 1 patient N=27 (4%)	IBX Pt. 1	<i>C. albicans</i>	FU	Oral Fluconazole
	FLU Pt. 1	<i>C. glabrata</i>	TOC	Topical Terconazole
Fluconazole 7 patients N=24 (29%)	FLU Pt. 2	<i>C. albicans</i>	Between TOC and FU	Oral Fluconazole
	FLU Pt. 3	<i>C. albicans</i>	Between TOC and FU	Oral Fluconazole Topical Clotrimazole
	FLU Pt. 4	<i>C. albicans</i>	FU	Oral Fluconazole Topical Terconazole
	FLU Pt. 5	<i>C. albicans</i>	FU	Oral Fluconazole
	FLU Pt. 6	<i>C. kefyr</i> , <i>C. tropicalis</i>	FU	Oral Fluconazole
	FLU Pt. 7	<i>C. albicans</i>	FU	Oral Fluconazole

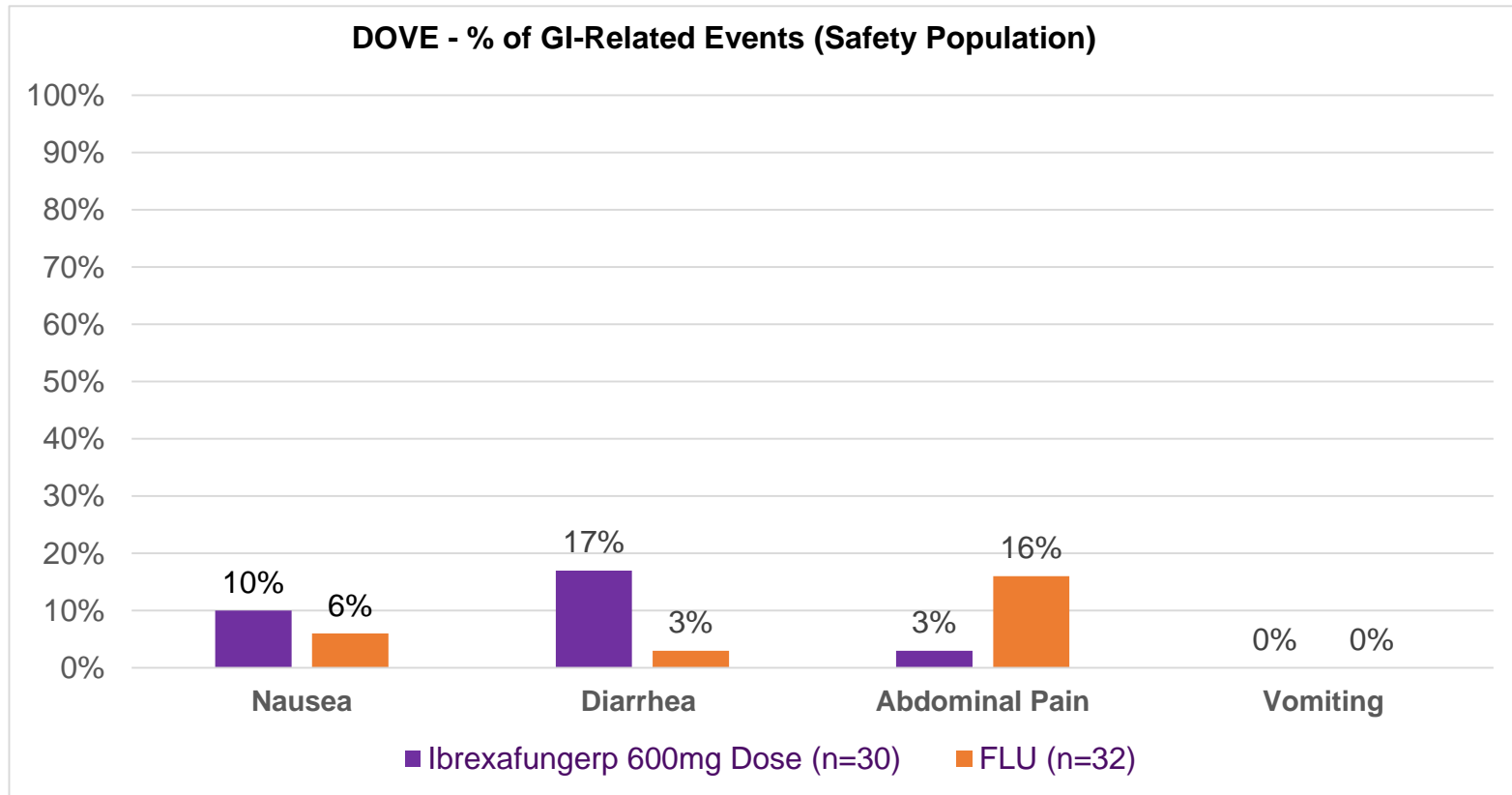
**Almost all of the failures received Oral FLU**

# DOVE Study: Individual Patient Vaginal S&S Score during Study Period



Vaginal Signs & Symptoms	Ibrexafungerp	Fluconazole
Mean score of patients with S&S score >0 at Follow-up visit	1.7	5.9

# DOVE Study Key Tolerability Results Ibrexafungerp 600mg Dose

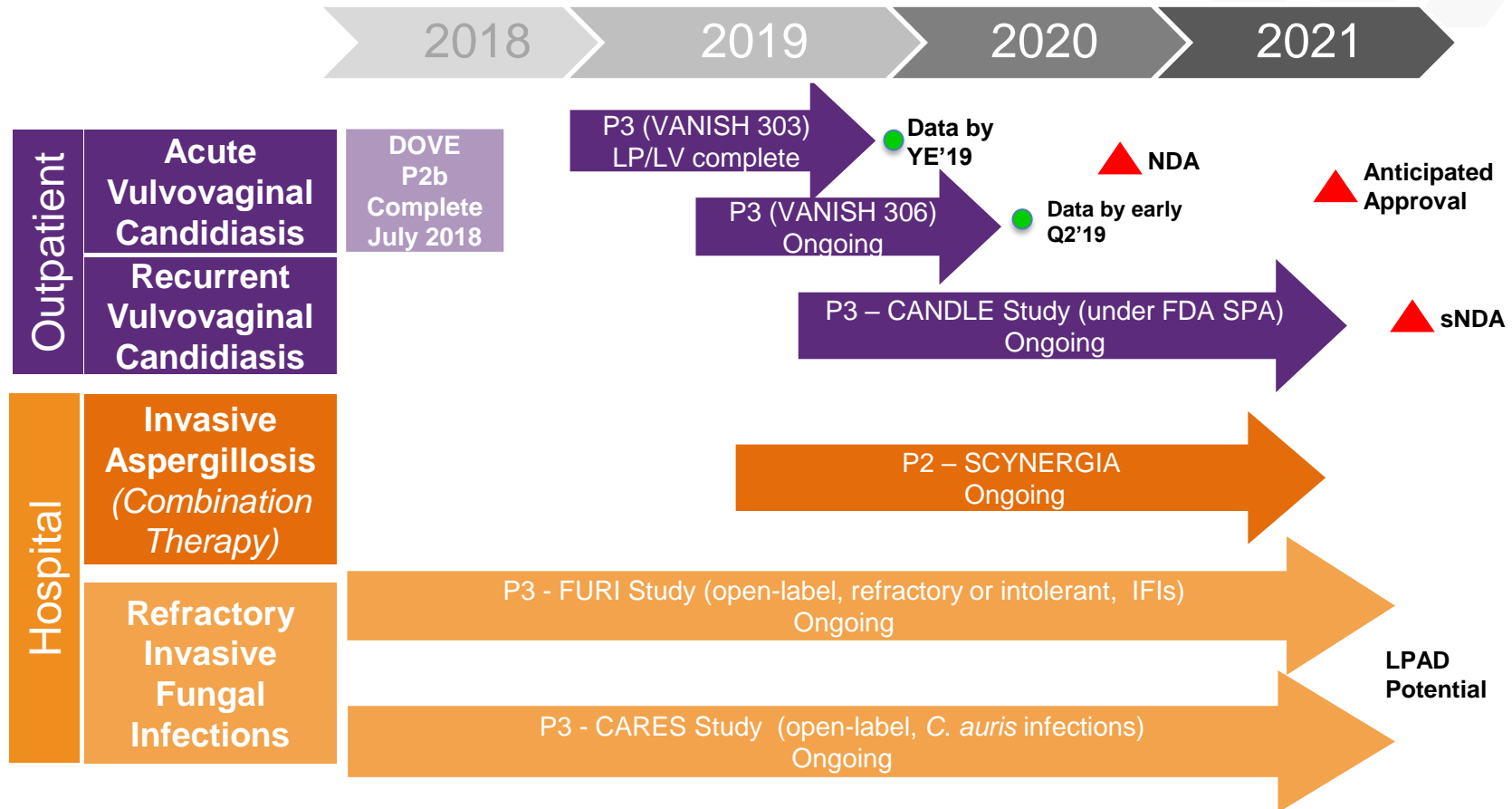


- Most Adverse Events were mild to moderate and lasting 1 day
- No Serious Adverse Events
- No Discontinuations

# DOVE Study Key Results

- All six arms showed evidence of antifungal activity.
- The 1-day ibrexafugerp dose regimens overall comparable efficacy to 3-days dose regimens.
- The 300mg BID for 1 day dose showed the best combination of clinical efficacy and tolerability.
- This dose regimen was selected for Phase 3 program

# Ibrexafungerp: Ongoing Programs / Timing



Other potential oral indications: Prophylaxis, Chronic Fungal Infections, Invasive Candidiasis



*Thank you*