A Phase 2b, Dose-Finding Study Evaluating Oral Ibrexafungerp in Vulvovaginal Candidiasis (DOVE)

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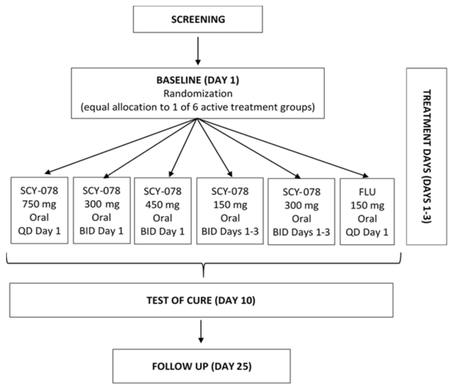
BACKGROUND

Ibrexafungerp (formerly SCY-078) is a novel IV/oral antifungal agent currently in development for the treatment of invasive and mucocutaneous fungal infections. ibrexafungerp has broad activity against *Candida* spp., including azole-resistant strains. A phase 2b, dose-finding study was conducted to evaluate the safety and efficacy of oral ibrexafungerp in subjects with moderate to severe vulvovaginal candidiasis (VVC).

METHODS

Randomized, double-blind, double-dummy study including 5 oral ibrexafungerp treatment groups (750mg-QD 1 day, 300mg-BID 1 day, 450mg-BID 1 day, 150mg-BID for 3 days, and 300-BID for 3 days) and an active comparator (oral fluconazole [FLU] 150mg single dose). (Figure 1) Subjects were evaluated at Day-10 and Day-25 for clinical cure and mycological eradication.

Figure 1: Oral Ibrexafungerp dosing regimens



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.

RESULTS

153 subjects with culture-confirmed VVC comprised the primary population for analysis (mITT). We compared the 1-day dose regimens (750 mg QD, 300 mg BID and 450 mg BID) versus the 3-day dose regimens (150 mg BID and 300 mg BID): the clinical outcomes between the two groups were similar. Of the 1-day dose regimens, the ibrexafungerp dose of 300mg BID for 1 day (600mg-dose) showed the best combination of clinical efficacy and tolerability. At Day-10, clinical cure, defined as complete resolution of all signs and symptoms, was observed in 14 of 27 (52%) subjects in the ibrexafungerp 600mg-dose arm and 14 of 24 (58%) subjects in the FLU arm. At Day-25, the rate of clinical cure in the ibrexafungerp 600mg-dose arm reached 70% compared to 50% in the FLU arm. At Day-10 and Day-25, the mycological eradication rates were 63% and 48% for the ibrexafungerp 600mg-dose arm and 63% and 38% for the FLU arm.(Figure 2 and 3)

Figure 2.: Efficacy at TOC (Day10)

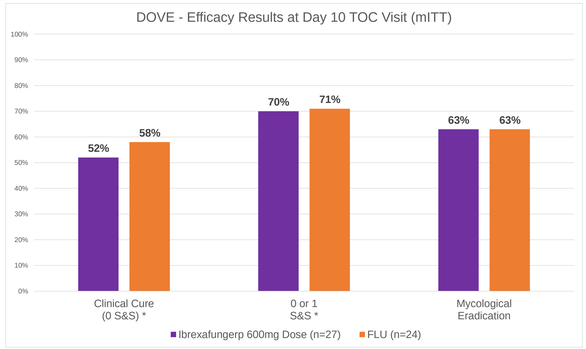
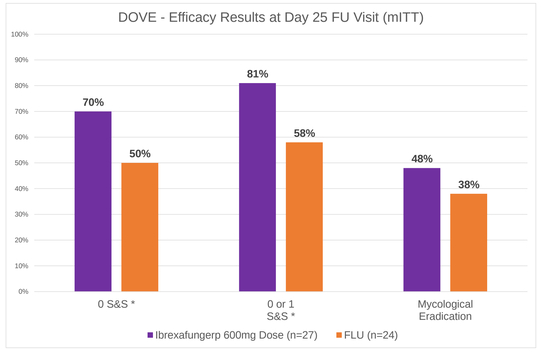


Figure 3: Efficacy at FU visit (Day25)



Additional analysis showed that patients receiving ibrexafungerp required less rescue therapy during the study, 4% vs 29% for fluconazole (Figure 4) and ibrexafungerp signs and symptoms score (S&S) continued to improve over the 25 days whereas fluconazole had an improved S&S at day 10, but saw a rise in the score at FU visit (day 25) (Figure 5).
At the 300 mg BID dose, the most common adverse events were GI related, with diarrhea being the most common at 10% for ibrexafungerp and abdominal pain at 16% for fluconazole (Figure 6) .

**Signs and Symptoms [S&S] score defined as 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, mild, moderate or severe, with a corresponding score from 0 to 3. The total composite scale goes from 0 to 18 points.*

Figure 4: % patient requiring rescue therapy

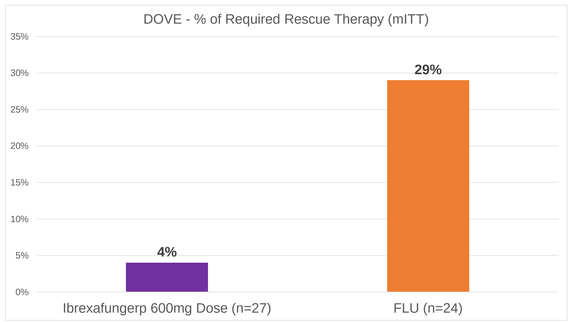


Figure 5: Signs and Symptoms Score from baseline to FU visit

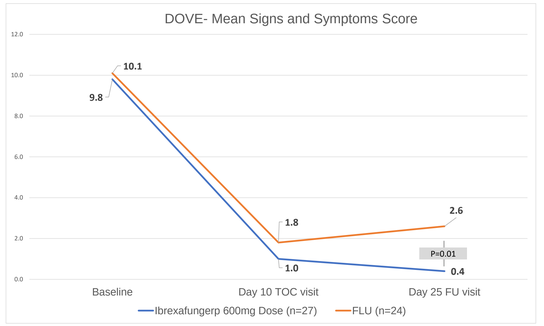
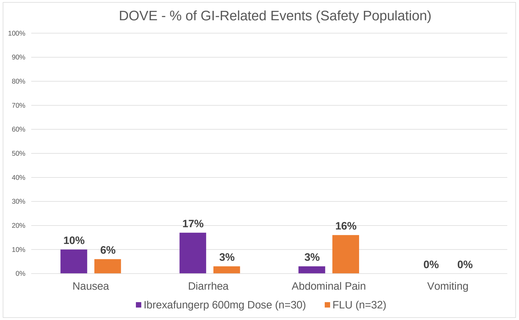


Figure 6: GI Adverse Events The most common AEs were mild nausea and diarrhea.



CONCLUSIONS

These results support the selection of ibrexafungerp 600mg-dose for Phase 3 registration studies in VVC.

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