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# Susceptibility Testing of SCY-078 Against *Candida* Isolates Obtained from a Clinical Study of Oral SCY-078 vs. Oral Fluconazole in Subjects with Moderate to Severe Vulvovaginal Candidiasis Demonstrates no Resistance Development


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## INTRODUCTION & PURPOSE

SCY-078 is a novel intravenous and oral triterpenoid antifungal in clinical development for the treatment of invasive and mucocutaneous fungal infections. It has broad-spectrum activity against both *Candida and Aspergillus*.

SCY-078, a glucan synthase inhibitor with fungicidal activity against *Candida* spp., exhibits an extensive tissue distribution, making it a suitable candidate for the treatment of vulvovaginal candidiasis (VVC).

The purpose of this study was to evaluate the safety and efficacy of oral SCY-078 in subjects with moderate to severe VVC. Here we present the result of the *in vitro* activity of SCY-078 against clinical isolates obtained from subjects enrolled in this proof-of-concept study.

## METHODS: STUDY DESIGN

Subjects were randomized in a 1:1:1 ratio to one of 3 treatment arms

- Oral SCY-078 loading dose (1250mg), followed by 750mg QD for 2 days
- Oral SCY-078 loading dose (1250mg), followed by 750mg QD for 4 days
- Oral Fluconazole (FLU) 150mg for 1 day

Subjects were evaluated on Day 24 (test of cure visit) Day 60, Day 90 and 120 days (end of study). The analysis included:

- Clinical cure, mycological eradication, and therapeutic cure (defined as combination of clinical cure and mycological eradication)

Vaginal samples were collected at baseline (pre-treatment) and on Day 24, Day 60, Day 90 and Day 120 day for species identification and susceptibility testing

Determination of *Candida* sp. was done via API 20C AUX or growth pattern on CHROMagar®

Minimum inhibitory concentrations (MICs) for SCY-078 and fluconazole, were determined using CLSI M27-A3 methodology

## CLINICAL STUDY RESULTS

96 subjects were enrolled (IIT population), and 70 subjects had cultured-confirmed *Candida* spp. infection (per protocol population, PP).

**Efficacy Evaluation at Day 24 (per Protocol Population)**

| N<br>Rates % | SCY-078[b]<br>(n= 50) | Fluconazole<br>(n= 20) | Difference between SCY-078 vs. Fluconazole |
|---|---|---|---|
| Clinical Cure<br>Updated FDA Definition[a] | 35<br>*70%* | 11<br>*55%* | 15% |
| Mycological Eradication | 35<br>*70%* | 13<br>*65%* | 5% |

a Clinical cure defined as absence of all sign and symptoms
b Combined 3 days and 5 days dosing regimens

**Efficacy Evaluation at Month-4 (per Protocol Population)**

| N<br>Rates % | SCY-078[b]<br>(n= 50) | Fluconazole<br>(n= 20) | Difference between SCY-078 vs. Fluconazole |
|---|---|---|---|
| Relapse rate [a] | 2<br>*4%* | 3<br>*15%* | 11 % |
| Negative Culture | 37<br>*74%* | 12<br>*60%* | 14 % |

a Symptomatic and cultured-confirmed VVC episode requiring treatment
b Combined 3 days and 5 days dosing regimens

## BASELINE MYCOLOGY RESULTS

The majority of subjects presented with *C. albicans* (N=60 [86%]).
All of the baseline isolates were susceptible to SCY-078 and fluconazole.

| Organism | N | Microbiologic Outcome | SCY-078 (µg/mL) | Fluconazole (µg/mL) |
|---|---|---|---|---|
| *Candida albicans* | 60 | Range | 0.063 – 0.5 | ≤0.125 – 2 |
| | | $MIC_{50}$ | 0.25 | ≤0.125 |
| | | $MIC_{90}$ | 0.25 | 0.5 |
| | | Mode | 0.25 | ≤0.125 |
| *Candida glabrata* | 2 | Range | 0.5 | 0.5 - 2 |
| *Candida parapsilosis* | 2 | Range | 0.25 | 0.25 |

One subject each presented with *C. tropicalis and C. nivariensis.*
Four subjects had multiple *Candida spp.* identified at baseline: one with *C. albicans/C. glabrata* coinfection, one with *C. albicans/C. tropicalis* coinfection, one with *C. parapsilosis/C.krusei* coinfection, and one with *C. lusitaniae/C. krusei* coinfection.

## POST-BASELINE MYCOLOGY RESULTS

No significant differences in MICs were observed between baseline and post-treatment isolates during the 4-month follow up period.
The most common post-baseline isolate was *C. albicans.* The MICs of post-treatment *C. albicans* isolates by treatment arm are displayed below.

| Treatment Group | Post treatment *C. albicans* | Microbiologic Outcome | SCY-078 (µg/mL) | Fluconazole (µg/mL) |
|---|---|---|---|---|
| *SCY-078 (combined)* | 22 | Range | <0.031 – 0.25 | |
| | | $MIC_{50}$ | 0.25 | |
| | | $MIC_{90}$ | 0.25 | |
| | | Mode | 0.25 | |
| *Fluconazole* | 11 | Range | | <0.125 - 4 |
| | | $MIC_{50}$ | | <0.125 |
| | | $MIC_{90}$ | | 1 |
| | | Mode | | <0.125 |

No significant differences in MICs were observed between baseline and post-treatment isolates among subjects presenting with non-*albicans Candida* infections.

## CONCLUSION

The results of this study indicate that SCY-078 possesses potent activity against *Candida spp.* resulting in high mycological and clinical cure rates in VVC. The rate of mycological response after treatment with SCY-078 was maintained during the 4-month follow up and there was no development of resistance following treatment.