A Multicenter, Randomized, Evaluator Blinded, Active-Controlled Study to Evaluate the Safety and Efficacy of Oral SCY-078 vs. Oral Fluconazole in 96 Subjects with Moderate to Severe Vulvovaginal Candidiasis

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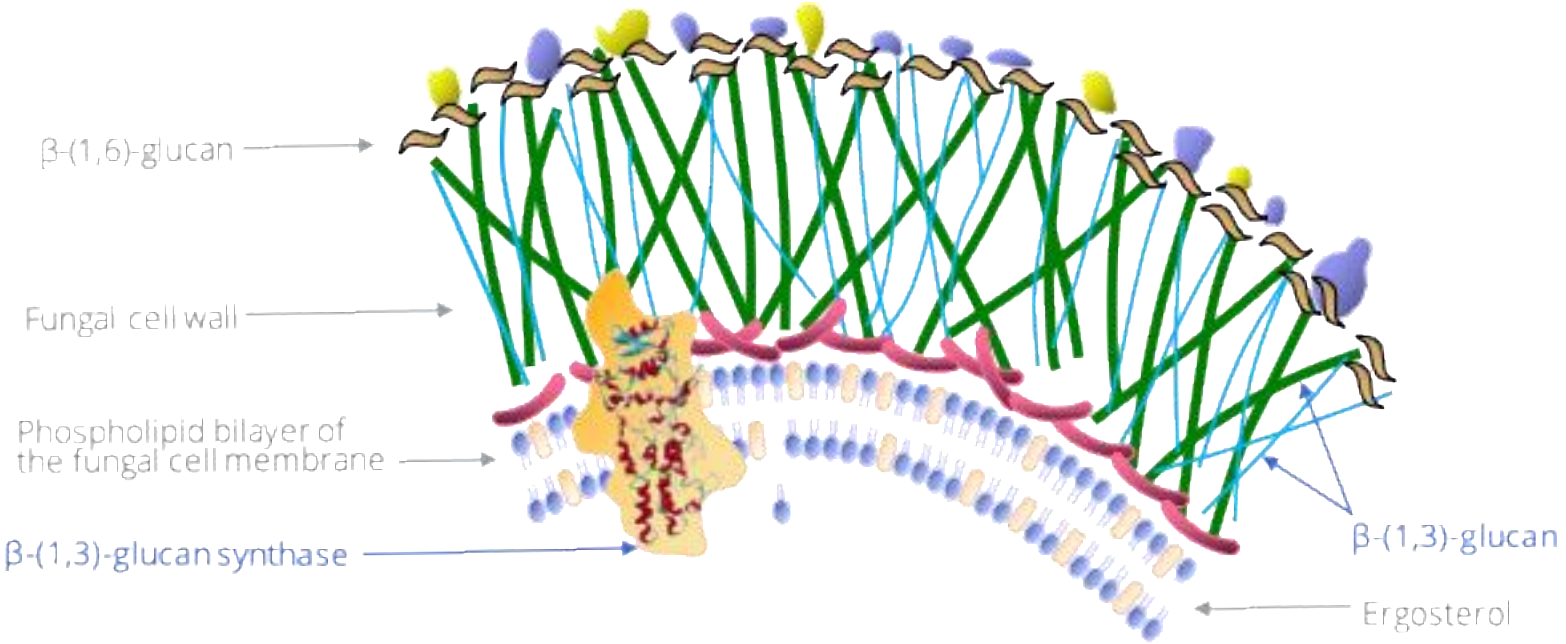
SCY-078 – An Innovative Antifungal

- Novel Class: Triterpenoid with MOA glucan synthase inhibitor. Semi-synthetic derivative of a natural product
- Being developed for invasive and mucotaneous fungal infections

SCY-078 – Validated Mechanism of Action

- SCY-078 targets synthesis of β-(1,3)-glucan in fungal cell wall
  - Mechanism validated by echinocandins
  - Disruption of fungal cell wall with fungicidal effect in *Candida*
  - No cross-resistance with Azoles because of different mechanism

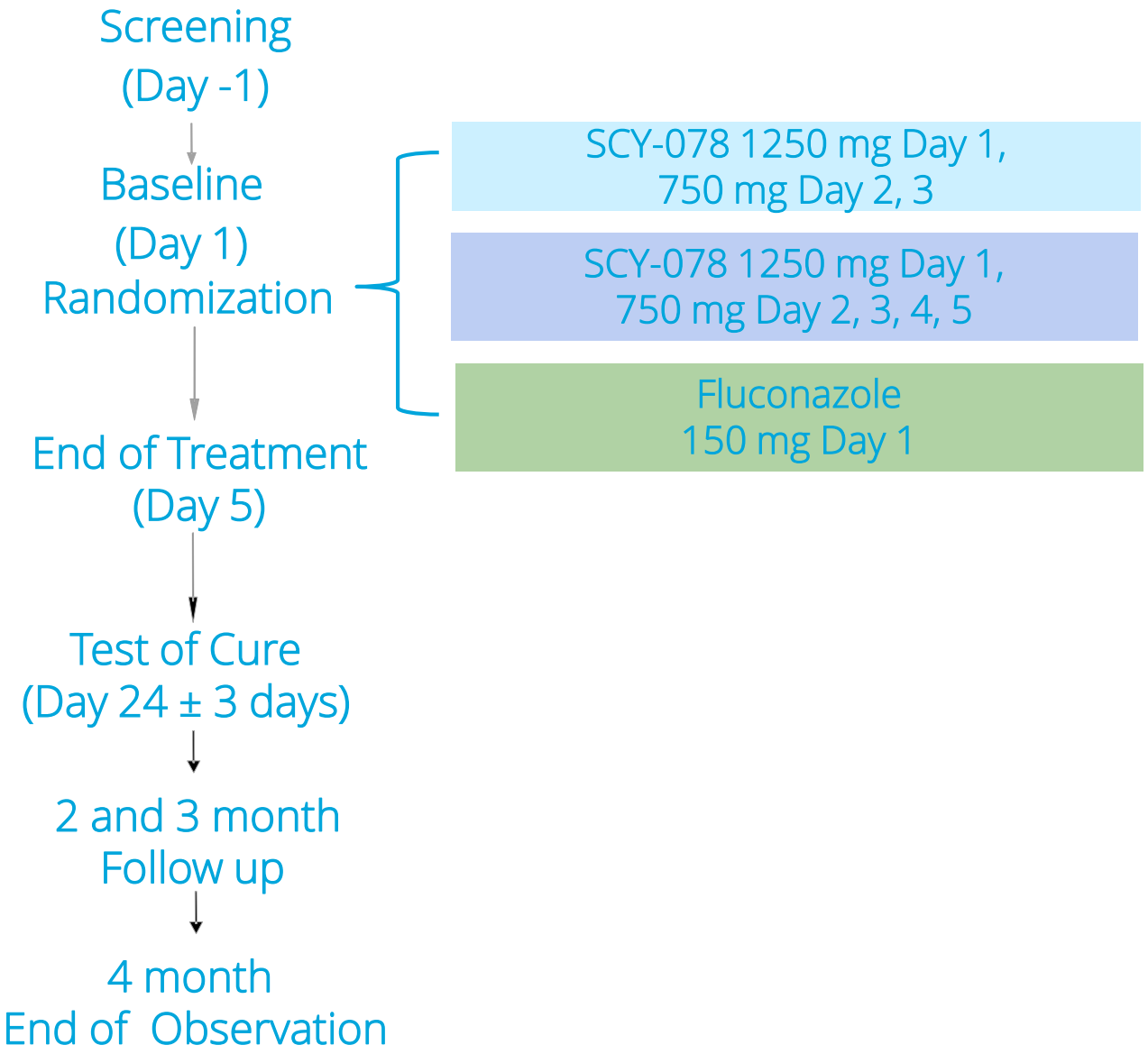


Adapted by Kartsonis et al, Drug Resistance Update, 2003
Anderson Freitas Pinheiro et al. International Journal of Quantum Chemistry, 2012

SCY-078-203 Study Design

- Oral treatment for vulvovaginal candidiasis
  - Multicenter, randomized, evaluator-blinded study
  - Patients with moderate to severe VVC
    - Sign and Symptoms ≥7 + Positive Potassium Hydroxide (KOH) test from vaginal sample
    - 3 episodes in the past year (confirmed by microscopy or response to antifungal therapy)
  - Two dose-regimens of oral SCY-078 compared to Fluconazole
  - Endpoints:
    - PRIMARY: Safety and Efficacy (clinical & microbiological outcome) at Day 24
    - SECONDARY: Relapse rates, clinical & microbiological outcomes up to Month 4
  - Enrollment total of 96 patients (32 per arm)

SCY-078-203 Study Design



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SCY-078-203 Populations

- Intent to Treat (ITT):
  - The ITT population will consist of all subjects who received at least 1 dose of randomized study drug (SCY-078 or fluconazole)
    - Signs and Symptoms + KOH +
    - Started Treatment +
- Per protocol: (PP)
  - A per-protocol population will be defined as those subjects who have a positive KOH test and a confirmed positive mycological culture for yeast at Visit 1, and who have completed the study drug treatment and have TOC evaluations.
    - Signs and Symptoms + KOH + Culture (yeast) +
    - Completed treatment +
    - Test of Cure Visit +

Populations N	SCY-078 (3-Days)	SCY-078 (5-Days)	SCY-078 (Combined)	Fluconazole
ITT	32	32	64	32
PP	24	26	50	20

SCY-078-203 Efficacy Definitions

- Clinical Cure:
  - Resolution of signs and symptoms without further antifungal treatment.
  - Any sign or symptom with a score of 1 or 2 at entry should be absent (score = 0)
  - Any sign or symptom with a score of 3 (severe) at entry should have a score of 0 or 1
- Mycological Eradication:
  - Negative culture for baseline yeast pathogen
- Therapeutic Cure:
  - Patients meeting both, Mycological eradication + Clinical cure

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SCY-078-203 Efficacy at Day 24 (PP)

PP N Rates %	SCY-078 (3-Days) (n= 24)	SCY-078 (5-Days) (n= 26)	SCY-078 (Combined) (n= 50)	Fluconazole (n= 20)	Delta Combined SCY-078 vs. Fluconazole
Clinical Cure	19 79.2%	19 73.1%	38 76%	13 65%	11%
Mycological Eradication	19 79.2%	16 61.5%	35 70%	13 65%	5%
Therapeutic Cure	14 58.3%	13 50%	27 54%	11 55%	-1%

P-values for all comparisons > 0.5

SCY-078-203 Efficacy at Month-4 (PP)

PP N Rates %	SCY-078 (3-Days) (n= 24)	SCY-078 (5-Days) (n= 26)	SCY-078 (Combined) (n= 50)	Fluconazole (n= 20)	Delta Combined SCY-078 vs. Fluconazole
Relapse rate – episodes requiring antifungal therapy	1 4.2%	1 3.8%	2 4%	3 15%	- 11%
Clinical Cure at M-4	21 87.5%	23 88.46%	44 88%	13 65%	23%
"0" Signs and Symptoms	19 79.1%	21 80.7%	39 78%	12 60%	18%
Negative Culture	18 75%	19 73%	37 74%	12 60%	14%

SCY-078-203 Adverse Events

- No severe AEs
- No Serious AEs
- No discontinuations due to AEs
- The majority of subjects receiving SCY-078 reported mild nausea, diarrhea and or vomiting particularly after the loading dose with resolution typically by day 2

SCY-078 Summary

- New Class: A novel Triterpenoid antifungal
- Fungicidal against *Candida spp.*
- Ongoing phase 2 dose-ranging study in acute VVC
- May provide a non-azole oral treatment for VVC in the future

Thank You