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
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

Screening (Day -1)

Baseline (Day 1)

Randomization

End of Treatment (Day 5)

Test of Cure (Day 24 ± 3 days)

2 and 3 month Follow up

4 month End of Observation

SCY-078 1250 mg Day 1, 750 mg Day 2, 3

SCY-078 1250 mg Day 1, 750 mg Day 2, 3, 4, 5

Fluconazole 150 mg Day 1
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 +

<table>
<thead>
<tr>
<th>Populations</th>
<th>N</th>
<th>SCY-078 (3-Days)</th>
<th>SCY-078 (5-Days)</th>
<th>SCY-078 (Combined)</th>
<th>Fluconazole</th>
</tr>
</thead>
<tbody>
<tr>
<td>ITT</td>
<td></td>
<td>32</td>
<td>32</td>
<td>64</td>
<td>32</td>
</tr>
<tr>
<td>PP</td>
<td></td>
<td>24</td>
<td>26</td>
<td>50</td>
<td>20</td>
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</tbody>
</table>
**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
SCY-078-203 Efficacy at Day 24 (PP)

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

P-values for all comparisons > 0.5
# SCY-078-203 Efficacy at Month-4 (PP)

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