Pharmacokinetics, Safety, and Target Attainment of Single and Multiple Doses of CD101 IV – A Novel, Once-Weekly Echinocandin

T. Sandison, V. Ong, and D. Thye
Cidara Therapeutics, Inc., San Diego, CA

INTRODUCTION

CD101 is a novel echinocandin in development for prevention and treatment of serious fungal infections. As a semisynthetic derivative of Candida and Aspergillus apiculata, it includes azole-resistant strains1,4 and has demonstrated safety and efficacy in animal models of candidiasis and aspergillosis2,4,12 in a mouse model of cryptococcal pneumonia. PK/PD analysis of CD101 was conducted to evaluate the probability of achieving therapeutic targets against Candida.

METHODS

Methods:
- Quadratic cohorts of 6 healthy subjects (n=4; CD101, n=2; placebo).
- Double-blind, placebo-controlled, single- and multiple-dose studies (100 mg q2, 200 mg q2, 400 mg q2) infused intravenously over 1 hour. PK was assessed via CD101 plasma concentrations collected from pharmacokinetic and safety assessments.
- Two Phase 1 studies were conducted to determine the safety, tolerability, and PK profile of single- and multiple-dosing of CD101 (100 mg IV) in healthy adults (NCT02518664 and NCT02551149, respectively).

RESULTS

Study Design and Treatments

- These were randomized, double-blind, placebo-controlled, single-center, dose-escalation studies in which CD101 or placebo was infused over 1 hour in the following dose cohorts:
- In the single-dose study (N=32), subjects were randomized to receive one dose of CD101 100 mg, 200 mg, 400 mg, or placebo. Details of the multiple-dose study (N=24) are shown below. Both studies randomized 6 CD101 and 2 placebo subjects per cohort.

Multiple-dose Ascending Dose Study Design

<table>
<thead>
<tr>
<th>Study N (6)</th>
<th>Dose (mg)</th>
<th>No. of Subjects</th>
<th>Male</th>
<th>Female</th>
<th>Age (y)</th>
<th>Weight (kg)</th>
<th>BMI (kg/m²)</th>
<th>CD101 Conc. 12 h after IV (µg/mL)</th>
<th>CD101 Conc. 12 h after IV (µg/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cohort 1</td>
<td>300</td>
<td>6</td>
<td>2</td>
<td>4</td>
<td>56±8</td>
<td>67±13</td>
<td>23±3</td>
<td>46±14</td>
<td>39±11</td>
</tr>
<tr>
<td>Cohort 2</td>
<td>400</td>
<td>6</td>
<td>2</td>
<td>4</td>
<td>56±8</td>
<td>67±13</td>
<td>23±3</td>
<td>81±18</td>
<td>78±18</td>
</tr>
<tr>
<td>Cohort 3</td>
<td>500</td>
<td>6</td>
<td>2</td>
<td>4</td>
<td>56±8</td>
<td>67±13</td>
<td>23±3</td>
<td>115±22</td>
<td>111±22</td>
</tr>
<tr>
<td>Cohort 4</td>
<td>600</td>
<td>6</td>
<td>2</td>
<td>4</td>
<td>56±8</td>
<td>67±13</td>
<td>23±3</td>
<td>150±28</td>
<td>149±28</td>
</tr>
</tbody>
</table>

CONCLUSIONS

- These two Phase 1 studies established the safety and PK of single- and multiple-dosing of CD101 IV in healthy adults.
- No serious adverse events or withdrawals due to AEs were observed. In the single-dose study, 1 subject withdrew due to AEs.
- Safety assessments were conducted using adverse events (AEs), vital signs, physical examination, laboratory tests, and safety laboratory tests up to 21 days after dosing. Data from these clinical trials were used to develop a population PK model for CD101. The pharmacokinetic parameters of CD101 were calculated using the NONMEM® software with a weighting scheme that minimized the weighted residuals.
- All subjects included in safety and PK analyses; one subject withdrew due to an AE.

ACKNOWLEDGMENTS / DISCLOSURES

Cidara Therapeutics. D.T. was an employee of Cidara Therapeutics when this work was conducted. T.S. and V.O. are employees of Cidara Therapeutics at the time this work was performed. T.S. and V.O. are employees of Cidara Therapeutics. D.T. is an employee of Cidara Therapeutics. This work was funded by Cidara Therapeutics. Literature was prepared by InFocus Communications and was funded by Cidara Therapeutics. Miesel L, et al. ASM Microbe 2016. Voon Ong, Ph.D., Cidara Therapeutics, Inc, 6310 Nancy Ridge Dr, Suite 169, San Diego, CA 92121 USA vong@cidara.com

REFERENCES