CD101: A Novel Echinocandin

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TIMM - Belgrade, Serbia
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Disclosures

Dr. Sandison is an employee of and stockholder in Cidara Therapeutics
Cidara’s Platforms

CD101 IV Echinocandin Antifungal

Candidemia / invasive candidiasis
Prophylaxis

Cloudbreak™ Immunotherapy

MDR Gram-negative bacteria
CD101: A Novel Echinocandin

Structural modification yields improved chemical & biological properties

Permanent Charge and Highly Stable Ring Structure:

- **Prolongs PK:** 1x Weekly Dosing
- **Allows High Exposures:** Treats Less Susceptible Pathogens
- **Eliminates Toxic Degradation Products:** Improved Safety & Dose Range
- **Enables Multiple Formulations:** Intravenous & Subcutaneous
Drug distribution in liver after single dose CD101 at 20 mg/kg determined by MALDI MS Imaging

Fungi location stained by GMS

Multidoses Micafungin vs. single dose CD101

Zhao and Perlin, Microbe 2016; and unpublished

CD101 Penetrates and Accumulates at High Levels at the Site of Infection
Dose Fractionation Study of CD101 in Mouse Candidiasis Model

Dose: 2mg/kg

N = 5 Mice/Group
1 Week
Same Weekly Exposure / Group
Front Loading Echinocandins Improves Efficacy

N = 5 Mice/Group
1 Week
Same Weekly Exposure / Group

← Less disease →

Vehicle

Daily

Twice weekly

Single dose

Change in Log_{10} CFU at 168h
CD101: Improved Target Attainment

Percent probabilities of PK-PD target attainment in *Candida* spp.

<table>
<thead>
<tr>
<th>MIC mg/L</th>
<th>C. albicans</th>
<th>C. glabrata</th>
<th>C. auris</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.008</td>
<td>100.0</td>
<td>100.0</td>
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<td>0.015</td>
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<td>22.8</td>
</tr>
<tr>
<td>8.000</td>
<td>0.0</td>
<td>4.4</td>
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<table>
<thead>
<tr>
<th>Caspofungin</th>
<th>C. albicans</th>
<th>C. glabrata</th>
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<tbody>
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<td>0.2</td>
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TIMM 2017/ IDSA 2017/ data on file
CD101 PK/PD: Exposure Drives Better Target Attainment especially when facing less susceptible pathogens

Caspofungin (14 daily doses)

CD101 (3 weekly doses)

\[ \text{Weekly } \frac{fAUC}{MIC} \]

Target \( \frac{AUC}{MIC}=10 \)

MIC=0.25 for caspofungin. MIC=0.12 for CD101
Bader. Emerging Candida glabrata Resistance and Echinocandin Dosing: A Call to Arms! IDWeek 2016
STRIVE trial: Phase 2 Candidemia & Invasive Candidiasis

Study Design

**CD101 IV**

- **Dose:** 400/400/(400)mg
- **n=30**

<table>
<thead>
<tr>
<th>Week</th>
<th>1</th>
<th>2</th>
<th>3</th>
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<tr>
<td>Day</td>
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<td>8</td>
<td>15</td>
<td>22</td>
<td>28</td>
<td>35</td>
<td>42</td>
<td>49</td>
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</table>

**Mycological response**

**Mycological & clinical response:**

1° ENDPOINT

**Mycological & clinical response (IC only)**

**Optional dose**

- **Day 5**
- **Week 1**

**CD101 IV**

- **Dose:** 400/200/(200)mg
- **n=30**

<table>
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**Mycological response**

**Mycological & clinical response:**

**Optional dose**

- **Day 5**
- **Week 1**

**CD101 IV**

- **Dose:** 70/50/(50)mg
- **n=30**

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**Mycological response**

**Mycological & clinical response:**

**Optional dose**

- **Day 5**
- **Week 1**

**Caspofungin**

- **70mg Dose**
- **50mg Dose**

**n=30**

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Current Prophylaxis Requires Multiple Drugs For Coverage

Day
-10 0 10 20 30 40 50 60 70 80

SOC for Candida and Aspergillus

Fluconazole
Posaconazole or Voriconazole

or... Posaconazole or Voriconazole

SOC for Pneumocystis (PCP)

Anti-PCP: Bactrim, dapsone or atovaquone

Risk of IFI

High
Low
Transplant
Pre-engraftment
Candida
Aspergillus

Post-engraftment
Pneumocystis
Aspergillus

Day
-10 0 10 20 30 40 50 60 70 80
Aspergillus prophylaxis with CD101 - 100% success at humanized doses

STUDY DESIGN

6 mice per arm

Controls: Amphotericin B control 3 mg/kg; CD101 at 3 mg/kg; one hour after infection

9 CD101 groups at 5, 10 and 20 mg/kg as prophylaxis was once at Day -5, -3 or -1 before infection

All animals immunosuppressed

Day 0, infected with A. fumigatus

10-20 mg/kg ≈ expected humanized dose
Mice clear CD101 2-3 fold faster than humans.
CD101 Shows Equivalent Efficacy to TMP/SMX in PCP Prophylaxis Mouse Model

STUDY DESIGN

10 mice per arm

Infected with *P. murina* by intranasal inoculation

Immunosuppression with dexamethasone throughout study

CD101 was administered at the same time the mice were infected

Quantification of PCP from lung

"Prophylaxis with CD101, which blocked cyst/asci formation, offers a new means to prevent PJP"
CD101: Simplified Single Drug Paradigm

Day

SOC for Candida and Aspergillus

SOC for Pneumocystis (PCP)

Risk of IFI

High

Low

Candida Aspergillus

Pneumocystis Aspergillus

Pre-engraftment

Post-engraftment

Transplant

Engraftment
Phase 3 Antifungal Prophylaxis Trial in HSCT Patients

**Planned 2018**

**CD101 Arm (n=220)**

1. **Week 1**
   - **CD101 IV**
   - **Azole placebo**
   - **Bactrim placebo**

2. **Day 1**

1° Day 90 Fungal Free Survival - Non-Inferiority
2° Day 90 Safety/Tolerability - Superiority

**Comparator Arm (n=220)**

1. **Week 1**
   - **CD101 IV Placebo**
   - **Azole***
   - **Bactrim**

2. **Day 1**

*Fluconazole or Posaconazole

Adaptive design: interim analysis @ 35% enrollment for futility/sample size.
Apx. 15 sites globally, with planned initiation in 2018. Timing and size pending regulatory input.
Thank You