CD101: A Novel Echinocandin

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TIMM - Belgrade, Serbia
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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

Powered by CARB-X
CD101: A Novel Echinocandin

- Prolongs PK
- Allows high exposures
- Eliminates toxic degradation products
- Enables multiple formulations

Once weekly dosing
Treats less susceptible pathogens
Improved safety & dose range
Intravenous & subcutaneous

Structural modification yields improved chemical & biological properties
CD101 Penetrates and Accumulates at High Levels at the Site of Infection

Drug distribution in liver after single dose CD101 at 20 mg/kg determined by MALDI MS Imaging

Fungi location stained by GMS

Zhao and Perlin, Microbe 2016; and unpublished
Dose Fractionation Study of CD101 in Mouse Candidiasis Model

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

Free-Drug Concentration (mg/L) vs. Time (hours)

Dose: 2mg/kg

Lakota ASM 2016
Front Loading Echinocandins Improves Efficacy

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

Less disease ↔ More disease

Vehicle

Daily

Twice weekly

Single dose

Change in $\log_{10}$ CFU at 168h

Lakota ASM 2016
## CD101: Improved Target Attainment

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

<table>
<thead>
<tr>
<th>MIC mg/L</th>
<th><em>C. albicans</em></th>
<th><em>C. glabrata</em></th>
<th><em>C. auris</em></th>
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<tr>
<td>0.008</td>
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<td>0.0</td>
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<td>22.8</td>
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<td>8.000</td>
<td>0.0</td>
<td>4.4</td>
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- **≥90% probability of target attainment**
- **CD101** (400mg, weekly for 3 weeks)
- **Caspofungin** (70mg 1xq24; 50mg 13xq24h)

### C. albicans
- 100.0
- 100.0
- 100.0
- 100.0
- 100.0
- 100.0
- 97.8
- 100.0
- 98.7
- 40.1
- 0.0
- 0.0

### C. glabrata
- 100.0
- 100.0
- 100.0
- 100.0
- 100.0
- 100.0
- 97.2
- 100.0
- 22.8
- 0.2
- 0.0

Rows represent different strains of *Candida*

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)

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 400/400/(400)mg

<table>
<thead>
<tr>
<th>Week</th>
<th>Dose</th>
<th>Optional dose</th>
<th>Mycological response</th>
<th>Mycological &amp; clinical response: 1° ENDPOINT</th>
<th>Mycological &amp; clinical response (IC only)</th>
<th>Mycological &amp; clinical response</th>
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#### CD101 IV 400/200/(200)mg

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#### Caspofungin 70/50/(50)mg

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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

Pre-engraftment

Post-engraftment

Transplant

Engraftment
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’

Source: Cushion et al. ASM. 2016
CD101: Simplified Single Drug Paradigm

SOC for Candida and Aspergillus

SOC for Pneumocystis (PCP)

Risk of IFI

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

CD101

SOC for Candida and Aspergillus

SOC for Pneumocystis (PCP)

Risk of IFI

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

Transplant

Pre-engraftment

Post-engraftment

Engraftment

High

Low

Candida

Aspergillus

Pneumocystis

Aspergillus

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

Transplant

Pre-engraftment

Post-engraftment

Engraftment

High

Low

Candida

Aspergillus

Pneumocystis

Aspergillus
Phase 3 Antifungal Prophylaxis Trial in HSCT Patients
Planned 2018

CD101 Arm (n=220)

Comparator Arm (n=220)

Follow up

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