Susceptibility of recent *Candida auris* isolates to the novel echinocandin CD101 and comparator antifungal agents

Emily L. Larkin, Lisa Long, Mahmoud A. Ghannoun

Center for Medical Mycology, Department of Dermatology, Case Western Reserve University

School of Medicine and University Hospitals Cleveland Medical Center, Cleveland, OH 44106-5028, USA

Poster# 9037

Background: *Candida auris* has emerged clinically as a highly virulent yeast species. Therapeutic options are often limited as many isolates possess resistance to one or more major antifungal drug classes (echinocandins, azoles and polyenes). CD101 is a novel echinocandin that safely achieves high plasma exposures and has a long half-life. These PK/PD attributes enable CD101 to produce front-loaded drug exposures with less-frequent dosing compared with other echinocandins. In this study, the *in vitro* susceptibility of a panel of recent *C. auris* isolates to CD101 and relevant antifungal comparators was investigated through minimum inhibitory concentration (MIC) assays.

Material/methods:
- 16 *C. auris* isolates were obtained from patients in Germany, Japan, India, and South Korea collected from 2009 - 2016
- CLSI M27-A3 broth microdilution methodology was used to determine MICs
- MIC assays utilized RPMI 1640 medium with 3-(N-Morpholino)propanesulfonic acid, yeast inoculum of 0.5 -2.5 x 10³ cells/ml, and incubation at 35 °C

### Table 1. CD101 and comparator antifungal MIC values for a panel of *C. auris* clinical isolates (n=16)

<table>
<thead>
<tr>
<th>MIC (µg/mL)</th>
<th>CD101</th>
<th>ANID</th>
<th>MICA</th>
<th>CAS</th>
<th>FLU</th>
<th>ITRA</th>
<th>VORI</th>
<th>AMB</th>
</tr>
</thead>
<tbody>
<tr>
<td>Range</td>
<td>0.031 - 1</td>
<td>0.125 - 0.25</td>
<td>0.25 - 2</td>
<td>0.25 - 1</td>
<td>1 - &gt;64</td>
<td>&lt;0.063 - 1</td>
<td>&lt;0.063 - 1</td>
<td>0.5 - 8</td>
</tr>
<tr>
<td>MIC₅₀</td>
<td>0.125</td>
<td>0.125</td>
<td>1</td>
<td>0.5</td>
<td>16</td>
<td>0.5</td>
<td>0.5</td>
<td>2</td>
</tr>
<tr>
<td>MIC₉₀</td>
<td>0.25</td>
<td>0.25</td>
<td>1</td>
<td>1</td>
<td>&gt;64</td>
<td>1</td>
<td>1</td>
<td>4</td>
</tr>
</tbody>
</table>

### Material/methods (continued)
- Quality control strains: *C. parapsilosis* ATCC 22019 and *C. krusei* ATCC 6258
- Drugs used: CD101, anidulafungin (ANID), micafungin (MICA), caspofungin (CAS), fluconazole (FLU), itraconazole (ITRA), voriconazole (VORI) and amphotericin B (AMB)
- Visual endpoints were the lowest concentration of drug that caused complete inhibition (100%) (AMB) or ≥50% decreased in fungal growth (CD101, ANID, MICA, CAS, FLC, ITRA, VORI) relative to growth control

### Results:
- Table 1 lists the 24 h MIC values for all compounds with the exception of ITRA which was read at 48 h
- CD101 was equipotent to ANID and 4-fold more potent than MICA and CAS
- FLU was much less active when compared to ITRA and VORI MIC₉₀ of >64 µg/mL and 1 µg/mL, respectively
- AMB MIC values typically fell in between those for the echinocandins and FLU
- ATCC 22109 and ATCC 6258 were within quality control ranges for all tested drugs

### Conclusions:
- 8 out of 16 isolates possessed susceptibility profiles that, for other *Candida* species, would be characterized as resistant to at least three of the antifungal agents evaluated
- The potent activity of CD101 against this panel, coupled with its front-loaded, high area under the curve/max concentration (AUC/Cₘ₉₅) plasma drug exposure, support the potential clinical utility of CD101 in the treatment of *C. auris* infections

### References: