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

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**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).[1] 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.[2] 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[3]
- MIC assays utilized RPMI 1640 medium with 3-(N-Morpholino) propanesulfonic acid, yeast inoculum of 0.5 -2.5 x $10^3$ 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)

| | MIC (µg/mL) | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | CD101 | ANID | MICA | CAS | FLU | ITRA | VORI | AMB |
| **Range** | 0.031 - 1 | 0.125 - 0.25 | 0.25 - 2 | 0.25 - 1 | 1 - >64 | <0.063 - 1 | <0.063 - 1 | 0.5 - 8 |
| **$MIC_{50}$** | 0.125 | 0.125 | 1 | 0.5 | 16 | 0.5 | 0.5 | 2 |
| **$MIC_{90}$** | 0.25 | 0.25 | 1 | 1 | >64 | 1 | 1 | 4 |

**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 $MIC_{90}$ 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 ($AUC/C_{max}$) plasma drug exposure, support the potential clinical utility of CD101 in the treatment of *C. auris* infections

**References:**

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2. **Sandison, T., V. Ong, J. Lee, and D. Thye.** 2017. Safety and Pharmacokinetics of CD101 IV, a Novel Echinocandin, in Healthy Adults. Antimicrob Agents Chemother **61:**e01627-16.

3. **Clinical and Laboratory Standards Institute.** 2008. Reference method for broth dilution antifungal susceptibility testing of yeasts--third edition: approved standard M27-A3, vol. CLSI, Wayne, PA, USA.