Efficacy of CD101 to Treat Echinocandin-Resistant *Candida albicans* in a Murine Model of Invasive Candidiasis

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**ABSTRACT**

**Background:** CD101 is a novel, long-acting echinocandin being developed for the treatment of invasive *Candida* infections. CD101 has demonstrated potent in vitro activity against a broad range of *Candida* and *Aspergillus* species including antifungal-resistant strains. Herein, we have evaluated the in vivo efficacy of CD101 against echinocandin-susceptible and -resistant *C. albicans* strains in an invasive candidiasis murine model.

**Methods:** Female 6-week-old BALB/c mice weighting 18-22 g were rendered neutropenic by receiving 150 mg/kg and 100 mg/kg of cyclophosphamide via IP injection on day -4 and -1 prior to infection, respectively. Two *C. albicans* strains, ATCC 90028 (FKS WT) and DPL22 (fks/FKS mutant S645P/S), were used in this experiment. On day 0, mice were infected with 5x10^6 CFU WT or mutant strain via lateral tail vein injection. Groups of 10 mice were given single doses of vehicle, CD101 (20, 40, or 60 mg/kg) or micafungin (MCF) (10 mg/kg), which are doses that are equivalent to their anticipated human drug exposures after a single IV dose at 3 h post-inoculation via IP injection. At 24 h and 48 h post-inoculation, 5 mice from each group were euthanized, and kidneys were aseptically removed for enumeration of fungal burdens. Data analysis was performed using GraphPad Prism software. A P value of <0.05 is considered statistically significant.

**Results:** CD101 at all three doses exhibited activity against both WT and heterozygous fks/FKS mutant strains of *C. albicans*, as demonstrated by significant kidney burden reductions compared to infected controls in all treatment groups at both 24 h and 48 h post-inoculation time points. In WT infected mice, CD101 exhibited greater efficacy than MCF at 24 h post-inoculation at all three doses. Superiority relative to MCF was observed with the 60 mg/kg CD101 group at 48 h post-inoculation. In fks/FKS mutant infected mice, CD101 treatment significantly reduced kidney burdens by over 2 logs at 24 h post-inoculation compared to vehicle control (P<0.05). The 24 h burden reduction was not significantly different among three CD101 dosage groups or micafungin treatment group. However, better efficacy of CD101 compared to micafungin at 5 mg/kg was observed for all three doses at 48 h post-inoculation. B burden reduction was comparable in three CD101 groups (Figure 2).

**CONCLUSIONS**

- CD101 at the dose range of 20 to 60 mg/kg was effective to treat invasive candidiasis caused by both FKS wild-type and a heterozygous fks/FKS mutant *C. albicans* in a murine model.
- Compared to a standard 5 mg/kg micafungin regimen, better efficacy of CD101 was observed for all three studied doses at 24 h post-inoculation in wild-type infected mice. The highest dose (60 mg/kg) of CD101 was better than micafungin at 48 h post-inoculation.
- For fks/FKS mutant caused infection, better efficacy of CD101 relative to micafungin was observed at 48 h post-inoculation for all three studied doses.

**REFERENCES**


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