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Efficacy of once or twice daily oral SCY-247, a second-generation triterpenoid antifungal, in a murine model of *Candida auris* infection

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Introduction

Candida auris is a multidrug resistant fungus exhibiting a 200% increased in incidence in the U.S from 2019 to 2023. SCY-247 is a second generation triterpenoid antifungal in development for IV/oral administration.

Methods

Animals: Neutropenic CD-1 female mice (n=10 per group).

Inoculation: *C. auris* 1.5 × 10^7 blastospores/mouse intravenously.

Treatment: Started 2 hours post-inoculation for 7 days

- Vehicle control
- SCY-247 15 mg/kg PO BID
- SCY-247 30 mg/kg PO BID
- SCY-247 30 mg/kg PO QD
- Micafungin 5 mg/kg IP QD

Kidneys collected 2hr post infection from stasis control and on day 8 post infection from all groups for fungal burden analysis by colony forming units (CFUs/g). Differences in fungal burden were assessed for significance by T-test.

Pharmacokinetics in plasma and kidneys were determined and correlated to reductions in fungal burden.

For PK/PD analysis samples were assayed by LC-MSMS methods.

Goal

Assess the activity of 7-day dosing of oral SCY-247 treatment, once or twice daily in reducing the kidney fungal burden in a murine model of *C. auris* infection

Results

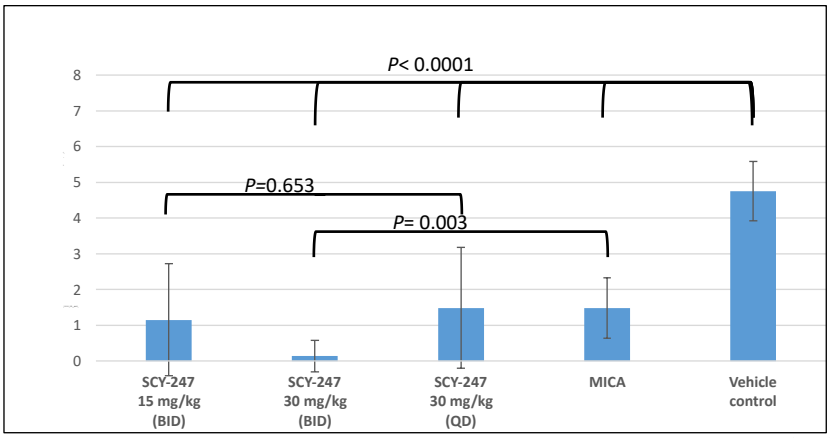

Figure 1: Kidney fungal burden (average log CFU/g ± SD) of mice infected with C. auris following treatment with SCY-247 (n=10)

- Kidney fungal burden was similar between stasis and vehicle control (4.66 and 4.75 $\log_{10}$ CFUs, respectively).
- Treatment with 15 and 30 mg/kg BID SCY-247 resulted in 3.60 $\log_{10}$ and 4.61 $\log_{10}$ reductions in CFUs versus vehicle control, (P<0.0001 for both).
- Treatment with SCY-247 30 mg/kg QD yielded a similar reduction in CFUs compared to SCY-247 15 mg/kg BID; (3.27 $\log_{10}$ vs 3.60 $\log_{10}$ CFUs, respectively, P=0.653).
- Results were consistent with $AUC_{0\text{-}24}$, rather than C_{max}, being the PK parameter driving efficacy as reported for other glucan synthase inhibitors.
- SCY-247 30mg/kg/day via QD or BID administration showed similar fungal burden reductions to micafungin.
- Treatment with SCY-247 at 30 mg/kg BID was significantly more effective than treatment with micafungin (4.61 $\log_{10}$ vs 3.28 $\log_{10}$ reduction, respectively, P=0.0003).
- SCY-247 achieved undetectable fungal burden in 50%, 60%, and 90% mice following 30 mg/kg QD, 15 mg/kg BID and 30 mg/kg BID treatment, respectively vs. 20% for micafungin.
- Values for plasma $AUC_{0\text{-}24}$ following either the first QD or second BID dose, were 49.0, 31.0 and 79.8 µg.hr/mL for the 30 mg/kg QD, 15 mg/kg BID and 30 mg/kg BID regimens, respectively.
- The half-life of SCY-247 was ~15 hr consistent with steady-state being achieved on day 3. Corresponding values for C_{max} were: 2.88, 1.89 and 4.36 µg/mL, respectively. SCY-247 distributed extensively to kidney with $AUC_{0\text{-}24}$ exposures ~20-fold higher than plasma.

Conclusion

SCY-247 demonstrated *in vivo* efficacy against invasive *C. auris* candidiasis. Significant reductions in fungal burden were observed in the kidneys of mice treated with SCY-247 in a dose dependent fashion with similar activity observed between QD and BID doses at 30 mg/kg/day. SCY-247 distributed extensively to kidney tissues and PK/PD analysis is consistent with $AUC_{0\text{-}24}$ rather than C_{max} being the PK parameter driving efficacy. These data support the potential utility of SCY-247 therapy against invasive infections caused by resistant *C. auris.*

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