Efficacy of Oral Ibrexafungerp (IBX, Formerly SCY-078) in the Treatment of *Candida auris* Infection in a Murine Disseminated Model

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BACKGROUND

Candida auris has recently been reported worldwide as a cause of invasive infections, with a mortality rate approaching 60 percent, double that caused by other species. Therefore, identifying antifungals that are effective against this emerging species that is multidrug resistant to available antifungals, is critically needed. Ibrexafungerp (IBX, formerly SCY-078) is a novel glucan synthase inhibitor with oral availability that is being evaluated for activity against *C. auris* and currently enrolling patients in a clinical trial, the Open-Label Study to Evaluate the Efficacy and Safety of SCY-078 in Patients with Candidiasis Caused by *Candida auris* (CARES)(NCT03363841)

METHODS

An inoculum of a clinical isolate of *C. auris* was prepared to a concentration of 3×10^7. Mice were immunocompromised with cyclophosphamide, inoculated via tail vein injection, and randomized into three treatment groups (10, 20, and 30 mg/kg twice a day (BID) by oral gavage) and vehicle control. Kidneys tissue fungal burden was determined at day 7 from 5 mice per group, with survival evaluation recorded in another 10 animals per group at 14 days. PK bioanalysis of IBX plasma concentrations was conducted 4, 8, and 12 hours post-morning dose (13^{th} dose) on day 7 (3 mice per time point).

RESULTS

Our data showed that tissue fungal burdens were lower than vehicle controls in all treatment groups, with the highest reduction in tissue burden observed in the 30 mg/kg dosing group (Table 1, Fig. 1). The 14-day survival rate was comparable across groups, with animals in the 10, 20 and 30 mg/kg groups having survival rates of 60%, 70% and 60%, respectively, compared to the vehicle group which had a survival rate of 20% (Table 2). Exposures in mice dosed with 10, 20 or 30 mg/kg BID are consistent with steady-state plasma exposure ($AUC_{0\text{-}24}$) values of 8.4, 24.3 and 40.2 ug*hr/mL, respectively.

Treatment Group	Average Log CFU	SD
Vehicle	6.41	0.66
SCY-078 10 mg/kg	4.86	1.44
SCY-078 20 mg/kg	6.05	0.77
SCY-078 30 mg/kg	2.69	1.65

Table 1. Tissue Fungal Burden

Treatment Group	% Survival at Day 14	P-value Compared to Vehicle Control
Vehicle	20	-
SCY-078 10 mg/kg	60	0.20
SCY-078 20 mg/kg	70	0.02
SCY-078 30 mg/kg	60	0.08

Table 2. Survival

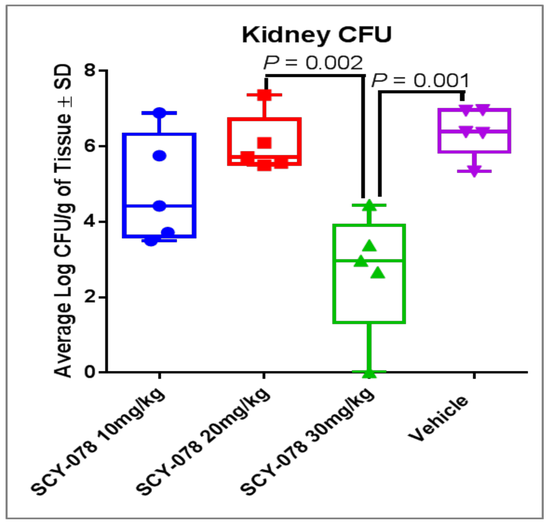

Figure 1. Tissue fungal burden

CONCLUSIONS

Our findings show that Ibrexafungerp possesses potent antifungal activity against the *C. auris* strain tested, as determined by kidney fungal burden and survival rates. This data indicates that IBX could have utility in the treatment of *C. auris* infections.

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