Efficacy of Ibrexafungerp (IBX, formerly SCY-078) in the Treatment of *Candida auris* Cutaneous Infection in a Guinea Pig Model

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BACKGROUND

Candida auris, an emerging multi-drug resistant species recently reported worldwide as a cause of invasive infections and its persistence on the skin of patients may be associated with its transmission contributing to outbreaks in health care facilities. Ibrexafungerp **(**formerly SCY-078**),** a novel orally bioavailable glucan synthase inhibitor with demonstrated *in vitro* activity against *C. auris*, was evaluated for efficacy in an experimental *in vivo* cutaneous model

METHODS

- Guinea pigs (*n*=5 per group) were randomized into 5 treatment groups: 10, 20, and 30 mg/kg of Ibrexafungerp twice daily (BID) by gavage, micafungin 5 mg/kg once daily IP, and vehicle control. Animals received a single dose of prednisolone 30 mg/kg, subcutaneously, one day prior and again at three days post infection. A 100 µl cell suspension containing 10^8 blastospores of *C. auris* was applied to an abraded area on the back of animals. At Day 7, tissue biopsies were examined histologically, and tissue fungal burden was analyzed by colony counts from skin samples. PK bioanalysis of Ibrexafungerp plasma concentrations was conducted following the final dose (Day 7).

RESULTS

Tissue fungal burdens were lower than vehicle controls in all treatment groups, with a significant reduction in tissue fungal burden in the 10 mg/kg Ibrexafungerp dosing group. Histological examination showed that no fungal elements were observed in the biopsy samples treated with Ibrexafungerp or micafungin, as opposed to the untreated control group (arrow). There were no significant differences in the clinical scores (crusting, inflammation) among the treatment groups. Animals dosed with 10, 20 or 30 mg/kg BID of IBX had exposures (AUC $_{0\text{-}24}$) of 2.8, 5.6, and 15 ug*hr/ml.

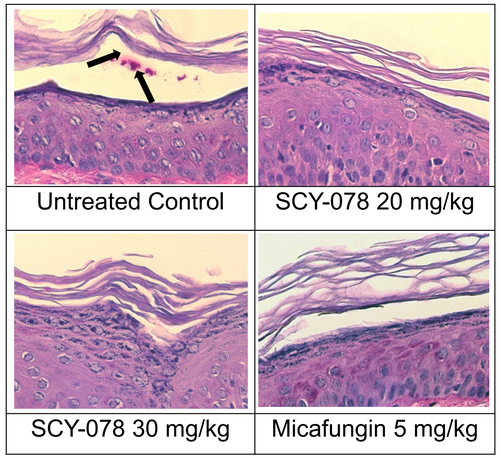

Figure 1. PAS stain of infected skin `

Treatment Group	Average Log CFU ± SD
Untreated	4.1 ± 0.3
SCY-078 10 mg/kg, twice a day	2.8 ± 0.7*
SCY-078 20 mg/kg, twice a day	3.7 ± 0.4
SCY-078 30 mg/kg, twice a day	3.6 ± 0.3
Micafungin 5 mg/kg, once a day	3.6 ± 1.2

Table 1. Average fungal tissue burden of skin

* *P*-value of 0.039

Treatment Group	Average Log CFU ± SD
Untreated	2.2 ± 0.2
SCY-078 10 mg/kg, twice a day	1.7 ± 0.4
SCY-078 20 mg/kg, twice a day	1.8 ± 0.4
SCY-078 30 mg/kg, twice a day	2.1 ± 0.4
Micafungin 5 mg/kg, once a day	2.1 ± 0.3

Table 2. Average clinical score of skin

CONCLUSIONS

The results from this experimental model show that IBX dosed orally distributed to the skin, and that treatment with IBX reduced the fungal burden in skin infected with *C. auris,* when compared to the untreated control, thus suggesting efficacy in the treatment of cutaneous infections and potential role in *C.auris* skin decolonization.

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