

Ibrexafungerp Demonstrates Potent and Consistent *In Vitro* Activity Against >400 Global *Candida auris* Isolates, Including isolates with Elevated MIC's to Echinocandins

S. Barat, K. Borroto-Esoda, D. Angulo
SCYNEXIS, Inc., Jersey City, United States of America

Background: *Candida auris* is a urgent global threat; a pathogen associated with high mortality (up to 60%), multi-drug resistance, the ability to spread from person-to-person and surface-to-person, presenting high risk for outbreaks in healthcare facilities. Echinocandins are the first-line treatment for patients with *Candida auris* infections given the high degree of resistance to azoles and polyenes. Ibrexafungerp is a novel IV/oral glucan synthase inhibitor (triterpenoid) antifungal with activity against *Candida*, *Aspergillus* and *Pneumocystis* spp, in Phase 3 development. Given the potent activity of ibrexafungerp against *Candida* spp., Scynexis has embarked on a development program to understand the activity and effectiveness of ibrexafungerp against *Candida auris*. We will present a compilation of >400 *Candida auris* isolates from four studies, including 32 *Candida auris* isolates with elevated MIC's to the echinocandins.

Materials/methods: *In vitro* MIC data for ibrexafungerp against *Candida auris* isolates were compiled from across 4 independent studies with the majority of isolates originating in the US and India. *In vitro* susceptibility was determined by broth micro-dilution using CLSI (M27-S3) and/or EUCAST methods. Overall, 445 isolates were evaluated including 32 isolates with elevated MIC values to one or more echinocandins.

Results: The ibrexafungerp MIC₉₀ value against the 445 clinical isolates was 1 µg/mL; the modal and MIC₅₀ values were 0.5 µg/mL each. These results were consistent across the four studies and no differences were observed between MIC results generated using CLSI or EUCAST methods. Similar results were obtained for the 32 isolates with elevated MIC values to one or more of the echinocandins. Among this population, the mode, MIC₅₀ and MIC₉₀ were 0.5, 0.5, and 1 µg/mL, respectively. Only 1/32 of the echinocandin-resistant isolates had reduced sensitivity to ibrexafungerp (defined as > 2-dilutions vs the mode). This isolate was pan-resistant with elevated MICs to all three echinocandins (MICs = 4 µg/mL) as well as fluconazole (MIC >256 µg/mL) and amphotericin B (MIC = 1 µg/mL).

Conclusions: This data demonstrates that ibrexafungerp possesses potent and consistent *in vitro* activity against *Candida auris* and remains highly active against *C. auris* isolates with high MIC's to the echinocandins.