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

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October 21-25 • www.idweek.org
IDWeek 2020
Advancing Science, Improving Care
Chasing the Sun
24 hours of COVID-19 followed by IDWeek

BACKGROUND

Candida auris is an 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 *C. auris* infections given the high degree of resistance of this pathogen to azoles and polyenes. Ibrexafungerp is a novel IV/oral glucan synthase inhibitor (triterpenoid) antifungal with activity against *Candida*, *Aspergillus* and *Pneumocystis,* in Phase 3 development. Given the potent activity of ibrexafungerp against *Candida* spp., SCYNEXIS has embarked on a development program to understand the effectiveness of its compound against *C. auris*. We will present the activity of ibrexafungerp against a compilation of >400 *C. auris* isolates from four studies, including 32 *C. auris* isolates with elevated MIC's to the echinocandins.

METHODS

In vitro MIC data for ibrexafungerp against *Candida auris* isolates were compiled from across 4 independent studies (see References) 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 from around the globe were evaluated including 32 isolates with elevated MIC values to one or more echinocandins.

REFERENCES

[1]Berkow, E.L. et al., Antimicrob Agents Chemother., 2017 Jun 27
[2]Larkin, E. et al., Antimicrob Agents Chemother., 2017 Apr 24
[3]Zhu, YZ. et al., Int J Antimicrob Agents., 2020 Feb 21
[4]Arendrup, MC, et al., Antimicrob Agents Chemother., 2020 Feb 21

RESULTS

The ibrexafungerp MIC_{90} value against the 445 clinical isolates was 1 μg/mL; the modal and MIC_{50} 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.

Table 1. Ibrexafungerp MIC (mg/mL) distribution against all *C. auris* isolates

Ibrexafungerp MIC's (μg/ml)	Study #1 (N=107) [1] Berkow	Study #2 (N=16) [2] Larkin	Study #3 (N=200) [3] Zhu	Study #4 (N=122) [4] Arendrup	Overall (N=445)
MIC_{50}	1	1	0.5	0.5	0.5
MIC_{90}	1	1	1	1	1
Mode	1	1	0.5	0.5	0.5
Range	0.0625 – 2	0.5 – 2	0.0625 – 8	0.0625 - 2	0.625 - 8

MIC values were similar among the 32 isolates with elevated MIC values to one or more of the echinocandins as compared to other isolates with modal, MIC_{50} and MIC_{90} of 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 mg/mL) and amphotericin B (MIC = 1 μg/mL).

Table 2. Ibrexafungerp MIC (mg/mL) distribution against ECH-R *C. auris* isolates

Ibrexafungerp MIC's (μg/ml)	ECH-R (N=32)
MIC_{90}	0.5
MIC_{50}	1
Mode	0.5
Range	0.0625 – 8

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.