Successful Treatment of Two Patients with *Candida auris* Candidemia with the Investigational Agent, Oral Ibrexafungerp (formerly SCY-078), from the CARES Study

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29th ECCMID EUROPEAN CONGRESS OF CLINICAL MICROBIOLOGY AND INFECTIOUS DISEASES

Amsterdam, Netherlands
13 – 16 April 2019

BACKGROUND

Candida auris is a growing global threat pathogen and has been isolated in 20 countries to date. *C. auris* is a MDR fungi, associated with high mortality (up to 60%) that can spread from person-to-person and surface-to-person, leading to outbreaks in healthcare facilities. In a recent publication, *C. auris* was the 2nd most common *Candida* spp. (17%) isolate in a tertiary care hospital in India, with 55% of *C. auris* isolates having high MICs to fluconazole (≥64 mcg/ml).[1]

Figure 1: Countries from which *Candida auris* cases have been reported, as of January 31, 2019

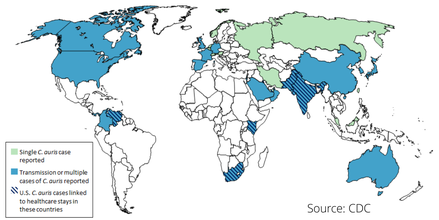

Table 1: Ibrexafungerp MIC data compared to isolates with elevated echinocandin MICs

	Minimum Inhibitory Concentration (µg/ml)			
Isolate	Anidulafungin	Caspofungin	Micafungin	Ibrexafungerp
1	8	1	4	1
2	16	1	4	1
3	1	16	1	1
4	2	16	2	1
5	4	0.5	0.5	0.5
6	>16	>16	>8	0.5
7	4	>16	1	1

Ibrexafungerp (formerly SCY-078) is a novel IV/oral glucan synthase inhibitor (triterpenoid) antifungal with activity against *Candida*, *Aspergillus* and *Pneumocystis,* in Phase 3 of development. *In vitro and in vivo* studies indicate that ibrexafungerp has activity against *C. auris*, including MDR strains. Berkow et al, tested Ibrexafungerp against 100 *C. auris* isolates, including 7 isolates with echinocandin-high MIC isolates of *C auris*. Ibrexafungerp MICs ranged from 0.0625-2 µg/ml and maintained similar MICs for the echinocandin-high MIC isolates (see Table 1).[2]

METHODS

The CARES study is an open-label study to evaluate the efficacy and safety of ibrexafungerp in patients with *C. auris* infections (Clinicaltrials.gov NCT03363841). This study is open for enrollment in the U.S. and India. Subjects receive a loading dose of oral ibrexafungerp 750 mg BID during the first 2 days and then 750 mg QD for up to 90 days and are followed for 6 weeks after end of therapy.

RESULTS

Table 2: We present our experience with 2 cases of candidemia due to *C.auris* that we enrolled in the CARES study.

Demographics	Medical History	Microbiology Day, relative to IBX start	Description	Antifungal therapy Day, relative to IBX start
58 years old Male Asian	DM, acute ischemic stroke, popliteal thrombosis, liver, spleen and kidney infarcts, and prolonged ICU stay.	Paired blood cultures: Day -11 *Candida auris* Fluconazole MIC >64 Voriconazole MIC 2 Ampho B MIC 0.5 Micafungin MIC 0.12 Day -4 *Candida auris* Day +3 Negative Day +5 Negative Day +12 Negative	The patient developed aspiration pneumonia and septic shock. He was initially treated with antibiotics and subsequently empirically added fluconazole. *C. auris* was recovered from blood culture and antifungal therapy was switched to micafungin. Clinical improvement was observed but blood culture collected after micafungin remained positive and ibrexafungerp was initiated. Blood cultures became negative, the patient continued to improve and completed 17 days of ibrexafungerp. The patient was considered to have achieved complete response at end of therapy (EOT), per investigator's assessment. The patient subsequently developed sepsis due to *K. pneumonia* and died of septic shock and multiple organ failure on Day 43 after EOT.	Fluconazole IV from -10 to Day -5 Micafungin IV from Day -5 to Day -1 Ibrexafungerp from Day 1 to Day +17 Ibrexafungerp related AEs included, loose stools (mild) from Day +2 to Day + 4
64 years old Female Asian	DM, HTN, CKD on MHD	Paired blood cultures: Day -3 *Candida auris* Day +3 *Candida auris* Day +9 Negative Day +21 Negative	The patient presented with a LRTI, fever and hypotension. The patient was started on antibiotics and showed improvement but fever persisted. *C. auris* was isolated from blood cultures and ibrexafungerp was initiated. The patient's blood cultures became negative and the patient continued to improve completing 22 days of ibrexafungerp. The patient was considered to have achieved complete response at EOT, per investigator's assessment. At the end of the 6 week follow up, the patient was alive and with no evidence of recurrence of the fungal infection.	Ibrexafungerp from Day 1 to Day +22 No Ibrexafungerp related AEs were observed

Days are negative (-) for events before start of Ibrexafungerp and positive (+) for events after start of antifungal therapy, unless indicated otherwise.

CONCLUSIONS

These cases provide initial evidence of efficacy and safety of ibrexafungerp in the treatment of candidemia caused by *C. auris,* including in patients who failed previous therapies. Continued enrollment in the CARES study is warranted.

REFERENCES

[1]Five-year profile of candidaemia at an Indian trauma centre: High rates of *Candida auris* blood stream infections, P. Mathur et al., Mycoses May 2018

[2]*In Vitro* Activity of a Novel Glucan Synthase Inhibitor, SCY-078, against Clinical Isolates of *Candida auris,* Berkow et al., AAC, May 2017

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