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In Vitro Activity of a Novel Glucan Synthase Inhibitor, SCY-078, against Clinical Isolates of *Candida auris*

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Candida auris, an emerging fungal pathogen that is associated with high mortality, has been identified in many countries across the world. It is often mistaken for other *Candida* species in the clinical laboratory and has shown a marked ability to withstand standard infection control practices. More troubling, *C. auris* can exhibit *in vitro* resistance to multiple antifungal agents—creating a challenge for clinicians directing treatment (1–3). As the emergence of this serious threat to public health continues, it will be important to evaluate the efficacy of novel antifungal agents as existing options may be inadequate.

SCY-078 is a triterpene glucan synthase inhibitor (GSI) that has been shown to exhibit both *in vitro* and *in vivo* activity against the most common *Candida* species, including echinocandin-resistant isolates (4). This compound differs from other GSIs (i.e., echinocandins) in that it is orally bioavailable. Additionally, unlike that of the echinocandins, the activity of this compound is not compromised by the most common mutations within the protein target Fks (5).

Here, we evaluate the *in vitro* susceptibility of SCY-078 against a collection of 100 isolates of the emerging pathogen *Candida auris*. Isolates represent each of the four known clades of *C. auris* and originate from countries all over the world, including India, Pakistan, Colombia, South Africa, and the United States (3). The collection includes isolates known to have elevated MICs against the echinocandins. All isolates were subjected to broth microdilution according to the standards of the Clinical and Laboratory Standards Institute reference methodology M27-A3 (6). Antifungal panels were read visually after 24 h of incubation for a 50% decrease in growth compared to a drug-free control.

The distribution of MIC values of SCY-078 ranged from 0.0625 μg/ml to 2 μg/ml (Table 1). The overall mode was 1 μg/ml, and the MIC_{50} and MIC_{90} were 0.5 μg/ml and 1 μg/ml, respectively. SCY-078 showed activity against all clades of *C. auris* with very little variation in activity between the clades. These data are consistent with what has been observed with other species of *Candida* (4, 7).

The distribution of MIC values among the collection for the echinocandins ranged from 0.03 to >8 μg/ml for micafungin, 0.03 to >16 μg/ml for caspofungin, and 0.125 to >16 μg/ml for anidulafungin. Among seven isolates with elevated MICs to one or more echinocandins, the MIC range of SCY-078 was 0.5 to 1 μg/ml with a MIC_{50} of

TABLE 1 Distribution of MIC values

MIC	0.03	0.0625	0.125	0.25	0.5	1	2	4	8
No. of isolates		4	3	12	31	46	4		

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TABLE 2 SCY-078 MIC data compared to isolates with elevated echinocandin MICs

Isolate	MIC (μg/ml) of drug:			
	Anidulafungin	Caspofungin	Micafungin	SCY-078
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

1 μg/ml (Table 2). For the sake of such a compact publication, we elected to display only those isolates which displayed echinocandin resistance in Table 2.

This report describes *in vitro* susceptibilities of a large collection of *C. auris* isolates to the novel glucan synthase inhibitor SCY-078 (7). This drug is the only β-1,3-glucan synthase inhibitor with both oral and intravenous formulations in development. While there are no interpretative breakpoints for *C. auris* against SCY-078, these MIC values are within the achievable serum level and indicate widespread activity (8). There are no significant differences among MIC values between the clades, indicating that any genetic diversity arising between geographically distinct isolates does not influence the activity of the compound. Furthermore, resistance to other β-1,3-glucan synthase inhibitors is not indicative of resistance to this compound. Echinocandin-resistant isolates exhibited MICs consistent with those of echinocandin-susceptible isolates. In conclusion, SCY-078 is a promising novel antifungal agent against *Candida auris*, and further investigation is warranted.

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