In vitro Efficacy of Second-Generation Triterpenoid Antifungal, SCY-247, against Multidrug- and Pandrug-resistant Candida auris

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STUDY HIGHLIGHTS

- For 293 *Candida auris* from New York and elsewhere, the SCY-247 MIC₅₀ range was 0.03125–4 mg/L (Fig. 1).
- SCY-247 modal MICs were lower than all the azoles, 16-fold lower than amphotericin B, and similar to the echinocandins.
- For seven pandrug-resistant *C. auris* isolates, the SCY-247 MIC $_{50}$ range was 0.125–8 mg/L; modal MIC $_{50}$ values were 2 mg/L, which was lower than echinocandins (4 mg/L for anidulafungin and micafungin and 16 mg/L for caspofungin).

INTRODUCTION

- Candida auris is a newly recognized global health threat by the CDC and WHO.
- In the USA, the New York –New Jersey metropolitan area remains a hotbed for multidrug- and pandrug-resistant *C. auris* strains.
- New antifungal drugs are needed against drug-resistant C. auris.
- We evaluated SCY-247 (Fig. 2), a second-generation IV/oral triterpenoid antifungal that targets β-(1,3)-d-glucan biosynthesis, for its in vitro efficacy against multidrug- and pandrug-resistant C. auris.

METHODS

- C. auris test panel included 300 isolates (predominantly Clade I),
 - 281 were collected in New York between 2014 and 2023
 - 227 clinical, 37 surveillance, and 17 environmental
 - 19 were from the CDC-FDA AR bank
 - 7 of the 300 isolates were pandrug-resistant
- Isolates were tested against SCY-247, fluconazole (FLZ), Voriconazole (VRC), Itraconazole (ITR), Isavuconazole (ISA), Posaconazole (POS), Anidulafungin (AND), Caspofungin (CAS), Micafungin (MCF), Amphotericin B (AMB), and Flucytosine (FLC)
- CLSI M-27 Ed4 reference method was used to prepare in-house drug panels and included QC strains C. krusei ATCC 6258 and C. parapsilosis ATCC 22019.
- MIC₅₀ was recorded as the minimum concentration that led to 50% reduction in fungal growth compared with the control.
- Data was analyzed with Microsoft Excel, and the ECOFF determined according to Turnidge J, Kalhmeter G, Kronvall G.. Clin Microbiol Infect 2006; 12:418-25

RESULTS

Antifungal	No. Isolates	MIC50	MIC Range	Median	Mode
SCY-247	293	0.125	0.03-2	0.5	0.125
FLZ	293	>256	8->256	>256	>256
VRC	293	2	0.01-8	2	2
ITR	292	0.5	0.06-1	0.5	0.5
ISA	293	0.05	0.008-4	1	1
POS	293	0.25	0.008-2	0.25	0.25
AND	293	0.12	0.03-16	0.5	0.25
CAS	193	0.03	0.015-16	0.12	0.12
MCF	292	0.12	0.06-8	0.12	0.12
AMB	293	2	0.25-24	1	2
FLC	250	0.064	0.02-32	0.094	0.064

Table 1. SCY-247 Antifungal test results for 274 New York *Candida auris* isolates & 19 CDC-FDA AR Bank

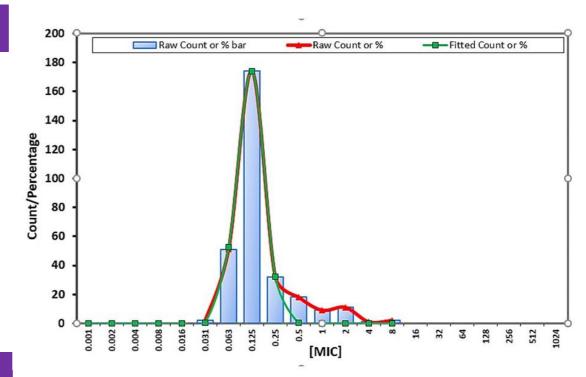


Fig. 1. SCY-247 WT-UL for C. auris per ECOFFinder

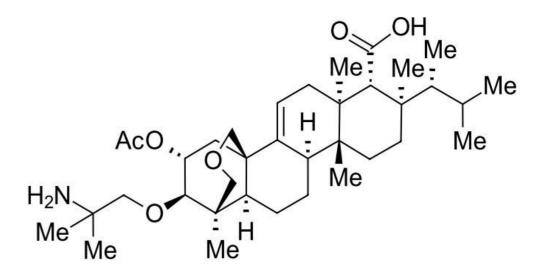


Fig. 2. SCY-247 chemical structure.

Antifungal	MIC50	MIC Range
SCY-247	2	0.125-8
FLZ	256	>256
VRC	2	2-16
ITR	1	0.5-1
ISA	4	0.5-4
POS	0.5	0.25-1
AND	4	4
CAS	16	2-16
MCF	4	4-8
AMB	1	0.75-4
FLC	8	0.06-8

Table 2. SCY-247 and comparator drugs activity for seven pandrug-resistant *Candida auris*

Conclusions

- 1.SCY-247 is a promising antifungal against *C. auris*
- 2. Clinical studies are needed to evaluate SCY-247 therapeutic potential for *C. auris* infections

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