308
06/04/17

Assessment of the In Vitro Antifungal Activity of SCY-078 Against a Panel of Susceptible and Resistant, Clinical *Candida* Isolates from Europe

Katyna Borroto-Esoda[1], S. Birchall[2], C. B. Moore[3], D. Angulo[1];

[1]Scynexis Inc, Jersey City, NJ, [2]Evotec (UK) Ltd, Manchester, UK, [3]Univ. Hosp. of South Manchester, Manchester, UK

SCYNEXIS, Inc.
Tel. 201-884-5485
info@scynexis.com

INTRODUCTION & PURPOSE

SCY-078 is a novel intravenous and oral triterpenoid antifungal agent that is currently in clinical development for the treatment of both invasive and mucocutaneous fungal infections. It has broad-spectrum activity against both *Candida and Aspergillus*.

SCY-078 has demonstrated *in vitro* activity against wildtype and drug-resistant *Candida* spp. Based on evaluation of wildtype and echinocandin resistant *C. glabrata* isolates, a preliminary epidemiological cutoff value of 2 µg/mL has been proposed for this species*.

The purpose of this study to evaluate the *in vitro* antifungal activity of SCY-078 against a panel of recent clinical *Candida* isolates from the EU

METHODS

A panel of 270 clinical *Candida* strains isolated from referring hospitals throughout the UK between January 2015 and March 2016 were used to assess the *in vitro* antifungal activity of SCY-078. The collection comprised *C. albicans* (*n* = 99), *C. glabrata* (*n* = 72), *C. guilliermondii* (*n* = 17), *C. krusei* (*n* = 14), *C. lusitaniae* (*n* = 10), *C. parapsilosis* (*n* = 41), *C. dubliniensis* (*n* = 6), *C. inconspicua* (*n* = 1), *C. kefyr* (*n* = 2) and *C. tropicalis* (*n* = 9).

Antifungal susceptibility test assays were performed according to the European Committee on Antimicrobial Susceptibility Testing (EUCAST) document E.DEF 7.3 Method for the determination of broth dilution minimum inhibitory concentrations (MICs) of antifungal agents for yeasts.

The MIC of SCY-078, azole antifungals and echinocandins was determined as the lowest concentration of drug giving inhibition of growth of ≥50% of that of the drug-free control. For amphotericin B, the MIC was determined as the lowest concentration giving rise to an inhibition of growth of ≥90% of that of the drug-free control. MIC_{50} and MIC_{90} values were defined as the concentration of test articles at which the growth of 50% ($n \times 0.5$) or 90% ($n \times 0.9$) of test species, or all test strains, respectively, was inhibited.

RESULTS

MIC_{50} & MIC_{90} Results Summary

Test Article MIC_{50} / MIC_{90} (µg/mL)

Species	MIC_{50} MIC_{90}	SCY-078	Amphotericin B	Anidulafungin	Micafungin	Caspofungin	Fluconazole	Voriconazole	Posaconazole
C. albicans (n= 99)	MIC_{50}	0.25	1	0.125	0.125	0.125	0.25	≤0.008	0.125
	MIC_{90}	1	1	0.25	0.25	0.5	2	0.03	0.25
C. glabrata (n= 72)	MIC_{50}	1	1	0.25	0.06	0.25	2	0.125	0.5
	MIC_{90}	1	1	1	0.25	1	32	1	1
C. guilliermondii (n= 17)	MIC_{50}	2	1	2	1	1	4	0.125	1
	MIC_{90}	>4	1	4	1	2	>64	1	1
C. krusei (n= 14)	MIC_{50}	1	1	0.125	0.25	0.5	64	0.25	0.25
	MIC_{90}	2	2	0.5	1	1	>64	1	1
C. lusitaniae (n= 10)	MIC_{50}	2	1	0.25	0.25	0.5	0.125	≤0.008	0.06
	MIC_{90}	>4	1	1	1	1	16	0.03	0.125
C. *parapsilosis* (n= 41)	MIC_{50}	1	1	2	2	1	0.5	0.016	0.125
	MIC_{90}	2	1	4	4	2	2	0.03	0.25

SCY-078 MICs vs DRUG RESISTANT *C. glabrata*

C. glabrata Isolates	Total (N=72)	Anidulafungin Resistant (N=64)	Micafungin Resistant (N=43)	Anidulafungin and Micafungin Resistant (N=41)	Fluconazole Resistant (N=7)
SCY-078 MIC (µg/mL)	MIC_{50} = 1 MIC_{90} = 1 Range 0.125 - 2	MIC_{50} = 1 MIC_{90} = 1 Range 0.25 - 2	MIC_{50} = 1 MIC_{90} = 1 Range 0.25 - 2	MIC_{50} = 1 MIC_{90} = 1 Range 0.25 - 2	Range 0.25 - 1

CONCLUSION

SCY-078 demonstrated potent, broad spectrum activity against a panel of clinical *Candida* isolates.
Notably, SCY-078 retained activity against all of the echinocandin- and azole-resistant *C. glabrata* isolates tested.