Poster #44

SCY-078; The First Orally Bioavailable, Glucan Synthase Inhibitor, Demonstrates Potent *In vitro* Activity Against Azole-Resistant *Candida spp.*

Scynexis Inc
(201-884-5485)
Steve.wring@scynexis.com

[1]K. Borroto-Esoda, D. Angulo, [2]S. Moser, [2]J. Whiddon, [3]P. Pappas, [4]D. Perlin and [1]S. Wring
[1]Scynexis Inc, Jersey City NJ [2]Univ. of Alabama, Birmingham Division of Infections Diseases, Dept of Clinical Micro/Pathology, [3]Univ. of Alabama, Birmingham Department of Pathology, [4]Public Health Research Institute, Rutgers University, NJ

Background

- Broad use of the azole-class of antifungal compounds has led to an increased incidence of infections caused by azole-resistant (intrinsic and acquired) *Candida spp.*
- Antifungal therapy for azole-resistant candidemia is limited to the echinocandin (ECH) and polyene classes of compounds, which unlike the azoles, are only available as intravenous (IV) formulations.
- SCY-078, like ECHs is a 1,3-ß-D-glucan synthesis inhibitor (GSI); however, in contrast to ECH and amphotericin B, it is orally bioavailable being the first in class of structurally novel triterpene antifungals in clinical development for the treatment of *Candida spp.* infections.
- Here we report *in vitro* activity of SCY-078 against azole resistant *Candida spp.*

Methods

- *In vitro* MIC data (50% inhibition at 24 h) for SCY-078 against multiple *Candida spp.* were compiled from across 3 independent studies and included 34 *C. albicans*, 174 *C. glabrata*, 4 *C. parapsilosis*, and 5 *C. tropicalis isolates* with fluconazole (FLU) resistance plus WT controls. Isolates were collected between 2005-2015.
- *In vitro* susceptibility was determined by broth micro-dilution using CLSI methods (M27-S3).
- Fluconazole was used as a control for azole resistance across studies.
- Resistance to FLU was defined as MIC ≥8 and ≥64 µg/mL *for C. albicans* and *C. glabrata*, respectively (CLSI guidelines M27-S4).
- Resistance to SCY-078 was defined as MIC values >4-fold than that observed for WT isolates.

Results Summary

- MIC_{50} values for SCY-078 ranged from 0.03 to 0.5 µg/mL across WT *Candida spp.*
- There were no significant differences in MIC_{50} values obtained for SCY-078 against FLU-resistant strains as compared to WT.
- Overall, SCY-078 was active (MIC similar to WT) against 202/217 (93%) of the FLU-resistant strains tested in these studies

Resistance to Fluconazole Observed Across *Candida Spp*

Fluconazole MIC[a] (µg/mL) - Study 1		
Candida spp.	WT	Flu-R
C. albicans	0.25 (N=29)	64 (N=13)
C. glabrata	32 (N=29)	128 (N=12)
C. tropicalis	0.5 (N=21)	16 – 128 (N=4)
C. parapsilosis	1 (N=15)	8 – 64 (N=5)

[a]Values represent ranges for spp with <10 strains, MICs for spp with N>10
Data from Pfaller et al. JAC 2013 Vol 68

Fluconazole MIC (µg/mL) - Study 2[a]			Fluconazole MIC (µg/mL) - Study 3[b]		
Candida spp.	WT	Flu-R	*Candida spp.*	WT	Flu-R
C. albicans	0.12 (N=10)	>64 (N=21)	*C. glabrata*	8 (N=137)	≥64 (N=162)

[a]Isolates collected at PHRI. [b]Isolates colected at UAB Mycology reference laboratory

SCY-078 Displayed Similar MIC values across WT and FLU-R *Candida Spp*

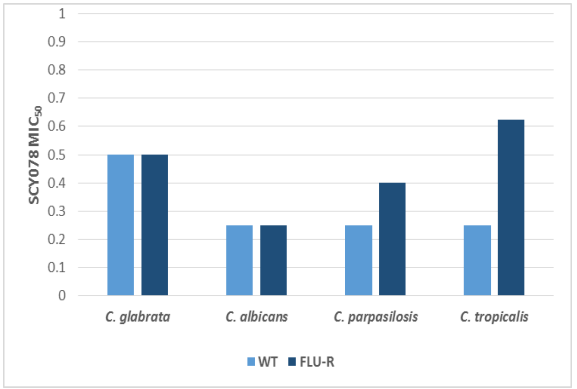
SCY-078 MIC[a] (µg/mL) - Study 1		
Candida spp.	WT	Flu-R
C. albicans	0.12 (N=29)	0.25 (N=13)
C. glabrata	0.5 (N=29)	0.5 (N=12)
C. tropicalis	0.25 (N=21)	0.25 - 1 (N=4)
C. parapsilosis	0.25 (N=15)	0.25 – 0.5 (N=5)

[a]Values represent ranges for spp with <10 strains, MICs for spp with N>10
Data from Pfaller et al. JAC 2013 Vol 68

SCY-078 MIC (µg/mL) - Study 2			SCY-078 MIC (µg/mL) - Study 3		
Candida spp.	WT	Flu-R	*Candida spp.*	WT	Flu-R
C. albicans	0.03 (N=10)	0.03 (N=21)	*C. glabrata*	0.5 (N=137)	0.5 (N=162)

[a]Isolates collected at PHRI. [b]Isolates collected at UAB Mycology reference laboratory

SCY-078 Demonstrated Potent Activity Against FLU-R *Candida*



Resistance to SCY-078 (MIC values >4-fold that of WT) was observed among 8/174 *C. glabrata*, 5/34 *C. albicans*, 0/5 *C. parapsilosis* and 2/4 *C. tropicalis* isolates.

Conclusions

SCY-078 demonstrated potent *in vitro* antifungal activity against 93% of the azole-resistant *Candida spp* tested. These results suggest that SCY-078 has the potential to be the first, orally bioavailable therapeutic option for the treatment of Invasive Candidiasis infections caused by azole-resistant *Candida* strains.