Poster #46

SCY-078 Displays Significant *In-Vitro* Activity Against Multi Drug Resistant (MDR) *Candida albicans* and *Candida glabrata* Isolates

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

K. Borroto-Esoda[1], D. Angulo[1], S. Moser[3], J. Whiddon[3], P. Pappas[2], and S. Wring[1]

[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

Background

- Patients infected with multi-drug resistant (MDR) *Candida* typically experience worsened clinical outcomes[a].
- 2016 IDSA treatment guidelines for candidiasis recommend lipid formulations of amphotericin B (LFAMB) for these patients[b].
- However, LFAMB is associated with significant adverse events that limits its use[c].
- SCY-078 is a 1,3-β-D-glucan synthesis inhibitor (GSI) and first-in-class of structurally novel triterpene antifungals in clinical development as both oral and intravenous formulations for the treatment of candidemia and invasive candidiasis.
- SCY-078 has demonstrated *in vitro* activity against echinocandin (ECH) and fluconazole (FLU) resistant strains (see posters 45 and 44).
- Here we report the *in vitro* activity of SCY-078 against multi-drug resistant (MDR) *Candida* strains with resistance to both ECHs and FLU.

Methods

- To identify MDR strains, *in vitro* MIC data for caspofungin (CASP), micafungin (MICA) and fluconazole (FLU) were analyzed across 2 independent studies that evaluated over 400 clinical *Candida spp* isolates collected between 2005 and 2015.
- In both studies, the *in vitro* susceptibility (MIC: 50% inhibition at 24 hrs) was determined by broth micro-dilution using CLSI methods (M27-S3).
- Resistance to CASP, MICA and FLU was determined according to the CLSI guidelines (M27-S4).
- Resistance to SCY-078 was defined as isolates having an MIC values >4-fold that of wild-type (WT)

Results Summary

- Twenty one clinical isolates comprising 8 *C. albicans* and 17 *C. glabrata* isolates met the criteria for ECH and FLU resistance.
- *In vitro* MIC values for FLU were ≥16 μg/mL and ≥64 μg/mL for *C. albicans* and *C. glabrata* respectively
- MIC values for CASP were ≥ 1 and ≥ 2 μg/mL against *C. albicans* and *C. glabrata*, respectively.
- MIC values for MICA against the C. *glabrata* strains was ≥ 0.25 μg/mL.
- Overall, SCY-078 was active *in vitro* against 6/8 (75%) of the MDR *C. albicans* strains and 12/17 (71%) *C. glabrata* strains tested.

Activity of SCY-078 and Comparators Against MDR *C. albicans* Isolates[d]

CLSI MIC (μg/mL)		
SCY-078*	CASP	FLU
0.5	1	64
0.5	2	16
0.25	2	128
0.125	2	64
2	1	128
0.25	1	128
0.25	1	32
1	8	64

[d]Data from Pfaller et.al, JAC 2013
*SCY-078 MIC_{50} vs WT *C. albicans* = 0.125 mg/mL: Resistance to SCY-078 defined as MIC ≥1 μg/mL against *C. albicans*

Activity of SCY-078 and Comparators Against MDR *C. glabrata* isolates[d]

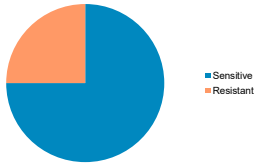
CLSI MIC (μg/mL)			
SCY-078	CASP	MICA	FLU
2	1	ND	128
1	2	ND	64
1	16	ND	128
1	16	ND	64
1	0.5	ND	64
1	8	ND	128
1	ND	4	64
2	ND	2	64
1	ND	2	64
2	ND	2	64
1	ND	1	64
2	ND	0.5	64
2	ND	0.5	64
1	ND	0.25	64
1	ND	0.25	64
1	ND	0.25	64
0.5	ND	0.25	64

[d]CASP data from Pfaller et.al., JAC 2013
*SCY-078 MIC_{50} vs. WT *C. glabrata* = 0.5 μg/mL: Resistance to SCY-078 defined as MIC ≥2 μg/mL against *C. glabrata*

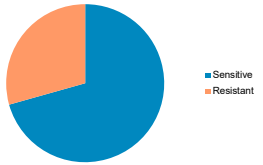
CLSI Resistance Guidelines:
C. albicans – CASP ≥1, MICA ≥1, FLU ≥8
C. glabrata – CASP ≥0.5, MICA ≥0.25., FLU ≥64

SCY-078 Retains Activity Against the Majority of MDR Clinical Isolates

75% of MDR-*C. Albicans* Isolates Remain Sensitive to Inhibition by SCY-078



71% of MDR-*C. Glabrata* Isolates Remain Sensitive to Inhibition by SCY-078



Conclusions

In vitro, the majority of MDR *C. albicans* and *C. glabrata* clinical isolates remained sensitive to inhibition by SCY-078 with MIC values ≤1 μg/mL. These results suggest that SCY-078 may be a suitable option for the treatment of selected infections caused by echinocandin and azole resistant *C. albicans* and *C. glabrata* strains.

References
[a]Farmakiotis et.al., Emerging Infectious Diseases 2014
[b]Pappas et.al., CID 2015
[c]Dupont, B. JAC 2002

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