1206

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Assessment of the *In Vitro* Antifungal Activity of SCY-078 Against a Collection of *C. parapsilosis* Clinical Isolates

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BACKGROUND

Global rates of candidemia caused by *C. parapsilosis* are increasing with differences detected between neonates and adult patients (50% vs. 12%, respectively) and across geographic regions (5% vs. 25% in Iceland and Spain, respectively). SCY-078 is a novel, oral and intravenous, triterpenoid glucan synthase inhibitor under development for the treatment of invasive candidiasis. This study evaluated the *in vitro* antifungal activity of SCY-078 against a collection of clinical *C. parapsilosis* isolates.

METHODS

- *In vitro* MIC data (50% inhibition at 24 hrs) for SCY-078 against *C. parapsilosis* were compiled from across 7 independent studies.
- The studies included more than 200 *C. parapsilosis* isolates collected between 2008-2015 in the US and EU and included 191 wild-type, 14 azole-resistant, and 6 echinocandin-resistant isolates.
- Across the studies, *in vitro* susceptibility was determined by broth micro-dilution using CLSI methods (M27-S3).
- Comparator compounds varied by study and included micafungin (MCF), caspofungin (CSP), and anidulafungin (ANF).

CONCLUSION

SCY-078 demonstrated potent activity against *C. parapsilosis* clinical isolates. Notably, SCY-078 was effective against all the echinocandin- and azole-resistant *C. parapsilosis* isolates tested.

RESULTS

MIC_{50} values obtained for SCY-078 against the wild-type *C. parapsilosis* isolates across the 7 studies ranged from 0.25 to 1 μg/mL, MIC_{90} values ranged from 0.25 -2 μg/mL. MIC_{90} values obtained for the echinocandins ranged from 0.5 to 2 μg/mL (CSP), 1 to 4 μg/mL (MCF) and 2 to 4μg/mL (ANF). SCY-078 was active against the 14 azole-resistant isolates (MIC ranging from 0.25 to 2 μg/mL). Similar activity was observed across the 6 echinocandin-resistant isolates with MIC values for SCY-078 ranging from 0.25 to 1 μg/mL. Consistent with reports of increased incidence of *C.parapsilosis* infections, this species represented from 14 –20% of all the *Candida* isolates collected in the 4 most recent studies in the US and EU (2013-2015).

Activity of SCY-078 and Comparator Compounds Against WT *C. parapsilosis* clinical isolates

	SCY078 MIC_{50} MIC_{90} (μg/mL)	CSP MIC_{50} MIC_{90} (μg/mL)	MCF MIC_{50} MIC_{90} (μg/mL)	ANF MIC_{50} MIC_{90} (μg/mL)
US Study1 2009[a] (N=15)	0.25 0.5	0.5 0.5	NA	NA
US Study 2 2012[b] (N=19)	0.5 2	0.5 1	NA	NA
US Study 3 2013[c] (N=43)	0.5 1	0.5 1	2 2	2 4
US Study 4 2013[d] (N=19)	0.25 0.25	0.25 0.5	1 2	1 2
EU Study 1 2012[e] (N=27)	0.25 0.5	0.5 1	NA	NA
EU Study 2 2015[f] (N=32)	0.25 0.5	NA	0.5 1	NA
EU Study 3 2016[g] (N=36)	1 2	1 2	2 4	2 4

[a]Pfaller et al. JAC 2013, [b]Jimenez-Ortigosa et al. AAC 2014, [c]Pfaller et al. AAC 2017, [d]Shell et al. AAC 2017, [e]Data on file (Eurofin), [f]Marcos-Sabrano et al. JAC 2017 , [g]Borroto-Esoda et al. ASM Microbe 2017

Activity of SCY-078 and Comparator Compounds Against Azole-Resistant *C. parapsilosis* clinical isolates

	SCY078 MIC (μg/mL)	CSP MIC (μg/mL)	MCF MIC (μg/mL)	ANF MIC (μg/mL)
US Study1 2009[a] (N=5)	0.25-0.5	0.25-0.5	NA	NA
US Study 4 2013[b] (N=1)	0.5	0.125	0.5	1
EU Study 1 2012[c] (N=4)	0.25-0.5	0.5-1	NA	NA
EU Study 2 2015[d] (N=1)	0.25	NA	0.25	NA
EU Study 3 2016[e] (N=3)	1-2	1-2	1-4	1-4

[a]Pfaller et al. JAC 2013, [b]Shell et al. AAC 2017, [c]Data on file (Eurofin), [d]Marcos-Sabrano et al. JAC 2017 , [e]Borroto-Esoda et al. ASM Microbe 2017

Activity of SCY-078 and Comparator Compounds Against Echinocandin-Resistant *C. parapsilosis* clinical isolates

	SCY078 MIC (μg/mL)	CSP MIC (μg/mL)	MCF MIC (μg/mL)	ANF MIC (μg/mL)
US Study 3 2013[a] (N=3)	0.25-1	0.5	2	1-4
US Study 4 2013[b] (N=1)	0.5	0.25	2	4
EU Study 3 2016[c] (N=2)	1-2	2-4	>4	4->4

[a]Pfaller et al. AAC 2017, [b]Shell et al. AAC 2017, [c]Borroto-Esoda et al. ASM Microbe 2017

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