

# 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<sub>50</sub> 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<sub>90</sub> values ranged from 0.25 -2 µg/mL. MIC<sub>90</sub> values obtained for the echinocandins ranged from 0.5 to 2 µg/mL (CSP), 1 to 4 µg/mL (MCF) and 2 to 4 µg/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 <sub>50</sub> MIC <sub>90</sub> (µg/mL)	CSP MIC <sub>50</sub> MIC <sub>90</sub> (µg/mL)	MCF MIC <sub>50</sub> MIC <sub>90</sub> (µg/mL)	ANF MIC <sub>50</sub> MIC <sub>90</sub> (µg/mL)
US Study1 2009 <sup>a</sup> (N=15)	0.25 0.5	0.5 0.5	NA	NA
US Study 2 2012 <sup>b</sup> (N=19)	0.5 2	0.5 1	NA	NA
US Study 3 2013 <sup>c</sup> (N=43)	0.5 1	0.5 1	2 2	2 4
US Study 4 2013 <sup>d</sup> (N=19)	0.25 0.25	0.25 0.5	1 2	1 2
EU Study 1 2012 <sup>e</sup> (N=27)	0.25 0.5	0.5 1	NA	NA
EU Study 2 2015 <sup>f</sup> (N=32)	0.25 0.5	NA	0.5 1	NA
EU Study 3 2016 <sup>g</sup> (N=36)	1 2	1 2	2 4	2 4

<sup>a</sup>Pfaller et al. JAC 2013, <sup>b</sup>Jimenez-Ortigosa et al. AAC 2014, <sup>c</sup>Pfaller et al. AAC 2017, <sup>d</sup>Shell et al. AAC 2017, <sup>e</sup>Data on file (Eurofin), <sup>f</sup>Marcos-Sabrano et al. JAC 2017, <sup>g</sup>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 <sup>a</sup> (N=5)	0.25-0.5	0.25-0.5	NA	NA
US Study 4 2013 <sup>b</sup> (N=1)	0.5	0.125	0.5	1
EU Study 1 2012 <sup>c</sup> (N=4)	0.25-0.5	0.5-1	NA	NA
EU Study 2 2015 <sup>d</sup> (N=1)	0.25	NA	0.25	NA
EU Study 3 2016 <sup>e</sup> (N=3)	1-2	1-2	1-4	1-4

<sup>a</sup>Pfaller et al. JAC 2013, <sup>b</sup>Shell et al. AAC 2017, <sup>c</sup>Data on file (Eurofin), <sup>d</sup>Marcos-Sabrano et al. JAC 2017, <sup>e</sup>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 <sup>a</sup> (N=3)	0.25-1	0.5	2	1-4
US Study 4 2013 <sup>b</sup> (N=1)	0.5	0.25	2	4
EU Study 3 2016 <sup>c</sup> (N=2)	1-2	2-4	>4	4->4

<sup>a</sup>Pfaller et al. AAC 2017, <sup>b</sup>Shell et al. AAC 2017, <sup>c</sup>Borroto-Esoda et al. ASM Microbe 2017