

Activity of Rezafungin against Clinical *Candida* and *Aspergillus* spp. Isolates Collected in Asia-Pacific Countries (2014-2018)

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OBJECTIVES

Rezafungin (RZF) is a novel echinocandin with an extended half-life and high, front-loaded drug exposure that allows for once-weekly dosing. RZF is undergoing Phase 3 development for treatment of invasive candidiasis and candidemia as well as for the prevention of invasive fungal disease caused by *Candida* and *Aspergillus* spp. and *Pneumocystis jirovecii* in allogeneic blood and marrow transplant patients. Here we analyzed RZF activity against *Candida* and *Aspergillus* spp. isolates collected from countries within the Asia-Pacific region between 2014 and 2018.

METHODS

The in vitro activity of RZF was evaluated as part of the JMI Laboratories international SENTRY Antimicrobial Surveillance Program. CLSI broth microdilution MIC/MEC values (M27, M38) were generated for RZF and comparators anidulafungin (ANF), caspofungin (CSF), micafungin (MCF), fluconazole (FLU; yeasts only), itraconazole (ITR, moulds only), posaconazole (POS), voriconazole (VOR), and amphotericin B (AMB). A total of 3,419 isolates of *Candida* spp. (*C. albicans*, *C. glabrata*, *C. tropicalis*, *C. parapsilosis*, *C. krusei*, and *C. dubliniensis*) and *Aspergillus* spp. (*A. fumigatus* and *A. flavus*) were collected globally during the 2014-2018 surveillance programs^{1,2,3}, 432 of which were from AP countries (Australia, Korea, New Zealand, Philippines, Singapore, and Thailand).

RESULTS

Table 1. Rezafungin MIC/MEC values for Asia-Pacific vs. Global surveillance isolates

| Species | RZF MIC/MEC (µg/mL) | | | | | | | |
|------------------------|----------------------|-------------------|-------------------|----------------|------------------|-------------------|-------------------|--------------|
| | Asia-Pacific (n=432) | | | | Global (n=3,419) | | | |
| | n | MIC ₅₀ | MIC ₉₀ | Range | n | MIC ₅₀ | MIC ₉₀ | Range |
| <i>C. albicans</i> | 187 | 0.03 | 0.06 | ≤0.008 - 0.12 | 1390 | 0.03 | 0.06 | 0.002 - 0.25 |
| <i>C. glabrata</i> | 66 | 0.03 | 0.06 | 0.03 - 0.12 | 595 | 0.06 | 0.12 | 0.002 - 4 |
| <i>C. tropicalis</i> | 70 | 0.015 | 0.03 | ≤0.008 - 0.12 | 302 | 0.03 | 0.06 | 0.008 - 2 |
| <i>C. parapsilosis</i> | 48 | 1 | 2 | 0.5 - 2 | 504 | 1 | 2 | 0.015 - 4 |
| <i>C. krusei</i> | 14 | 0.03 | 0.12 | 0.015 - 0.12 | 107 | 0.03 | 0.06 | 0.015 - 0.12 |
| <i>C. dubliniensis</i> | 7 | 0.03 | 0.12 | 0.03 - 0.12 | 116 | 0.06 | 0.12 | 0.015 - 0.12 |
| <i>A. fumigatus</i> | 30 | 0.015 | 0.015 | ≤0.008 - 0.03 | 336 | 0.015 | 0.03 | 0.004 - 0.03 |
| <i>A. flavus</i> | 10 | 0.008 | 0.015 | ≤0.008 - 0.015 | 69 | ≤0.008 | 0.015 | 0.004 - 0.03 |

- RZF had potent activity against *Candida* spp. isolates from Asia-Pacific with MIC₅₀ values of 0.015-0.03 µg/mL and MIC₉₀ values of 0.03-0.12 µg/mL for non-*parapsilosis* spp. MIC₅₀ and MIC₉₀ values for *C. parapsilosis* were 1 and 2 µg/mL, respectively.
- Asia-Pacific RZF MIC/MEC_{50/90} values were largely equivalent to or within 1 dilution of Global values.

Table 2. Rezafungin and comparator antifungal MIC/MEC values for Asia-Pacific surveillance isolates

| Species | n | MIC _{50/90} (µg/mL) | | | | | | | | |
|------------------------|-----|------------------------------|-------------|------------|--------------|------------|-------|-----------|--------------|-------|
| | | RZF | ANF | CSF | MCF | FLU | ITR | POS | VOR | AMB |
| <i>C. albicans</i> | 187 | 0.03/0.06 | 0.015/0.03 | 0.015/0.03 | 0.015/0.03 | 0.06/0.25 | | 0.03/0.06 | ≤0.008/0.015 | 0.5/1 |
| <i>C. glabrata</i> | 66 | 0.03/0.06 | 0.06/0.12 | 0.03/0.06 | 0.015/0.03 | 4/16 | | 0.5/1 | 0.12/0.5 | 1/1 |
| <i>C. tropicalis</i> | 70 | 0.015/0.03 | 0.015/0.03 | 0.015/0.03 | 0.015/0.03 | 0.25/1 | | 0.03/0.12 | 0.015/0.06 | 1/1 |
| <i>C. parapsilosis</i> | 48 | 1/2 | 2/2 | 0.25/0.5 | 1/2 | 0.5/2 | | 0.06/0.12 | 0.015/0.03 | 1/1 |
| <i>C. krusei</i> | 14 | 0.03/0.12 | 0.03/0.12 | 0.06/0.12 | 0.06/0.12 | 32/32 | | 0.5/0.5 | 0.25/0.5 | 1/2 |
| <i>C. dubliniensis</i> | 7 | 0.03/0.12 | 0.03/0.12 | 0.03/0.03 | 0.03/0.03 | ≤0.12/0.12 | | 0.03/0.06 | ≤0.008/0.008 | 0.5/1 |
| <i>A. fumigatus</i> | 30 | 0.015/0.015 | 0.015/0.03 | 0.03/0.03 | ≤0.008/0.015 | | 0.5/1 | 0.25/0.5 | 0.5/0.5 | 1/2 |
| <i>A. flavus</i> | 10 | 0.008/0.015 | 0.015/0.015 | 0.03/0.03 | 0.015/0.03 | | 0.5/1 | 0.25/0.5 | 0.5/1 | 2/2 |

- The RZF susceptibility to yeast and mould isolates collected from Asia-Pacific hospitals was comparable to their susceptibility to approved echinocandins.
- RZF (MIC_{50/90}, 0.03/0.06-0.12 µg/mL) and other echinocandins (MIC_{50/90}, 0.015-0.06/0.03-0.12 µg/mL) were active against species with elevated azole MIC values, such as *C. glabrata* and *C. krusei*.

CONCLUSION

- RZF demonstrated potent antifungal activity against contemporary isolates of *Candida* and *Aspergillus* spp. collected in Asia-Pacific countries, in line with clinically available echinocandins.
- The activity of RZF against Asia-Pacific surveillance isolates was consistent with isolates collected globally.

REFERENCES

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DISCLOSURES / ACKNOWLEDGEMENTS

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