Evaluation of the Post-Antifungal Effect of Rezafungin and Micafungin against Candida albicans, Candida parapsilosis, and Candida glabrata

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Introduction

- Post-antifungal effect (PAFE) is defined as the growth suppression of fungal cells after their exposure to an antifungal agent.
- Understanding PAFE helps evaluate dosage regimens for an antifungal agent.

Materials and Methods

- Six Candida spp. isolates were tested, including 2 C. albicans (ATCC 90028 and #1 clinical isolate), 2 C. parapsilosis (ATCC 22019 and #2 clinical isolate), and 2 C. glabrata (#3 and #4 clinical isolates).
- Antifungal susceptibility testing was performed using the Clinical and Laboratory Standards Institute (CLSI) reference broth microdilution method.
- Rezafungin (Cidara Therapeutics) and micafungin (Gilead Health) were tested.
- Each isolate was tested in triplicate to establish baseline MIC values (CLSI).
- Modal MIC values were used to determine drug concentrations for PAFE testing.

Results

- PAFE and MIC results for rezafungin and micafungin are shown in Table 1.
- C. albicans
  - Rezafungin PAFE results were >40 h against the C. albicans clinical isolate for all concentrations tested.
  - The C. albicans ATCC 90028 control failed to regain >1 log CFU/mL after the final cell wash compared to the untreated growth control.

- Micafungin PAFE results were equivalent to rezafungin PAFE values (>40 h) for all concentrations tested.

- Modal MIC values were used to determine drug concentrations for PAFE testing.

- PAFE was calculated as the difference in time required for isolates to grow 1-log10 after undergoing the same process performed on the test culture.

- Colony counts were performed at T0 (pre-exposure), after the 1-h drug exposure, and after a 1-h exposure to the antifungal agent, the cells were washed three times with RPMI with 1% glucose and then reconstituted in RPMI with 1% glucose containing 1X, 4X, or 16X MIC.

- After a 1-h exposure to the antifungal agent, the cells were washed three times with RPMI with 1% glucose and reconstituted with prewarmed RPMI to a final volume of 1X MIC.

- Colony counts were performed at T0 (pre-exposure), after the 1-h drug exposure, and after the cell wash (T1).

- The growth control that was not exposed to an antifungal agent was used to determine the standard 1-log10 increase.

- After a 1-h exposure to the antifungal agent, the cells were washed three times with RPMI with 1% glucose and reconstituted with prewarmed RPMI to a final volume of 1X MIC.

- Colony counts were performed at T0 (pre-exposure), after the 1-h drug exposure, and after the cell wash (T1).

- The micafungin PAFE value was 20.4 h for C. glabrata isolate #4.

- Micafungin PAFE results were equivalent to rezafungin PAFE values (>40 h) for all concentrations tested.

- The rezafungin PAFE value was 20.4 h for C. glabrata #1 isolate, while the rezafungin PAFE was >46.7 h.

Conclusion

- Rezafungin showed sustained growth inhibition following drug removal and displayed equivalent or longer PAFE values than micafungin against all tested Candida spp.

Acknowledgements

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References


Contact

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Table 1. PAFE for rezafungin and micafungin against C. albicans, C. parapsilosis, and C. glabrata

| Antifungal/Strain | Baseline MIC (µg/mL) | MIC of isolate (µg/mL) | PAFE (hours) from drug removal | Log10 (CFU/mL) | Rezafungin | Micafungin
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Abbreviations: ND, not determined