Rezafungin (RZF) is more effective than micafungin (MFG) in treating FKS-mutant Candida glabrata (CG) intra-abdominal candidiasis (IAC).

Kevin Squires,1 Shaoji Cheng,1 Yinan Zhao,1 David Perlin,2 Cornelius J Clancy,1 M. Hong Nguyen1

1Department of Medicine, Division of Infectious Diseases, University of Pittsburgh, Pittsburgh, PA, USA; 2Public Health Research Institute, New York Medical College, Rutgers Biomedical and Health Sciences, Newark, New York, USA

Contact information: M. Hong Nguyen, M.D., University of Pittsburgh
412-383-5193

INTRODUCTION

- IAC is among the 5 most common causes of IC.
- Echinocandins is the gold standard therapy for IC, including IAC; however, there are limited data on echinocandin pharmacokinetics/pharmacodynamics (PK-PD) at sites of Candida infection.
- Echinocandin treatment failures and emergence of resistance are common among patients with IAC, in particular due to C. glabrata.
- RZF is a novel echinocandin with high plasma drug exposures and long half-life, suitable for prolonged dosing intervals.

OBJECTIVES

- To compare the efficacy of RZF versus MFG in a murine model of intra-abdominal abscesses (IAA) due to C. glabrata
- To determine the spatial and quantitative distribution of RZF and MFG in tissues of mice with IAA

METHODS

- Murine model of IAA
  - Male 6-8 week-old mice (18-25 g) were infected intraperitoneally (IP) with 1x10^7 CFU of CG B02 (wild-type FKS) or 2 clinical isolates with FKS2 mutations (F6595S or F6598a)

RESULTS

Table 1. RZF and other echinocandins MICs against FKS wild-type and mutant C. glabrata

<table>
<thead>
<tr>
<th>Isolates</th>
<th>RZF MIC (\mu)g/mL</th>
<th>MFG MIC (\mu)g/mL</th>
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<tbody>
<tr>
<td>B02</td>
<td>0.035</td>
<td>0.35</td>
</tr>
<tr>
<td>21</td>
<td>F6595 - FKS2</td>
<td>0.06 - 0.5</td>
</tr>
<tr>
<td>4</td>
<td>F6598 - FKS2</td>
<td>0.35 - 1</td>
</tr>
</tbody>
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Fig. 1. RZF and MFG against FKS wild-type and mutants C. glabrata isolates in murine IAC

For B02 (FKS wild-type), one dose of RZF was as efficacious as daily administration of MFG at humanized dosing.

Fig. 2. RZF (20 mg/kg versus 50 mg/kg) and MFG against mutant C. glabrata isolates in murine IAA

For mutant isolates, RZF achieved significantly greater reductions in C. glabrata burdens within IAA than did MFG.

Fig. 3. RZF and MFG distribution (MALDI imaging) and concentrations (LC/MS) in infected pancreas tissues

CONCLUSIONS

- RZF achieves greater and more prolonged penetration at sites of IAA than MFG, which correlates with significantly greater activity against FKS mutant C. glabrata clinical isolates.
- RZF demonstrated similar efficacy against the FKS wild-type isolate with less frequent dosing than MFG.
- These results support RZF extended dosing intervals and its potential as treatment of IAA.