



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

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## INTRODUCTION

- IAC is among the 2 most common causes of IC
- Echinocandin 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 abscess (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  $1 \times 10^7$  CFU of CG BG2 (wild-type *FKS*) or 2 clinical isolates with *FKS2* mutations (F659S or F659del)

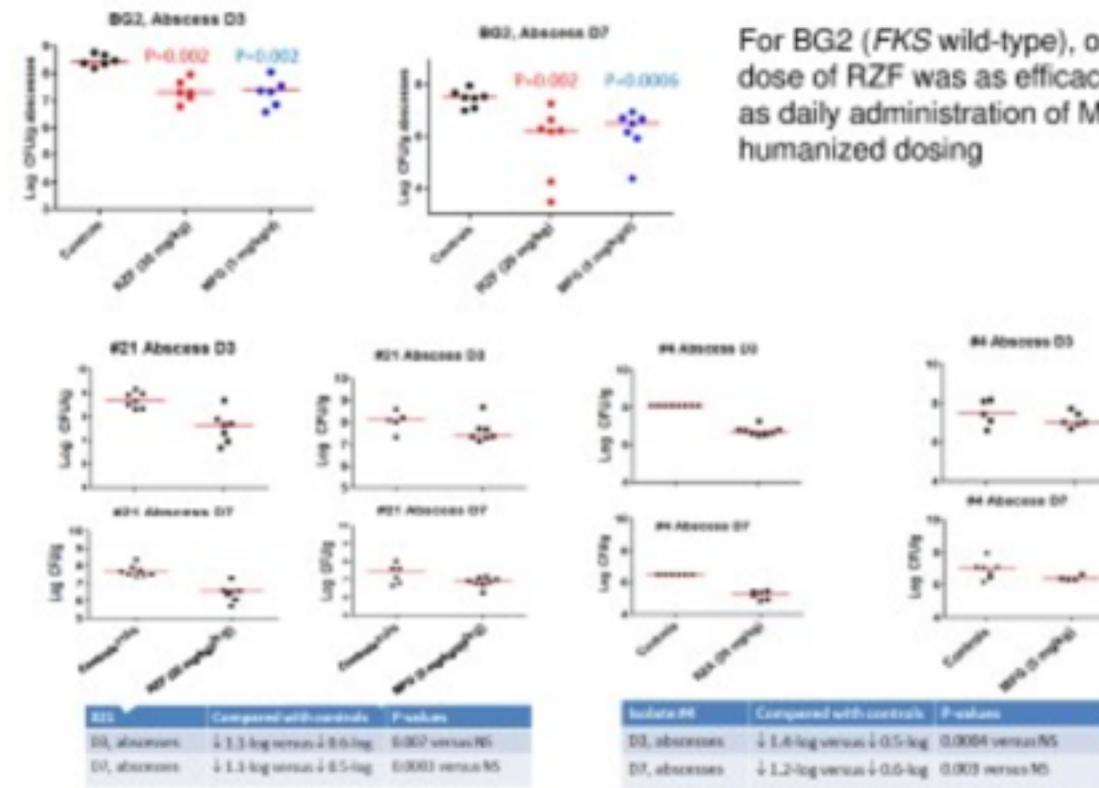


## RESULTS

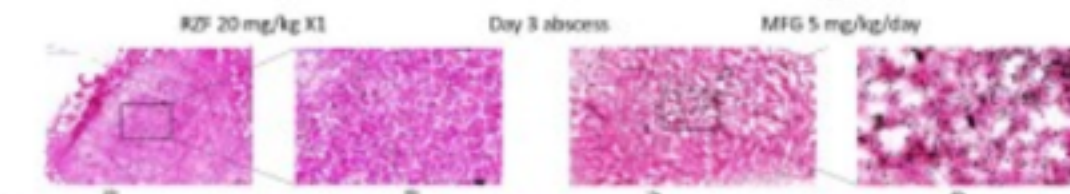
Table 1. RZF and other echinocandins MICs against *FKS* wild-type and mutant *C. glabrata*

Isolates		RZF MIC μg/mL	MFG MIC μg/mL
BG2	<i>FKS</i> wild-type	<0.015	0.03
21	F659S - <i>FKS2</i>	0.06	0.5
4	F659del - <i>FKS2</i>	0.25	1

Fig. 1. RZF and MFG against *FKS* wild-type and mutants *C. glabrata* isolates in murine IAC



For BG2 (*FKS* wild-type), one dose of RZF was as efficacious as daily administration of MFG at humanized dosing



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

## RESULTS

Fig. 2. RZF (20 mg/kg versus 60 mg/kg) and MFG against mutant *C. glabrata* isolates in murine IAA

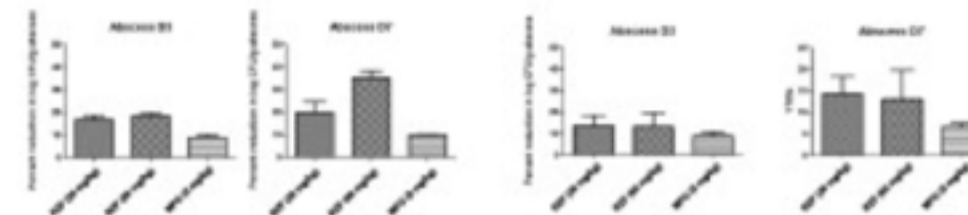
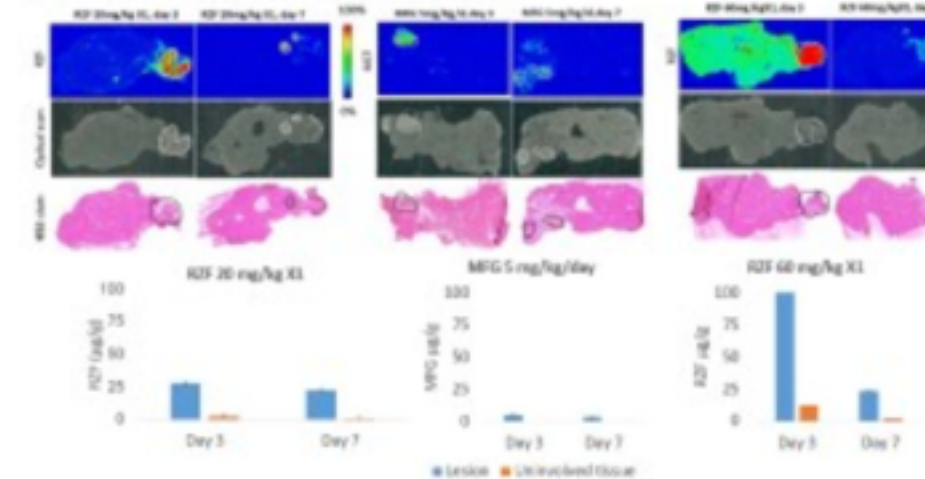


Fig. 3. RZF and MFG distribution (MALDI imaging) and concentrations (LC/MS) in infected pancreas tissues



## 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