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O0741 Rezafungin (RZA) is more effective than micafungin in treating of FKS-mutant *Candida glabrata* intra-abdominal candidiasis

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Background: Echinocandin resistance among Candida occurs when *FKS* genes are mutated. RZF is a novel echinocandin with long plasma half-life, suitable for prolonged dosing intervals. We used RZF or MCF to treat mice with CG IAC.

Materials/methods: Female 6-8 week-old mice were infected intraperitoneally (IP) with $1x10^7$CFU of CG BG2 (wild-type FKS) or 2 clinical isolates with *FKS2* mutations (F659S or F659del). RZF (20 mg/kg, single dose IV) or MCF (5 mg/kg, IV daily x3d) was given 6h before infection. Mice were sacrificed at 3d and 7d after infection for burden determination in peritoneal fluid and abscess (IAA).

Results: RZF and MCF MICs against BG2, F659S and F659del isolates were ≤0.015, 0.06 and 0.25 µg/mL, respectively, and 0.03, 0.5 and 0.75 µg/mL. For mice infected with BG2, RZF and MCF both achieved significant reductions compared to controls in mean burdens in PF at both time points. However, RZF achieved greater kills than MCF, with mean PF reductions of 0.83 *vs* 0.34 (3d), and 0.64 *vs* 0.35 (7d), and IAA reductions of 1.6 *vs* 0.21 (3d) and 1.27 *vs* 0.45 (7d) ($p<0.03$ for both). RZF also caused significant reductions in mean burdens of F659S compared with controls in PF (0.71 at 3d and 0.5 at 7d), and IAA (1.28 at 3d and 1.21 at 7d). In contrast, MCF caused less reductions in burdens of F659S compared with controls in PF (0.29 at 3d and none at 7d), and IAA (0.48 at 3d and 0.4 at 7d). For F659del, mean reductions for RZF and MCF compared with controls were: PF: 1.60 *vs* 1.02 (3d), and 0.93 *vs* 0.6 (7d); IAA: 1.28 *vs* 1.38 (3d), and 1.67 *vs* 1.48 (7d). MALDI-mass spectrometry imaging and laser capture-HPLC of IAA demonstrated that RZF attains better penetration for prolonged duration within necrotic cores than MCF.

Conclusions: RZF achieved greater and more prolonged penetration at sites of IAC than MCF, which correlates with significantly greater activity against FKS mutant CG clinical strains. RZF demonstrated greater effectiveness with less frequent dosing than MCF, supporting extended dosing intervals in patients, and promising use as treatment and prophylaxis against IAC.