00508

Rezafungin Activity against Candida spp. and Aspergillus spp. Isolates Causing Invasive Infections in European Medical Centres (2019–2021)

06. Fungal infection & disease

6c. Antifungal susceptibility testing & resistance (incl. surveillance)

Likely attendance

Onsite

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Background

Rezafungin (RZF) is an echinocandin (ECH) in development to treat candidemia and invasive candidiasis and prevent invasive fungal disease caused by *Candida*, *Aspergillus*, and *Pneumocystis* spp. We evaluated the *in vitro* activity of RZF, caspofungin (CSF), micafungin (MCF), and anidulafungin (ANF) against European fungal isolates causing invasive infection.

Methods

981 isolates were collected (1/patient) in 2019–2021 from 19 medical centres located in Western Europe (W-EU; *n*=755; 15 centres; 9 countries) and Eastern Europe (E-EU; *n*=226; 4 centres; 4 countries). Isolates were identified by MALDI-TOF and/or sequencing and tested by CLSI broth microdilution. CLSI breakpoints (BP) were applied (provisional for RZF). RZF non-susceptible (NS) isolates were submitted to *FKS* sequencing by whole genome sequencing.

Results

Isolates included *Candida albicans* (CA; 403 isolates), *Candida parapsilosis* (CP; 173), *Candida glabrata* (CG; 155), *Candida tropicalis* (CT; 80), *Candida krusei* (CK; 27), *Candida dubliniensis* (CD; 12), *Aspergillus fumigatus* (AF; 115), and *Aspergillus* section *Flavi* (ASF; 16). RFZ inhibited 99.7%/100% of CA from W-EU/E-EU, 99.1%/100% of CG, 88.9%/100% of CD, and all CP, CT, and CK (MIC50/90 in Table) at their susceptibility (S)-BP. RZF had similar activity to the other ECHs against CA (99.7%S), CG (99.1%S), CT (100.0%S), CK (100.0%S), and CD (MIC50 range, 0.015–0.03 mg/L) from W-EU. Except for CSF against CG (97.8%S) and ANF against CP (95.2%S), ECHs inhibited all Candida isolates from E-EU at their respective S-BP. Only 1 CA (Germany), 1 CD (Germany), and 1 CG (Spain), were NS to RZF. CA and CG NS strains were resistant to all ECH and displayed S645P alteration in Fks1 or S663P alteration in Fks2, respectively. No alterations were observed in the CD strain. All AF isolates were inhibited by RZF at ≤0.06 mg/L. ANF, MCF, and CSF inhibited all AF at ≤0.12 mg/L. RZF (MEC range, 0.015–0.03 mg/L) and other

ECHs (MEC range, 0.004–0.06 mg/L) were also active against 10 voriconazole-NS AF isolates (9 W-EU, 1 E-EU). RZF and other ECHs inhibited all ASF isolates at ≤0.06 mg/L.

Conclusions

RZF was very active against European *Candida* spp., AF, and ASF isolates causing invasive infections, including voriconazole-NS AF isolates.

Table 1

Organism (no. of isolates from W-EU/E-EU)	MIC_{50}/MIC_{90} or MEC_{50}/MEC_{90} (mg/L) CLSI %S							
	W-EU				E-EU			
	RZF	ANF	CSF	MCF	RZF	ANF	CSF	MCF
C. albicans (329/74)	0.03/0.06	0.03/0.06	0.015/0.03	0.015/0.03	0.03/0.06	0.03/0.06	0.015/0.03	0.015/0.015
	99.7	99.7	99.7	99.7	100	100	100	100
C. glabrata (109/46)	0.06/0.06	0.06/0.12	0.03/0.06	0.015/0.03	0.06/0.06	0.06/0.12	0.03/0.06	0.015/0.03
	99.1	99.1	99.1	99.1	100	100	97.8	100
C. parapsilosis (131/42)	1/2	2/4	0.25/0.5	1/1	1/1	2/2	0.25/0.5	1/1
	100	86.3	100	100	100	95.2	100	100
C. tropicalis (57/23)	0.03/0.06	0.03/0.06	0.015/0.03	0.03/0.06	0.03/0.06	0.03/0.06	0.03/0.06	0.03/0.06
	100	100	100	100	100	100	100	100
C. dubliniensis (9/3)	0.03/-	0.03/-	0.03/-	0.015/-	0.06/-	0.12/-	0.03/-	0.03/-
	88.9	NA	NA	NA	100	NA	NA	NA
C. krusei (19/8)	0.03/0.06	0.06/0.12	0.12/0.12	0.12/0.12	0.03/-	0.06/-	0.06/-	0.06/-
	100	100	100	100	100	100	100	100
A. fumigatus (94/21)	0.015/0.03	0.03/0.06	0.015/0.03	0.008/0.015	0.03/0.06	0.03/0.06	0.015/0.06	0.008/0.008
	NA	NA	NA	NA	NA	NA	NA	NA
VRC-NS AF (9/1)	0.015/-	0.03/-	0.015/-	0.008/-	0.03/-	0.03/-	0.03/-	0.008/-
	NA	NA	NA	NA	NA	NA	NA	NA
A. section *Flavi* (7/9)	0.008/-	0.008/-	0.015/-	0.015/-	0.015/-	0.015/-	0.008/-	0.008/-
	NA	NA	NA	NA	NA	NA	NA	NA

S, susceptible; RZF, rezafungin; ANF, anidulafungin; CSF, caspofungin; MCF, micafungin; VRC-NS, voriconazole non-susceptible; AF, *Aspergillus fumigatus*; NA, not available; "-", MIC_{90} not calculated due to the low number of isolates (<10 isolates).

Keyword 1
Fungi and clinical mycology
Keyword 2
New and non-traditional drugs
Keyword 3
Antimicrobial resistance

Conflicts of interest

Do you have any conflicts of interest to declare?
No