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O0115 EUCAST susceptibility testing of rezafungin: MIC data for contemporary Danish clinical yeast isolates

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Background: Rezafungin is a new long-acting echinocandin currently undergoing Phase 3 development for candidaemia and invasive candidiasis and for prophylaxis against invasive fungal diseases in blood and marrow transplant patients. Here, we present EUCAST MICs for rezafungin and comparators against clinical yeast isolates from 2017.

Materials/methods: 404 clinical yeast isolates (Table) were included. 346/404 were blood isolates. EUCAST E.Def 7.3.1 susceptibility testing was performed for rezafungin, anidulafungin, micafungin, amphotericin B, voriconazole and fluconazole (2424 MICs total) with *Candida krusei* ATCC 6258 and *Candida parapsilosis* ATCC 22019 as reference strains. Wild-type upper MIC limits were determined for species with ≥15 isolates using the ECOFFinder programme and a 97.5% cut-off. *FKS* sequencing was performed for anidulafungin- and micafungin-resistant isolates.

Results: The *in vitro* activity of rezafungin and comparators and rezafungin wild-type upper limits are presented (table). Modal MIC/MIC_{50}/ranges (mg/L) were 0.06/0.06/0.06-0.125 for *C. krusei* ATCC 6258 and 2/2/1-2 for *C. parapsilosis* ATCC 22019.

Five of 372 (1.3%) common *Candida* spp. isolates were non-wild-type for rezafungin: *C. albicans* n=2 (1.3%) (both MIC 0.25 mg/L and resistant to micafungin, fluconazole and voriconazole) and *C. glabrata* n=3 (2.2%) (MICs of 0.5, 1, and 2, respectively; all three resistant to anidulafungin and micafungin, and one also to fluconazole and voriconazole). *FKS* sequencing demonstrated a P1354S alteration outside hotspot 2 in one *C. albicans* (sequencing pending for the other) and FKS1/FKS2 alterations in 3/3 non-WT *C. glabrata*: WT/S663F, L630Q/S663F, and Y1249STOP/L664Q (+Y658N outside hotspot 2), respectively. In comparison, three *C. glabrata* were categorised anidulafungin-resistant and 12 (seven *C. albicans* and five *C. glabrata*) as micafungin-resistant (corresponding to 0.81% and 3.23%, respectively). Moreover, 42/372 (11.3%) common *Candida* spp. isolates were fluconazole-resistant and 17 (4.6%) were voriconazole-resistant using >0.25 mg/L as the resistance breakpoint for all. Finally, no amphotericin B resistance was found among the common *Candida* spp. isolates but one rare isolate (*C. doubushaemulonis*) was amphotericin B-resistant (MIC=4 mg/L).

Conclusions: Rezafungin non-WT *Candida* spp. isolates were rare and less frequent than resistance found for micafungin, fluconazole and voriconazole. With pharmacokinetics allowing for once-weekly IV dosing, rezafungin may be an attractive alternative to current antifungals.

Table. Modal MIC (range) ECOFF mg/L, of rezafungin and comparators against 404 Danish isolates.

	N	RZF	ANF	MCF	AMB	FLC	VRC
Most prevalent *Candida*	372						
C. albicans	151	0.06 (0.016-0.25) 0.125	≤0.004 (≤0.004-0.016)	0.016 (≤0.004-0.06)	0.25 (0.125-0.5)	0.25 (0.03->32)	≤0.004 (≤0.004-2)
C. dubliniensis	19	0.125 (0.03-0.25) 0.25	0.016 (≤0.004-0.03)	0.016 (0.008-0.06)	0.06 (0.03-0.25)	0.125 (0.06->32)	≤0.004 (≤0.004->4)
C. glabrata	134	0.125 (0.03-2) 0.25	0.016 (0.008-1)	0.016 (0.008-0.5)	0.25 (0.06-1)	4 (0.5->32)	0.06 (0.016->4)
C. krusei	24	0.06 (0.03-0.25) 0.25	0.03 (0.016-0.03)	0.125 (0.06-0.25)	0.5 (0.5-1)	32 (8->32)	0.125 (0.125-1)
C. parapsilosis	19	2 (1-4) 8	1 (0.5-2)	2 (1-2)	0.5 (0.25-1)	1 (0.5-4)	0.016 (0.008-0.06)
C. tropicalis	25	0.125 (0.06-0.25) 0.25	0.016 (≤0.004-0.03)	0.03 (0.016-0.06)	0.25 (0.25-1)	0.25 (0.125-16)	0.016 (0.008->4)
S. cerevisiae	6	(0.125-0.25)	(0.016-0.125)	(0.06-0.125)	(0.06-1)	(2-16)	(0.06-0.25)
Other *Candida*	21	(0.03-2)	(≤0.004-1)	(0.016-0.5)	(0.125->4)	(0.125->32)	(0.008->4)
Cryptococcus neoformans	3	(>4)	(>4)	(>4)	(0.03-0.25)	(2-8)	(0.016-0.06)
Rare yeast	2	(>4)	(>4)	(>4)	(0.25)	(32)	(0.25)