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P2174 EUCAST reference testing of rezafungin susceptibility: impact of choice of plastic plates

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Background: Rezafungin is a new long-acting echinocandin currently undergoing Phase 3 clinical trials. Epidemiological cut-off values are necessary for clinical breakpoint setting but have not been established, in part due to an unexplained interlaboratory variation observed particularly for *C. albicans*. Here we investigated if the choice of microtitre susceptibility testing (AFST) trays contributed to interlaboratory variability of rezafungin. Anidulafungin was included as comparator.

Materials/methods: EUCAST E.Def 7.3.1 AFST using tissue/cell-culture treated (TC-plates) and untreated polystyrene plates (UT-plates) from four manufacturers was performed. Six control strains (*C. albicans* CNM-CL-F8555, ATCC 64548 and ATCC 64550, *C. krusei* CNM-CL-3403 and ATCC 6258, and *C. parapsilosis* ATCC 22019) were tested repetitively (yielding 520 MICs). Five to six wild-type and four to five *FKS* mutant clinical isolates of *C. albicans*, *C. glabrata*, *C. krusei*, and *C. tropicalis* and 5 wild-type *C. parapsilosis* were subsequently tested (580 MICs).

Results: Repetitive MICs for QC strains fell within 2/3 dilutions for rezafungin in 82%/100% and for anidulafungin in 90%/98% of the cases. The modal MIC for rezafungin and collated *C. albicans* control strain distributions were 0.016 mg/L across TC-plates but 0.03 mg/L across UT-plates. The modal anidulafungin MICs were 0.004 mg/L and 0.016 mg/L for TC-plates versus UT-plates. The difference was most pronounced with Falcon plates (TC-plates: rezafungin MICs 0.008-0.016 mg/L versus UT-plates: 0.016-0.125 mg/L) but not observed for *C. krusei* and *C. parapsilosis*.

For rezafungin, 11 MICs for mutants overlapped with the MIC range for wild-type isolates (TC-plates on 4 occasions; UT-plates on 7 occasions). For anidulafungin, overlaps were observed on 5 occasions (all UT-plates). Most overlaps (n=5 for rezafungin; n=3 for anidulafungin) were caused by a *C. tropicalis* harbouring a F650L alteration and *C. glabrata* harbouring a D666Y alteration (n=2 for rezafungin; n=1 for anidulafungin). On 12 occasions the MIC of mutant isolates were at the highest MIC of the wild-type range.

Conclusions: Intralaboratory variation was low for both compounds and all plates. Treated plates resulted in lower MICs most profoundly for *C. albicans*, for Falcon plates, and more for anidulafungin than rezafungin. Standardisation of plate choice for EUCAST AFST would help minimise interlaboratory variation.