Background

Rezafungin (RZF) is a once weekly echinocandin (ECH) with a long half-life and front-loaded drug exposure under development to treat candidemia. We evaluated the in vitro activity of RZF, caspofungin (CSF), micafungin (MCF), anidulafungin (ANF), and fluconazole (FLC) against Candida spp. causing bloodstream infection in Europe.

Methods

610 isolates were collected (1/patient) in 2019–2021 from 18 medical centres located in Western Europe (W-EU; n=438; 14 centres) and Eastern Europe (E-EU; n=172; 4 centres). Isolates were identified by MALDI-TOF and tested by CLSI broth microdilution. CLSI breakpoints (BP) were applied (provisional values for RZF). RZF non-susceptible (NS) isolates were submitted to whole genome sequencing.

Results

Isolates included Candida albicans (CA; 261 isolates), Candida parapsilosis (CP; 134), Candida glabrata (CG; 121), Candida tropicalis (CT; 67), Candida krusei (CK; 20), and Candida dubliniensis (CD; 7). RFZ inhibited all but 3 Candida spp. isolates at the susceptible (S) BP for each species. One CA (Germany), 1 CD (Germany), and 1 CG (Spain) were non-S to RZF. CA and CG non-S strains were resistant to other ECHs and displayed either a S645P alteration in Fks1 or a S663P alteration in Fks2 genes, respectively. No alterations were observed in the CD strain. RZF had similar activity to the other ECHs against CA (98.9–100.0%S), CG (97.6–100.0%S), CP (100.0%S; except ANF, 89.2–95.1%S), CT (100.0%S), CK (100.0%S), and CD (MIC50 range, 0.015–0.12 mg/L), regardless of the region or year. FLC was active against CA (100.0%S) and CT (100.0%S), regardless of the region or year. FLC resistance (R) rates against CP isolates were 31.2%/17.1% from W-EU/E-EU and 18.9%/27.5%/31.6% for CP isolates from 2019/2020/2021, respectively. FLC-R rates against CG isolates were 5.0%/2.4% from W-EU/E-EU and 10.3%/4.4%/2.1% in 2019/2020/2021, respectively.
Conclusions

RZF was very active against CA, CG, CP, CT, CK, and CD causing candidemia in European medical centres. ECHs, including RZF, displayed similar activity against different *Candida* species. RZF and other ECHs S rates were stable over the 3-year period. However, FLC R rates progressively increased against CP and decreased against CG.

**Keyword 1**
Fungi and clinical mycology

**Keyword 2**
Antimicrobial susceptibility testing (AST)

**Keyword 3**
Antimicrobial resistance

*Conflicts of interest*

Do you have any conflicts of interest to declare?
No