

## O0784 Prevalence of MSH2 mutator genotype in echinocandin-resistant *Candida glabrata* from a 3-year global surveillance program

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**Background:** *Candida glabrata* (CGLA) isolates resistant to echinocandins and fluconazole are a worrisome cause of breakthrough infections. Isolates exhibiting alterations in the mismatch repair gene MSH2 have higher mutation rates and could be associated with resistance development. We evaluated 33 echinocandin non-wild-type (ECH-NWT) CGLA for the presence of MSH2 alterations.

**Materials/methods:** CGLA invasive clinical isolates were collected in 61 worldwide hospitals from 2014–2016. Isolates were susceptibility tested using CLSI reference broth microdilution. Echinocandin non-wild-type isolates were subjected to whole genome sequencing and multilocus sequence type (ST), FKS, and MSH2 were analyzed.

**Results:** Among 795 CGLA isolates, 33 (4.2%) were ECH-NWT and 7 of these were resistant to fluconazole (21.2%). Thirty of 33 ECH-NWT were recovered from blood cultures. Amino acid substitutions on FKS HS regions were detected among 24/33 (72.7%) isolates: 18 on FKS2 HS1 (10 S663P) and 7 on FKS1 HS1 alterations, 1 isolate harbouring alterations on both. Two isolates carried only non-HS FKS alterations. Isolates belonged to 15 distinct STs, including 2 previously unknown. ST3 was the most common (8 isolates) and was detected in 5 hospitals, followed by ST16 (4; 3 different hospitals), ST10 and ST2 (3 each; all from different hospitals). FKS HS alterations had no association with specific STs. MSH2 mutator genotypes were detected among 13 (39.4% of the ECH-NWT) isolates and included P208S/N890I, E231G/L269F, and V239L±A942T observed in 3, 4, and 6 isolates, respectively. Twelve of 13 isolates displaying MSH2 alterations belonged to 4 STs, and all isolates displaying the same ST had the same MSH2 genotype. These STs included 2 (3 isolates; V239L/A942T), 7 (2; V239L±A942T), 10 (3; P208S/N890I), and 16 (4; E231G/L269F). Among these isolates, 10 displayed FKS HS alterations and 3 had elevated fluconazole resistance.

**Conclusions:** ECH resistance among CGLA was <5%; however, almost 40% of the ECH-NWT CGLA isolates displayed MSH2 mutator genotypes. These isolates belonged to 4 STs and were not geographically related. These isolates are thought to be more prone to develop resistance upon exposure, causing breakthrough of antifungal treatment. Further studies should be performed to evaluate and closely monitor the clinical impact of these strains.