

P2167 Prevalence and mechanisms of resistance to azole antifungals of *Aspergillus fumigatus* isolates from respiratory specimens of patients from Lyon University Hospitals, France

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Background: Resistance of *Aspergillus fumigatus* strains to triazole antifungals is increasingly reported in Europe. The main mechanisms of resistance described are mutations in the *cyp51A* gene encoding a lanosterol 14- α -demethylase or its promoter. As few data are available in Southern France, our objective was to assess the burden of *Aspergillus* isolates with azole resistance from clinical specimens in Lyon University Hospitals

Materials/methods: In this retrospective cross-sectional study, 203 consecutive *A. fumigatus* isolates were identified during a seven-month period from February to September 2017 from respiratory specimens from 182 patients attending the inpatient and outpatient wards of the Pulmonary Medicine Departments of Lyon University Hospitals. Morphological identification was confirmed by sequence analysis of the β -tubulin gene. Minimum inhibitory concentrations were determined using E-test reagent strips for itraconazole, voriconazole, posaconazole, and isavuconazole. Resistance was defined according to the 2018 EUCAST clinical breakpoints. The molecular resistance mechanisms were searched for by sequence analysis of the *cyp51A* gene and its promoter region, as well as by gene expression analysis of the *cyp51* genes and genes encoding several efflux transporters.

Results: PCR and sequence analysis of the β -tubulin gene confirmed the identification of *Aspergillus fumigatus* for the 203 isolates. Four isolates presented with azole resistance: two isolates against itraconazole/posaconazole/isavuconazole and another two against all four triazoles. Out of these four strains, three presented silent polymorphisms in an intronic part of *cyp51A* and one presented simultaneously the F46Y, M172V and E427K mutations. No mutation was identified in the *cyp51A* promoter, but significant inductions of *cyp51A* and *cyp51B* gene expression were observed for all four isolates and three isolates, respectively. Significant inductions of *atrF* and *crd1B* gene expression were observed for two and three isolates, respectively. No significant induction of *MDR1-4*, *MFS56* and *M85* gene expression was observed.

Conclusions: The prevalence of azole resistance in our study population was 2.2% (95% CI 0.9-5.6). Only polymorphisms were found in the *cyp51A* gene and no mutation was found in its promoter. Nevertheless, significant inductions of the expression of the *cyp51* genes and two genes encoding efflux transporters were evidenced, underlying the diversity of resistance mechanisms to be explored.

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