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Prevalence and characterization of azole-resistant *Aspergillus fumigatus* in German CF-patients

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Background: *Aspergillus fumigatus* is the most prevalent fungus in the respiratory tract of patients with CF, ranging from 6% to 60%. Allergic bronchopulmonary aspergillosis and *Aspergillus* bronchitis are the most frequent complications. The aim of this study was to investigate the prevalence of azole-resistant *A. fumigatus* in respiratory secretions from German CF patients.

Material/methods: Thirteen university-based centres across Germany participated in the study. In total, 2,882 isolates of 966 CF patients were examined. Isolates were cultured on malt agar containing 4 mg/L itraconazole. In case of growth antifungal susceptibility testing of all azole-resistant isolates was performed by broth microdilution method according to EUCAST. Sequencing of the *cyp51A* gene of resistant isolates was performed to analyse mutations. Furthermore, genotyping by microsatellite PCR was done.

Results: 101 azole-resistant *A. fumigatus* isolates from 55 CF patients were found (prevalence 5.3%). The resistance rate varied between the centres. The Essen centre had the highest prevalence (9.1%) followed by Munich (7.8%), Muenster (6.0%) and Hannover (5.2%). Molecular characterisation of the isolates revealed that most of the isolates (n=87) carried a TR34/L98H mutation. Genotyping results by using a microsatellite PCR with nine different primers showed no major clustering of the isolates.

Conclusions: In summary, this is the first multicentre study analysing the prevalence of azole resistance in *A. fumigatus* isolates from CF patients in Germany. Because of a resistance rate of up to 9% susceptibility testing of *A. fumigatus* isolates is recommended in CF patients with azole-based antifungal treatment.