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P2170 First detection of TR34/L98H *Aspergillus fumigatus* mutants in Switzerland

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Background: Azole resistance in *Aspergillus fumigatus* has emerged as a global health problem and has been associated with high mortality rates in patients with invasive aspergillosis. The aim of this study is to assess the distribution and antifungal susceptibility profile of clinical respiratory *Aspergillus* spp. isolates in Switzerland. Here we present first preliminary results.

Materials/methods: This prospective multicenter study was conducted at all hospitals participating in the Fungal Infections Network of Switzerland (FUNGINOS). A one-year period starting from January 2018 was covered. All patients with detection of *Aspergillus* spp. in a respiratory sample were included. The main demographic, clinical and microbiological data were collected according to a specific case report form. All isolates were sent to a central laboratory for antifungal phenotypic susceptibility testing by Sensititre YeastOne panel. *Aspergillus* isolates with high minimum inhibitory concentration (MIC) for one of the tested triazoles were analysed by complete sequencing of the cyp51A gene and promoter region for detection of mutations.

Results: In the first 8 months, 136 respiratory samples with *Aspergillus* spp. were included. Samples were obtained from sputum (n=80, 59%), bronchoalveolar lavage or tracheobronchial aspiration (44, 32%), lung biopsy (7, 5%) and others (5, 4%). The isolates consisted of *A. fumigatus* (n=104, 76%), *A. niger* (15, 11%), *A. flavus* (7, 5%) and others (10, 7%). The results of the susceptibility testing to azole drugs are shown in Table 1. Two *A. fumigatus* strains were resistant to azoles and were found to carry the typical environmental TR_{34}/L98H mutation. The first isolate (Case 1) was obtained from a lung biopsy of a 62-year-old patient with proven invasive aspergillosis after allogeneic stem cell transplantation who had grade III graft-versus-host disease and had received long-term mold-active treatment. The other isolate (Case 2) was obtained from the sputum of a 73-year-old male patient with chronic obstructive pulmonary disease and was interpreted as colonisation.

Table 1. Results of the susceptibility testing to azoles of *A. fumigatus*, *A. niger* and *A. flavus* isolates

Species (n)		VRC (mg/L)	POS (mg/L)	ITR (mg/L)
A. fumigatus (104)	MIC_{50} / MIC_{90} (range)	0.5 / 0.5 (0.25 – 4)	0.25 / 0.25 (0.12 – 1)	0.5 / 0.5 (0.25 - >16)
A. niger (15)	MIC_{50} / MIC_{90} (range)	0.5 / 1 (0.25 – 1)	0.25 / 0.5 (0.12 – 0.5)	1 / 1 (0.5 – 1)
A. flavus (7)	MIC_{50} / MIC_{90} (range)	0.5 / 1 (0.5 – 1)	0.25 / 0.5 (0.25 – 0.5)	0.25 / 0.5 (0.25 – 0.5)
Case 1	MIC_{50}	4	1	>16
Case 2	MIC_{50}	2	1	2

MIC: minimum inhibitory concentration; VRC: voriconazole; POS: posaconazole; ITR: itraconazole

Conclusions: The prevalence of azole resistance among respiratory *Aspergillus* spp. isolates in Switzerland is low (<2%). We detected the first two cases of TR_{34}/L98H *A. fumigatus* mutants in clinical isolates in our country.