

P0170 **Antifungal susceptibility to azoles of clinical invasive Spanish *Aspergillus fumigatus* complex isolates: no sign of resistance at present**

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Background: Some reports are alerting on a rise in the number of azole-resistant *A. fumigatus* complex isolates in the North of Europe. The search for the presence of azole-resistant *A. fumigatus* complex isolates causing invasive disease in other regions is needed. We assessed the antifungal susceptibility of a collection of Spanish clinically significant *A. fumigatus* complex isolates to voriconazole (VRC), isavuconazole (ISA), itraconazole (ITC), posaconazole (POS), and amphotericin B (AMB) in order to check on the presence of resistant isolates.

Materials/methods: A total of 275 *A. fumigatus* complex isolates from 244 patients with proven/probable invasive aspergillosis admitted to Gregorio Marañón Hospital (Madrid, Spain) from January 1999 to June 2017 were studied. Isolates were molecularly identified and antifungal susceptibility was performed according to EUCAST 9.3.1 methodology. *Cyp51A* mutations were searched in *A. fumigatus* “sensu stricto” resistant isolates.

Results: Molecular identification yielded the following species distribution: *A. fumigatus* “sensu stricto” (n=275), *A. lentulus* (n=8), *Neosartorya udagawae* (n=3), *A. novofumigatus* (n=2), *A. felis* (n=1). The antifungal susceptibility of the isolates is shown in the table.

		AMB	ITC	VRC	POS	ISA
<i>A. fumigatus</i> sensu stricto (n=275)	GM	0.38	0.36	0.71	0.09	0.59
	MIC ₉₀ (Range)	0.5 (0.062 - 1)	0.5 (0.031 - ≥ 16)	1 (0.25 - 8)	0.125 (0.031 - 1)	1 (0.25 - 4)
	% of Resistance	0	0.7	0.7	0	0.7
Cryptic <i>A. fumigatus</i> species (n=14)	GM	3.28	1.16	2.56	0.19	1.41
	MIC ₉₀ (Range)	≥ 16 (0.25 - ≥ 16)	≥ 16 (0.25 - ≥ 16)	≥ 16 (0.5 - ≥ 16)	1 (0.062 - 1)	2 (1 - 8)
	% of Resistance	50	21.4	50	14.2	21.4
<i>A. fumigatus</i> complex (n=289)	GM	0.42	0.38	0.76	0.09	0.62
	MIC ₉₀ (Range)	0.5 (0.062 - ≥ 16)	0.5 (0.031 - ≥ 16)	1 (0.25 - ≥ 16)	0.25 (0.031 - 1)	1 (0.25 - 8)
	% of Resistance	2.4	1.7	2.7	0.7	1.7

The following isolates showed resistance: AMB [*A. lentulus* (n=7)]; ITC [*A. fumigatus* “sensu stricto” (n=2), *A. novofumigatus* (n=1), *N. udagawae* (n=1), *A. lentulus* (n=1)], VRC [*A. lentulus* (n=3), *A. fumigatus* “sensu stricto” (n=2), *N. udagawae* (n=1), *A. novofumigatus* (n=1), *A. felis* (n=1)]; POS [*A. novofumigatus* (n=1), *A. lentulus* (n=1)]; and ISA [*A. fumigatus* “sensu stricto” (n=2), *A. lentulus* (n=1), *A. novofumigatus* (n=1), *A. felis* (n=1)]. The *A. fumigatus* “sensu stricto” isolates (n=2) showing resistance to azoles harbored the G448S and TR₃₄L98H *cyp51A* substitutions and were isolated in 2011 and 2012, respectively.

Conclusions: Resistance in *A. fumigatus* “sensu stricto” isolates infecting patients admitted to our hospital was lower than 1%, and has not shown any sign of increase over the years. The overall rate

of resistance to azoles and amphotericin B in *A. fumigatus* complex was highly impacted by the presence of cryptic species.