P310

Susceptibility of emerging *Candida auris* isolates to the novel inhaled triazoles PC945/PC1244

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Introduction/Objectives

Candida auris **is an emerging multidrug-resistant species causing invasive infection (e.g. candidemia) with high mortality. A worldwide outbreak has been reported, the majority of cases identified as secondary nosocomial infections. Lower susceptibility of *C. auris* to current antifungals such as triazoles, polyenes and echinocandins limits treatment options. Both PC945[1] and PC1244[2] are novel inhaled anti-fungal triazoles with potent and persistent anti-fungal activities against *Aspergillus fumigatus*. Here, the activities of PC945 and PC1244 against *C. auris* were evaluated.**

Methods

- A collection of 50 clinical isolates deposited at National Culture Collection of Pathogenic Fungi (NCCPF) Chandigarh India were used in the study.
- Minimum inhibitory concentrations (MICs: azole endpoint) were determined using CLSI M27-A3 method.
- Quality control strains used - *C. parapsilosis* ATCC 22019 and *C. krusei* ATCC 6258.
- Broth microdilution MIC assays were performed for PC945 and PC1244, and the activities compared with those of fluconazole, voriconazole and posaconazole.

Results

- MIC values of all triazoles used (fluconazole, voriconazole and posaconazole) were in the normal range with quality control strains (*C. krusei/C. parapsilosis*) (Table 1).
- Majority (39 out of 50) isolates showed MIC (azole endpoint) of 64 or >64µg/mL for fluconazole, indicating many strains were fluconazole resistant (Figure 1).

Table 1: Susceptibility testing to reference isolates

(µg/mL)	*C. krusei (ATCC6258)*	*C. parapsilosis (ATCC22019)*
	MIC range (Mode)	MIC range (Mode)
Fluconazole	8 – 32 (16)	1 (1)
Voriconazole	0.125 – 0.5 (0.25)	0.031 – 0.125 (0.031)
Posaconazole	0.25 – 0.5 (0.25)	0.063 – 0.25 (0.125)
PC945	0.125 (0.125)	0.063 – 0.125 (0.125)
PC1244	0.25 – 0.5 (0.25)	0.063 – 0.125 (0.063)

- MIC_{90} of PC945 was 8-fold and 2-fold more potent than voriconazole and posaconazole respectively (Figure 1, Table 1).
- PC1244 was 4-fold more potent than voriconazole and equipotent to posaconazole (Figure 1, Table 1).
- Both PC945 and PC1244 showed complete inhibition of fungal growth with MIC_{50} and MIC_{90} of 0.25 and 0.5µg/mL respectively (Table 2).

Figure 1: Susceptibility of 50 *C. auris* clinical isolates to triazoles (CLSI, Azole endpoint)

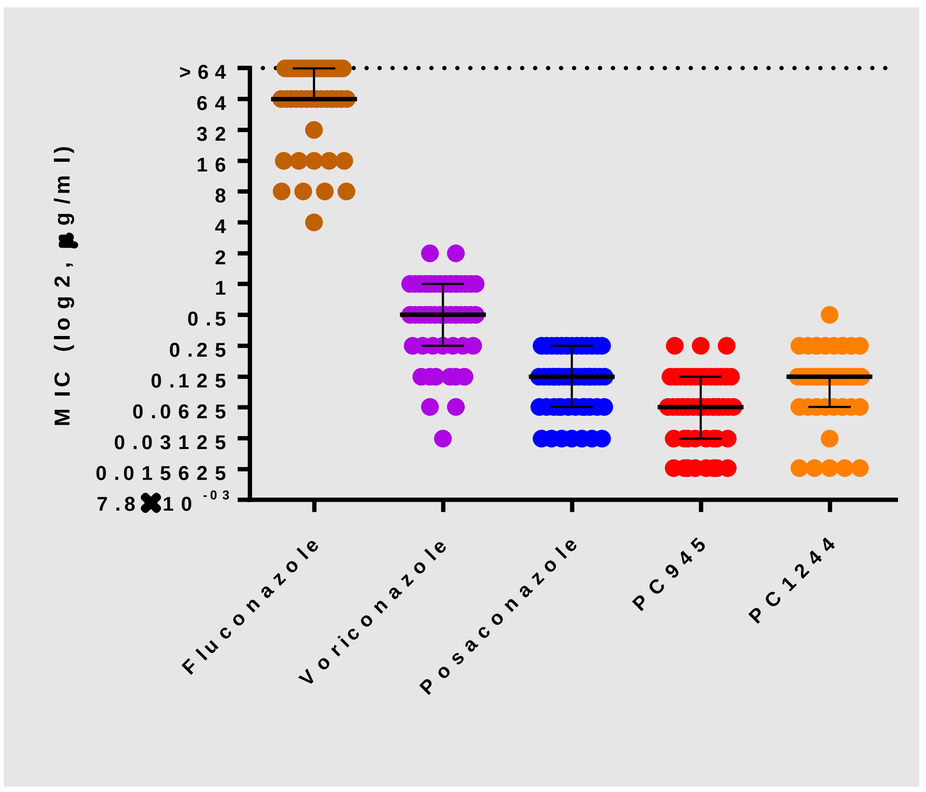

Table 2: MIC values of triazoles on growth of 50 *C. auris* clinical isolates.

		MIC median (µg/mL)	Interquartile range (µg/mL)	MIC_{50} (µg/mL)*1	MIC_{90} (µg/mL)*2
CLSI Azole-endpoint (MIC: approx. 50% growth inhibition)	Fluconazole	64	64 - >64	64	>64
	Voriconazole	0.5	0.25 – 1.0	0.5	1.0
	Posaconazole	0.125	0.063 – 0.25	0.125	0.25
	PC945	0.063	0.031 – 0.125	0.063	0.125
	PC1244	0.125	0.063 – 0.125	0.125	0.25
MIC (100%)	PC945	0.25	0.063 – 0.25	0.25	0.50
	PC1244	0.25	0.125 – 0.50	0.25	0.50

*1: MIC50, MIC required to inhibit the growth of 50% organisms

*2: MIC90, MIC required to inhibit the growth of 90% organisms

Conclusion

Majority of isolates were fluconazole resistant as reported. Posaconazole was one of the more active known azoles against *C. auris*. PC945 and PC1244 were found to demonstrate high levels of antifungal activity against *C. auris* with low MICs.

Bibliography

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