28th ECCMID EUROPEAN CONGRESS OF CLINICAL MICROBIOLOGY AND INFECTIOUS DISEASES
Madrid, Spain
21 – 24 April 2018

O0796 Candida auris is highly in vitro susceptible to APX001A in EUCAST antifungal susceptility testing

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Background: *Candida auris* is a multidrug-resistant yeast rapidly emerging as a significant cause of nosocomial infections. Here, we report the susceptibility of *C. auris* to the new antifungal investigational drug candidate APX001. The active moiety APX001A targets and inhibits the conserved fungal inositol acyltransferase enzyme Gwt1 thereby preventing GPI-anchored protein maturation and compromising fungal cell growth.

Materials/methods: EUCAST AFST according to E.Def 7.3.1 was performed on 122 Indian clinical *C. auris* isolates and the *C. auris* control strains KCTC17809, KCTC17810 and JCM15448. Cell-culture treated microtitre plates (Nunc, ThermoFisher Scientific, cat. no. 167008) were prepared using the ISO method for APX001A and fluconazole and serial dilution for amphotericin B, anidulafungin, micafungin, isavuconazole, itraconazole, posaconazole and voriconazole generating 1125 MICs in total. The results were compared to previously presented MICs for APX001A for the five most common *Candida* species.

Results: APX001A displayed potent *in vitro* activity against the clinical *C. auris* isolates with modal MIC, MIC_{50}, MIC_{90} and range of 0.016 mg/L, 0.016 mg/L, 0.03 mg/L and 0.001-0.125 mg/L, respectively. For the control strains, the MICs were 0.004 mg/L, 0.03 mg/L and 0.06 mg/L. On a mg/L basis, APX001A was the most effective antifungal tested. The MIC_{50} for posaconazole was one dilution step higher (0.03 mg/L) followed by the MIC_{50} for the remaining comparators anidulafungin, micafungin, isavuconazole and itraconazole (0.125 mg/L), voriconazole (0.5 mg/L), amphotericin B (1 mg/L), and fluconazole (256 mg/L).

When these data were compared to data from a previous study, *C. auris* was as susceptible to APX001A as the most common *Candida* species (MIC_{50} within ±2 dilutions). Thus, the MIC_{50} were as follows for comparison: *C. albicans* was 0.008 mg/L (range 0.001-0.03 mg/L), *C. dubliniensis* MIC_{50} 0.004 mg/L (range 0.002-0.03 mg/L), *C. glabrata* MIC_{50} 0.06 mg/L (range 0.008-0.25 mg/L), *C. parapsilosis* MIC_{50} 0.03 mg/L (range 0.008-0.03 mg/L) and *C. tropicalis* MIC_{50} 0.008 mg/L (range 0.004-0.125 mg/L).

Conclusions: The new antifungal compound APX001 shows promising *in vitro* activity suggesting it may be a welcomed therapeutic agent against *C. auris* for which therapeutic options are few.

Table. MICs of APX001A and comparator antifungals against the tested 122 clinical *C. auris* isolates. The MIC_{50} is highlighted in bold, the modal MIC underscored and the concentration range tested highlighted in white background. Off-scale MICs are shown in the first concentration outside the tested range.

	0.001	**0.002**	**0.004/<0.008**	**0.008**	**0.016**	**0.03**	**0.06**	**0.125**	**0.25**	**0.5**	**1**	**2**	**>2/4**	**8**	**16**	**32**	**64**	**128**	**256**	**>256**
APX001A	4	6	11	16	**41**	38	5	1												
AMB										14	**108**									
Ani					1	12	34	**30**	12	12	11	2	8							
Mic						5	30	**69**	9				8							
Flu											1				4	10	6	14	**33**	54
Isa			20	1	1	19	9	**19**	21	21	6	5								
Itr			2	2	9	5	14	**34**	36	19	1									
Psc			17	5	19	**34**	32	11	3	1										
Vor			1			1	1	16	13	**34**	38	13	5							