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# O0269 *In vitro* activity of APX001A and comparator agents against 1706 fungal isolates collected during an international surveillance programme (2017)

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**Background:** Current antifungal agents cover a majority of opportunistic fungal pathogens; however, breakthrough invasive fungal infections continue to occur and increasingly involve relatively uncommon yeasts and/or moulds that tend to exhibit decreased susceptibility to current agents. APX001A is a first-in-class small molecule inhibitor of the fungal Gwt1 enzyme which is required for acylation of inositol during glycosylphosphatidylinositol (GPI) anchor biosynthesis. It is active against the major fungal pathogens: *Candida* (except *C. krusei*), *Aspergillus*, and hard-to-treat moulds, including *Fusarium* and *Scedosporium*. In this study, we tested APX001A, anidulafungin (ANF), micafungin (MCF), fluconazole (FLU), and others against 1,706 contemporary clinical fungal isolates collected worldwide during 2017.

**Materials/methods:** 1,706 non-duplicate fungal isolates were collected from 68 medical centers in North America (37.3%), Europe (43.4%), Asia-Pacific (12.7%), and Latin America (6.6%). Among the isolates tested, 78.5% were *Candida* spp, 3.9% were non-*Candida* yeasts, including 30 *Cryptococcus neoformans* var. *grubii* (1.8%), 14.7% were *Aspergillus*, and 2.9% were other moulds. All isolates were tested by CLSI reference broth microdilution.

**Results:** APX001A ($MIC_{50/90}$, 0.008/0.06 mg/L) was the most active agent tested against *Candida* isolates (Table); corresponding ANF, MCF, and FLU $MIC_{90}$ values were 16- to 64-fold higher. Similarly, APX001A ($MIC_{50/90}$, 0.25/0.5 mg/L) was ≥8-fold more active than ANF, MCF, and FLU against *C. neoformans* var. *grubii*. Against *Aspergillus*, AXP001A ($MIC_{50/90}$, 0.015/0.03 mg/L) was comparable in activity to ANF and MCF. APX001A ($MIC_{90}$, 0.06 mg/L) was ≥128-fold more active than ANF and MCF against *Scedosporium* isolates.

| | $MIC_{50/90}$ (mg/L) | | | |
|---|---|---|---|---|
| **Organism (no. tested)** | **APX001A** | **Anidulafungin** | **Micafungin** | **Fluconazole** |
| *Candida* spp. (1,340) | 0.008/0.06 | 0.06/2 | 0.015/1 | 0.25/4 |
| *C. albicans* (414) | 0.008/0.008 | 0.015/0.03 | 0.015/0.015 | ≤0.12/0.25 |
| *C. glabrata* (321) | 0.06/0.12 | 0.06/0.12 | 0.015/0.03 | 4/32 |
| *C. parapsilosis* (270) | 0.008/0.015 | 2/2 | 1/1 | 0.25/2 |
| *C. tropicalis* (151) | 0.015/0.03 | 0.03/0.06 | 0.03/0.06 | 0.25/0.5 |
| *C. krusei* (43) | >2/>2 | 0.06/0.12 | 0.06/0.12 | 32/32 |
| *C. dubliniensis* (49) | 0.004/0.008 | 0.03/0.12 | 0.015/0.03 | ≤0.12/0.25 |
| *C. lusitaniae* (39) | 0.03/0.12 | 0.25/0.5 | 0.12/0.25 | 0.25/2 |
| Other *Candida* spp. (40) | 0.008/0.03 | 0.5/2 | 0.25/0.5 | 1/16 |
| *Cryptococcus neoformans* var. *grubii* (30) | 0.25/0.5 | >4/>4 | >4/>4 | 2/4 |
| *Aspergillus* spp. (251) | 0.015/0.03 | 0.015/0.03 | 0.015/0.015 | - / - |
| *A. fumigatus* (182) | 0.015/0.03 | 0.015/0.03 | ≤0.008/0.015 | - / - |
| Other *Aspergillus* spp.(18) | 0.015/0.03 | 0.03/0.12 | 0.03/0.12 | - / - |
| *Scedosporium* spp. (13) | 0.03/0.06 | 4/8 | >8/>8 | - / - |

**Conclusions:** APX001A demonstrated potent *in vitro* activity against 1,706 fungal isolates including echinocandin- and fluconazole-resistant strains. The extended spectrum of APX001A was also notable for its potency against many less common, yet antifungal-resistant strains such as *Candida auris*, *A. lentulus*, *A. ustus*, *Fusarium solani* species complex, and *Scedosporium*. Further studies are needed to demonstrate the utility of APX001A in difficult-to-treat resistant fungal infections.