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Paper Poster Session
Antifungal drug treatment

In vitro activity of isavuconazole against azole-resistant environmental Aspergillus fumigatus isolates, cryptic Candida strains and emerging yeasts

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Background: Isavuconazole is a novel broad-spectrum triazole agent. Since October 2015, isavuconazole is approved in Europe for the treatment of adult patients with invasive aspergillosis or mucormycosis when amphotericin B is inappropriate. Isavuconazole has *in vitro* activity against most medically important fungi, including species of *Candida*, *Aspergillus*, and *Cryptococcus* and activity against some of the agents of mucormycosis. Considering that isavuconazole shares the same mechanism of action with the other triazoles, cross-resistance is an important concern in the class. The aim of this study was to complete the isavuconazole spectrum establishing MIC for rare azole-resistant environmental *Aspergillus* strains, fluconazole resistant *Candida* spp and uncommon fungi by using EUCAST methodology.

Material/methods: A collection of wild-type *A. fumigatus* clinical isolates and environmental (TR34/L98H and TR46/Y121F/T289A) azole-resistant *A. fumigatus* isolates was evaluated for isavuconazole (Basilea Pharmaceutica Ltd) MIC determination by EUCAST standard methodology. Additionally, fluconazole resistant *Candida* spp, cryptic *Candida* species (*C. metapsilosis, C. nivariensis, C. auris, C. africana)* and other uncommon yeasts (*Trichosporon faecale, Cryptococcus gattii, Galactomyces candidus, Saprochaete suaveolens, Pichia kluyveri)* were also studied. *Candida krusei* ATCC 6258 and *C. parapsilosis* ATCC 22019 were used as control strains. For azole resistant *Aspergillus* and *Candida* isolates, isavuconazole was docked in the models of caCYP51 and AfCYP51.

Results: In this study isavuconazole demonstrated excellent *in vitro* activity against the crytic species *C. metapsilosis*, *C. nivariensis, C. auris* and *C. africana* and all the emerging yeasts. Furthermore this antifungal drug exhibited low MICs against *Candida* spp isolates including isolates with reduced fluconazole and/or voriconazole susceptibility as against wild type *Aspergillus fumigatus*. However, environmental azole-resistant *A. fumigatus* isolates also show high MICs (>8ug/ml) to isavuconazole.

Conclusions: In conclusion, the *in vitro* data presented in this study provide encouraging evidence of isavuconazole activity against unusual fungal pathogens and further contribute to outline its spectrum of activity. However, isavuconazole did not reverse resistance of TR34/L98H and TR46/Y121F/T289A isolates. Although this agent may be useful in the treatment of the rare yeasts, clinical data are needed to confirm these results.