

P1284

Paper Poster Session VI

Antifungal susceptibility

Combination antifungal activity on conidia and hyphae of *Fusarium* species

M. Drogari-Apiranthitou<sup>1</sup>, M. Siopi<sup>2</sup>, A. Bakossi<sup>1</sup>, J. Meletiadis<sup>2</sup>, G. Petrikos<sup>1</sup>

<sup>1</sup>Infectious Diseases Research Laboratory/4th Dept. of Internal Medicine- Attikon General University Hospital,

National and Kapodistrian University of Athens, Athens, Greece

<sup>2</sup>Laboratory of Clinical Microbiology- Attikon General University Hospital, National and Kapodistrian University of Athens, Athens, Greece

**Objectives** Combination therapy with antifungal drugs belonging to different classes (polyenes, azoles and echinocandins) is commonly used for difficult-to-treat fungal infections such as fusariosis. Data on antifungal susceptibility of hyphae, elements that better represent the fungal form in tissues, are scarce. We aimed to study the *in vitro* combined activity of antifungals against conidia and hyphae of *Fusarium* species, using a pharmacodynamic-based methodology.

**Methods** Sixteen clinical strains were tested in total: 5 *Fusarium solani* species complex (SC), 8 *F. fujikuroi* SC (5 *F. verticillioides*, 3 *F. proliferatum*), 2 *F. oxysporum* SC and one *Fusarium* spp. Hyphae were formed after a 12h incubation of conidia at 37°C. Dual combinations of Amphotericin B (AmB), anidulafungin (AND), posaconazole (POS) and voriconazole (VOR) were tested at concentrations ranging from 0.03-4 mg/L against conidia or hyphae in a checkerboard assay based on the EUCAST methodology. The MICs were determined with the XTT tetrazolium salt method and synergy was estimated by calculation of the fractional inhibitory concentration indices (FICIs) based on complete metabolic inhibition endpoint. *Aspergillus fumigatus* ATCC 204305 and *Candida krusei* ATCC 6258 were used as quality control strains.

**Results** The MICs of the antifungals alone did not differ significantly between conidia and hyphae. The FICIs against conidia or hyphae were also comparable. The combination AmB/AND showed synergy more frequently against conidia (54% of strains, median FICI 0.5, range 0.3-1) and the combination AmB/POS was more effective against hyphae (75% of strains, median FICI 0.3, range 0.3-0.6), but these differences were not statistically significant. Synergy was not species related. Antagonism was in no case observed.

**Conclusions** Synergy was frequently found with amphotericin B combined with anidulafungin against conidia, and with amphotericin B combined with posaconazole against hyphae of *Fusarium* strains. Combination therapy may be beneficial against infections caused by *Fusarium* species. Further studies in animal models are required in order to assess the clinical relevance of these combinations.