O227
1-hour Oral Session
From antifungal susceptibility to resistance

In vitro activity of isavuconazole against Candida and Aspergillus

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Background: Isavuconazole is a newly licensed compound in Europe. Here we report the in vitro activity of isavuconazole in comparison with voriconazole against for clinical isolates of Candida and Aspergillus isolates received in 2012-14 at the national reference laboratory for mycology in Denmark.

Material/methods: 1677 *Candida* and *Saccharomyces* isolates and 716 *Aspergillus* isolates were received. Species identification was done using morphology supplemented by MALDI-TOF mass spectrometry for the yeasts and thermotolerance and beta-tubulin sequencing for *Aspergillus*. EUCAST susceptibility testing was done following E-Def 7.2 for yeast. For *Aspergillus* screening for azole resistance was gradually implemented. Thus MIC determination was performed for 263/716 *Aspergillus* isolates following E-Def 9.2. Isolates were categorised as wild-type or non-wild-type isolates adopting EUCAST ECOFFs. For species without ECOFFs, a wild-type upper limit was determined as two 2-fold dilutions above the modal MIC was used. Thus isavuconazole/voriconazole ECOFF/ upper limit (mg/L) were: *A. flavus*: 2/2; *A. fumigatus*: 2/ 1; *A. nidulans*: 0.25/1; *A. niger*: 4/2; *A. terreus* 1/2, *C. albicans*: 0.03/0.125; *C. dubliniensis*: 0.03/0.125; *C. glabrata*: 0.125/1; *C. krusei* 0.125/1; *C. parapsilosis*: 0.03/0.125; *C. tropicalis* 0.03/0.125; *S. cerevisiae*: 0.125/0.25.

Results: Modal MIC (range) (mg/L) for isavuconazole against *Candida* species were as follows: *C. albicans*: ≤0.03 (≤0.03->4), *C. dubliniensis*: ≤0.03 (≤0.03), *C. glabrata*: ≤0.03 (≤0.03-4), *C. krusei*: ≤0.03 (≤0.03-0.5), *C. parapsilosis*: ≤0.03 (≤0.03–0.06), *C. tropicalis*: ≤0.03 (≤0.03->4), *S. cerevisiae*: ≤0.03 (≤0.03 -0.5) and other *Candida* ≤0.03 (≤0.03->4). Isavuconazole MICs above the wild-type upper limit were found for 0.84% of *C. albicans*, 14.89% of *C. glabrata*, 14.86% of *C. krusei*, 1.69% of *C. parapsilosis*, 14.29% of *C. tropicalis* and 10.00% of *S. cerevisiae*. In comparison, voriconazole MIC values above the ECOFFs were: 0.97% for *C. albicans*, 1.79% for *C. dubliniensis*, 9.45% for *C. glabrata*, 1.37% for *C. krusei*, 1.79% for *C. parapsilosis*, 19.12% for *C. tropicalis* and 5.00% for *S. cerevisiae*. Modal MIC (range) (mg/L) for isavuconazole against *Aspergillus* species were as follows: *A. calidoustus*: n.a. (4), *A. flavus*: 1 (0.5-2), *A. fumigatus*: 1 (≤0.125->4), *A. nidulans*: ≤0.125 (≤0.125-0.25), *A. niger*: 2 (1->4), *A. tamarii*: n.a (0.25), *A. terreus*: 1 (0.25->4), *A. tubingensis* n.a. (4 >4).

Isavuconazole MICs above the ECOFFs were found for 0% *A. flavus*, 14.12% *A. fumigatus*, 0% *A. nidulans*, 5.26% *A. niger* and 48.15% *A. terreus*. The similar percentages for voriconazole were: 0% *A. flavus*, 15.29% *A. fumigatus*, 0% *A. nidulans*, 0% *A. niger* and 22.22% *A. terreus*.

Conclusions: overall isavuconazole displayed a broad *in vitro* activity which was similar to that of voriconazole. Non wild-type isolates were found in up to 14% *C. glabrata*, *C. krusei, C. tropicalis* and *A. fumigatus*, but in part reflects the selected isolate population received at a reference laboratory.