

CLSI versus EUCAST for azoles susceptibility - the necessity to unify

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INTRODUCTION

Nowadays, standard antifungal susceptibility testing for molds is made employing two protocols: CLSI/EUCAST. They differ in technical details and in the quantitative criteria for the Clinical Break Points (CBP). As azole treatment is the cornerstone in the management of human aspergillosis, the differences in CBP according to the adopted protocol are likely to result in different therapeutical decisions. The purpose of this work was to evaluate MICs by CLSI for azoles, in clinical isolates of *Aspergillus*, and compare these results with those previously obtained using EUCAST [1].

MATERIALS and METHODS

Between January 2010 and March 2016, 227 *Aspergillus* were isolated from biological samples of 207 patients with proven or probable infections, and with colonization, who were admitted to Centro Hospitalar do Porto (CHUP), Centro Hospitalar Universitário S. João and Instituto Português de Oncologia do Porto (IPO). The susceptibilities were evaluated for itraconazole (ITZ), voriconazole (VCZ), posaconazole (PCZ) and isavuconazole (ICZ) following the CLSI M38-A2 protocol. The results were compared with those obtained with EUCAST [1].

RESULTS

The 227 different *Aspergillus* species (n), their respective MICs (mg/L) range, mean and essential agreement (EA) at two dilutions for all strains and the four tested azoles according CLSI and EUCAST are depicted in table 1.

In table 2, the number of *Aspergillus fumigatus sensu stricto* resistant (R) and non-wild type (NWT) strains are shown. Although the EA between both protocols was good (85.7-100%) for all tested combinations strain/antifungal, except for *A. lentulus*, the MICs ranges and means were lower for the CLSI, and the difference was remarkable for ICZ.

Table 2: *A. fumigatus sensu stricto* resistant (R) and non-wild type (NWT) strains

| Species (n) | Test method | ITZ | | VCZ | | PCZ | | ICZ | |
|---------------------------|-------------|-----|-----|-----|-----|-----|-----|-----|-----|
| | | R | NWT | R | NWT | R | NWT | R | NWT |
| <i>A. fumigatus</i> (190) | CLSI | 4 | 4 | 1 | 5 | 0 | 12 | NA | 9 |
| | EUCAST | 8 | 44 | 5 | 6 | 29 | NA | 149 | 34 |

NA: not applicable

CONCLUSIONS

In agreement with previous reports [2,3,4], the findings for the present population highlight the lower MICs by CLSI compared to EUCAST. In addition, they emphasize the need to unify both protocols, aiming to improve epidemiological comparisons and patient management.

REFERENCES

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Table 1: MICs (mg/L) range, mean and essential agreement (EA) for azoles drugs, according CLSI and EUCAST protocols

| Species (n) | Test method | ITZ | | EA % | VCZ | | EA % | PCZ | | EA % | ICZ | | EA % |
|-------------------------------|-------------|-----------|------|------|-----------|------|------|-----------|------|------|-----------|------|------|
| | | MIC range | Mean | | MIC range | Mean | | MIC range | Mean | | MIC range | Mean | |
| <i>A. fumigatus</i> (190) | CLSI | 0.12-16 | 0.81 | 92.1 | 0.12-16 | 0.48 | 100 | 0.03-2 | 0.18 | 96.8 | 0.25-16 | 0.86 | 97.4 |
| | EUCAST | 0.25-16 | 1.49 | | 0.25-16 | 0.77 | | 0.03-16 | 0.34 | | 0.5-8 | 2.32 | |
| <i>A. lentulus</i> (5) | CLSI | 1-16 | 4.2 | 20 | 1-16 | 4.6 | 100 | 0.25-1 | 0.45 | 60 | 2-16 | 6.4 | 80 |
| | EUCAST | 16-16 | 16 | | 2-16 | 6 | | 0.5-16 | 4.3 | | 16-16 | 16 | |
| <i>A. felis</i> (1) | CLSI | 2 | --- | ND | 2 | --- | ND | 0.25 | --- | ND | 2 | --- | ND |
| | EUCAST | 8 | --- | | 4 | --- | | 0.25 | --- | | 4 | --- | |
| <i>A. thermomutatus</i> (1) | CLSI | 16 | --- | ND | 4 | --- | ND | 0.5 | --- | ND | 2 | --- | ND |
| | EUCAST | 16 | --- | | 8 | --- | | 1 | --- | | 4 | --- | |
| <i>A. flavus/oryzae</i> (14) | CLSI | 0.5-1 | 0.75 | 92.9 | 1-16 | 2.5 | 100 | 0.25-1 | 0.48 | 100 | 1-16 | 2.9 | 92.9 |
| | EUCAST | 0.5-16 | 2.5 | | 1-16 | 2.8 | | 0.25-2 | 0.84 | | 2-16 | 8 | |
| <i>A. welwitschiae</i> (7) | CLSI | 1-16 | 3.3 | 85.7 | 0.5-1 | 0.79 | 100 | 0.12-0.5 | 0.3 | 85.7 | 1-2 | 1.6 | 100 |
| | EUCAST | 1-16 | 4.9 | | 0.5-1 | 0.71 | | 0.12-2 | 0.76 | | 2-8 | 4.6 | |
| <i>A. niger</i> (1) | CLSI | 1 | --- | ND | 1 | --- | ND | 0.25 | --- | ND | 2 | --- | ND |
| | EUCAST | 2 | --- | | 1 | --- | | 0.5 | --- | | 4 | --- | |
| <i>A. terreus</i> (4) | CLSI | 0.12-0.25 | 0.1 | 100 | 0.5-0.5 | 0.5 | 100 | 0.06-0.12 | 0.08 | 100 | 0.5-1 | 0.75 | 100 |
| | EUCAST | 0.25-0.5 | 0.38 | | 0.5-1 | 0.88 | | 0.06-0.25 | 0.17 | | 2-4 | 3 | |
| <i>A. pseudodeflectus</i> (2) | CLSI | 16-16 | 16 | ND | 8-8 | 8 | ND | 16-16 | 16 | ND | 8-8 | 8 | ND |
| | EUCAST | 16-16 | 16 | | 16-16 | 16 | | 16-16 | 16 | | 16-16 | 8 | |
| <i>A. nidulans</i> (1) | CLSI | 0.5 | --- | ND | 0.12 | --- | ND | 0.25 | --- | ND | 0.25 | --- | ND |
| | EUCAST | 1 | --- | | 0.25 | --- | | 0.5 | --- | | 1 | --- | |
| <i>A. sydowii</i> (1) | CLSI | 0.5 | --- | ND | 1 | --- | ND | 0.5 | --- | ND | 2 | --- | ND |
| | EUCAST | 16 | --- | | 1 | --- | | 1 | --- | | 8 | --- | |

ND: not determinated

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