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Session: 242. Antifungals
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Background. Invasive aspergillosis (IA) is a leading cause of morbidity and mortality in immunocompromised hosts. Triazole resistance in *Aspergillus fumigatus* is emerging globally. We performed antifungal susceptibility testing (AST) in Aspergillus isolates from Mexico and evaluated risk factors associated with 6 week mortality, including the MICs.

Methods. Aspergillus isolates from clinical samples were collected in a tertiary care center from 2014 to 2018. Species-level identification and broth microdilution following the CLSI M38 method were performed. MICs were interpreted according to epidemiological cutoff values. PCR and cyp51A gene sequencing were performed in *A. fumigatus* isolates with voriconazole (VRC) MIC >1 µg/mL. Data from the medical record were obtained to classify patients according to the MSG/EORTC criteria. The relationship between the MICs and 6-week mortality was described. Multivariate analysis of factors associated with six week mortality was performed.

Results. AST was performed on 85 Aspergillus isolates: 60/85 from patients with IA, 15/85 from patients with Aspergillus colonization, 2 patients with Aspergilloma, 1 with chronic otitis media and 1 with endophtalmitis. Information from 6 patients was unavailable. VRC MIC > 1 µg/mL was found in 3/38 (7.8%) A. fumigatus, from two patients with IA. Both had a TR34/L98H mutation in the cyp51A gene. Amphotericin B (AmB) MICs ≥ 2 were found in 16/49 (32%) *A. fumigatus*, 10/15 (66%) *A. flavus* and 1/14 (8%) *A. niger*. Forty-one patients with IA were treated: 29/41 (71%) with VRC or posaconazole, 7/41 (17%) with AmB and 5 with combination therapy. Overall, 6-week mortality was 30/49 (61.2%) among patients with IA; 2/2 (100%) when VRC MIC >1 µg/mL and 12/19 (63%) when AmB > 2 µg/mL, of which only 4 patients received initial treatment with AmB. Age older than 65 years (OR 11.8; 95% CI 1.14–123) and hepatic failure (OR 7.9; 95% CI 1.22–50.9) were independently associated with 6-week mortality in multivariate analysis.

Conclusion. We found a VRC MIC >1 µg/mL prevalence of 7.8% among *A. fumigatus* and a high prevalence of AmB MIC ≥ 2 among clinical isolates of Aspergillus in Mexico. Elevated mortality was seen in IA among older patients with hepatic failure. Larger epidemiological studies are warranted.

Disclosures. **All authors:** No reported disclosures.

2119. Matched-Paired Analysis of Patients Treated for Invasive Mucormycosis—Standard Treatment vs. Posaconazole New Formulations (MoveOn)

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Background. Current first-line (first) antifungal treatment for invasive mucormycosis (IM) consists of liposomal amphotericin B (AMB). Salvage (SAL) treatment options are limited and often based on posaconazole oral suspension (POS*susp*). However, with the approval of posaconazole new formulations (POS*new*), patients could benefit from improved pharmacokinetics, safety and tolerability. Our aim was to assess the effectiveness of POS*new* as first-line and SAL treatments for IM.

Methods. We performed a case-matched analysis with proven or probable IM patients from the FungiScope® Registry. 1st-POS*new* and 1st-AMB+POS*new* cases were matched with 1st-AMB-based treatment controls, and SAL-POS*new* cases were matched with SAL-POS*susp* controls. Each case was matched with up to three controls based on severity, hematological/oncological malignancy, surgery and/or renal dysfunction.

Results. Five patients receiving first-line POS*new* alone, 18 receiving first-line POS*new* combined with AMB, and 22 receiving salvage POS*new* were identified. By day 42, favorable response was reported for 80.0% (n = 4/5) of patients receiving first-line POS*new*, for 27.8% (n = 5/18) receiving first-line POS*new* plus AMB, and for 50.0% (n = 11/22) receiving salvage POS*new*. Day-42 all-cause mortality of patients receiving POS*new* was lower compared with mortality in their respective controls (20.0% (n = 1/5) in 1st-POS*new vs.* 53.3% (n = 8/15) in 1st-AMB; 33.3% (n = 6/18) in 1st-AMB+POS*new vs.* 52.0% (n = 26/50) in 1st-AMB; 0.0% (n = 0/22) in SAL-POS*new vs.* 4.4% (n = 2/45) in SAL-POS*susp*).

Conclusion. In the observed patients, POS*new* was effective in terms of treatment response and-associated mortality of IM. POS*new* may be an alternative for the treatment of IM.

Disclosures. **All authors:** No reported disclosures.

2120. Minimum Inhibitory Concentration Distribution of Fluconazole against Cryptococcus Species and the Fluconazole Exposure Prediction Model

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Background. Fluconazole is lifesaving for the treatment and prevention of cryptococcosis; however, optimal dosing is unknown. Initial fluconazole doses of 100 mg to 2000 mg/day have been used. Prevalence of fluconazole non-susceptible *Cryptococcus* is increasing over time, risking the efficacy of long-established standard dosing. Based on current minimum inhibitory concentration (MIC) distribution, we modeled fluconazole concentration and area under the curve (AUC) relative to MIC to propose a rational fluconazole dosing strategy.

Methods. First, we conducted a systematic review using the MEDLINE database for reports of fluconazole MIC distribution against clinical *Cryptococcus* isolates. Second, we utilized fluconazole concentrations from 92 Ugandans who received fluconazole 800 mg/day coupled with fluconazole's known pharmacokinetics to predict plasma fluconazole concentrations for doses ranging from 100 mg to 2000 mg via linear regression. Third, the fluconazole AUC above MIC ratio were calculated using Monte Carlo simulation and using the MIC distribution elucidated during the systemic review.

Results. We summarized 21 studies with 11,094 clinical *Cryptococcus* isolates. MICs were normally distributed with geometric mean of 3.4 mg/mL, median (MIC_{50}) of 4 mg/mL, and 90th percentile (MIC_{90}) of 16 mg/mL. The median MIC_{50} trended upwards from 4 mg/mL in 2000–2012 to 8 mg/mL in 2014–2018. Predicted sub-therapeutic fluconazole concentrations (below MIC) would occur in 38% with 100 mg, 20% with 200 mg, and 8% with 400 mg. AUC/MIC ratio > 100 would occur in 53% for 400 mg, 74% for 800 mg, 84% for 1200 mg, and 88% for 1,600 mg.

Conclusion. Currently recommended fluconazole doses may be inadequate for cryptococcosis. Further clinical studies are needed for rational fluconazole dose selection.

Figure 1. Fluconazole MIC Distribution for *Cryptococcus* from Years 2001-2012 and 2014-2018

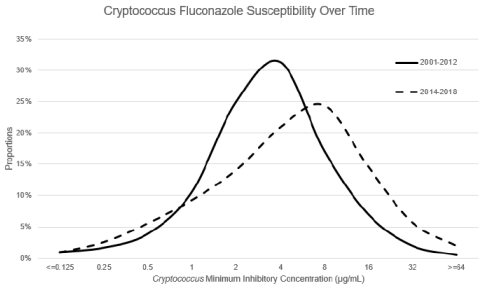

Figure 1. MIC distribution of 11,094 clinical isolates published from January 1, 2000 to May 31, 2018 were normally distributed with a geometric mean of 3.4 µg/mL, median MIC_{50} of 4 µg/mL, and 90th percentile MIC_{90} of 16 µg/mL. When divided into two groups, from the year 2000-2012 (13 studies, n=9,507) and year 2014-2018 (8 studies, n=1,542). The median MIC_{50} was up trending from 4 µg/mL to 8 µg/mL.

Figure 2. Proportion Achieving Target AUC/MIC Ratio

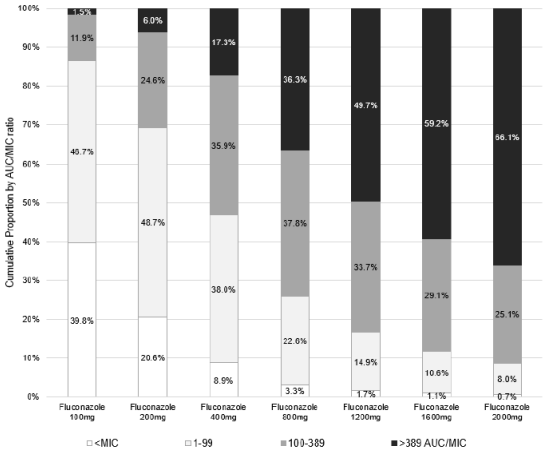

Figure 2. The percent of AUC/MIC ratio by category for various doses of fluconazole. The desire optimum target dose for induction therapy would be a>389 AUC/MIC ratio which is directly proportional to the fluconazole dose. The percent of <MIC reflects the percent of subtherapeutic fluconazole level which decreasing with a higher dose of fluconazole. At present ~20% of persons receiving 200mg/day are projected to not achieve plasma levels above MIC.

Disclosures. **All authors:** No reported disclosures.