The introduction of mammalian antifungal agents to the triazole spectrum has considerably improved the treatment of invasive mold infections. In clinical practice, caspofungin, micafungin, and liposomal amphotericin B remain the mainstays of antifungal therapy for the prevention and treatment of invasive aspergillosis (IA). There is a growing concern in our institution that merits monitoring by standardized susceptibility testing. Allopurinol and inosine have been used to improve susceptibility of Aspergillus fumigatus (A. fumigatus) to anidulafungin, voriconazole, and alternative agents. These observations have prompted a call for an expanded use of in vitro screening methods to detect emerging resistance. In this study, we compared the in vitro activity of anidulafungin, voriconazole, and comparator agents as determined by both CLSI and EUCAST broth microdilution methods (BMD) methods. CLSI BMD testing was performed as outlined in document M38-A2 (CLSI, 2008) by using MIC endpoints of 0.25-8 µg/ml for azoles and ≥0.5 µg/ml for echinocandins. For all isolates, MIC values were determined using an inoculum concentration of 5 X 10⁵ CFU/ml, and incubation at 35°C for 48 h. For all methods, the MIC was defined as the lowest concentration of drug that caused complete inhibition of fungal growth. In this study, we describe for the first time that both CLSI and EUCAST methods generate comparable results for susceptibility testing of Aspergillus spp.

Results: In vitro susceptibility testing of ANF and CAS was concordant for both methods. Certain isolates were only susceptible to CAS or ANF. Micafungin (MIC₉₀, 0.015 µg/ml) was the most potent agent against AMB-R strains of A. terreus (MEC₉₀, 0.12 µg/ml) > amphotericin B (MIC₉₀, 1 µg/ml) > caspofungin (MIC₉₀, 1 µg/ml) > voriconazole (MIC₉₀, 0.12 µg/ml) > anidulafungin (MIC₉₀, 0.12 µg/ml) > itraconazole (MIC₉₀, > 8 µg/ml; Table 3).

Conclusions: In vitro susceptibility testing of ANF, VRC, and other mammalian antifungal agents may be accomplished by either CLSI or EUCAST BMD methods with comparable results.

**RESULTS**

- All 78 isolates of Aspergillus spp. were examined. Strains with ≥2 µg/ml of azole resistance were determined by both CLSI and EUCAST methods.
- VRC and ANF were active against all azole-resistant isolates. ANF displayed the lowest MIC₉₀ (0.015 µg/ml) among azoles. For CAS, MIC₉₀ was 0.12 µg/ml. Itraconazole was ≥8 µg/ml for all isolates.
- The EA between the CLSI and EUCAST methods was 100.0% for caspofungin and voriconazole (Table 4). The EA between the CLSI and EUCAST methods was ≤0.0% for voriconazole and anidulafungin.
- The overall EA between CLSI and EUCAST results was 100.0% for caspofungin and voriconazole but only 61% (35/57) for anidulafungin.
- All MIC values for anidulafungin, caspofungin, and voriconazole were determined as described in the CLSI and EUCAST methods.
- The EA between the CLSI and EUCAST methods was 100.0% for caspofungin and voriconazole but only 61% (35/57) for anidulafungin.
- The overall EA between CLSI and EUCAST results was 100.0% for caspofungin and voriconazole but only 61% (35/57) for anidulafungin.
- The MIC data for the triazole-resistant strains were compared against the activities of the comparator agents. Anidulafungin was the most potent agent against the triazole-resistant strains. These compounds exhibit impressive activity against a spectrum of wild-type and resistant Aspergillus spp.
- Anidulafungin demonstrated excellent activity in vitro and against a variety of clinical isolates of Aspergillus spp. and Aspergillus terreus in clinical isolates.