# Activity of a Novel Echinocandin Biafungin (CD101) Tested against Most Common *Candida* and *Aspergillus* Species, Including Echinocandin- and Azole-resistant Strains

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## ABSTRACT

**Background**: A novel echinocandin, biafungin, displaying long-acting pharmacokinetics and chemical stability is being developed for once-weekly administration. The activities of biafungin and comparator agents were tested against 173 fungal isolates of the most clinically common species.

**Methods**: 106 CAN and 67 ASP were tested using CLSI and EUCAST reference broth microdilution methods against biafungin (50% inhibition) and comparators. Isolates included 27 echinocandin-resistant CAN (4 species) with identified *fks* hotspot (HS) mutations and 20 azole non-susceptible ASP (4 species).

**Results:** Against *C. albicans, C. glabrata* and *C. tropicalis*, the activity of biafungin ($MIC_{50}$, 0.06, 0.12 and 0.03 µg/ml, respectively by CLSI method) was comparable to anidulafungin (AND; $MIC_{50}$, 0.03, 0.12 and 0.03 µg/ml, respectively) and caspofungin (CSP; $MIC_{50}$, 0.12, 0.25 and 0.12 µg/ml, respectively; **Table**). *C. krusei* strains were very susceptible to biafungin, showing $MIC_{90}$ values of 0.06 µg/ml by both methods. Biafungin ($MIC_{50/90}$, 1/2 µg/ml) was comparable to AND and less potent than CSP against *C. parapsilosis* using CLSI methodology. CLSI and EUCAST methods displayed similar results for most species, but biafungin ($MIC_{50}$, 0.06 µg/ml) was eight-fold more active than CSP ($MIC_{50}$, 0.5 µg/ml) against *C. glabrata* using the EUCAST method. Overall, biafungin was two- to four-fold more active against *fks* HS mutants than CSP and results were comparable to AND. Biafungin was active against *A. fumigatus* ($MEC_{50/90}$, ≤0.008/0.015 µg/ml), *A. terreus* ($MEC_{50/90}$, 0.015/0.015 µg/ml), *A. niger* ($MEC_{50/90}$, ≤0.008/0.03 µg/ml) and *A. flavus* ($MEC_{50/90}$, ≤0.008/≤0.008 µg/ml) using CLSI method. EUCAST results for ASP were also low for all echinocandins and comparable to CLSI results.

**Conclusions:** Biafungin displayed comparable in vitro activity with other echinocandins against common wild-type CAN and ASP and resistant subsets that in combination with the long-acting profile warrants further development of this compound.

| | MIC/MEC$_{50/90}$ by CLSI (µg/ml; MIC/MEC$_{50/90}$ by EUCAST) | | |
|---|---|---|---|
| Organism (no. tested) | Biafungin | Anidulafungin | Caspofungin |
| *C. albicans* (25) | 0.06/0.5 (0.015/0.5) | 0.03/1 (≤0.008/0.25) | 0.12/1 (0.25/2) |
| *C. glabrata* (25) | 0.12/1 (0.06/0.5) | 0.12/1 (0.03/0.25) | 0.25/1 (0.5/2) |
| *C. tropicalis* (21) | 0.03/0.25 (0.06/0.5) | 0.03/0.5 (≤0.008/0.25) | 0.12/1 (0.25/2) |
| *C. krusei* (20) | 0.06/0.06 (0.06/0.06) | 0.06/0.12 (0.06/0.06) | 0.25/0.25 (0.5/1) |
| *C. parapsilosis* (15) | 1/2 (1/1) | 2/2 (0.5/1) | 0.5/0.5 (1/1) |
| *A. fumigatus* (20) | ≤0.008/0.015 (0.015/0.015) | ≤0.008/0.015 (0.015/0.015) | 0.06/0.12 (0.12/0.25) |

## INTRODUCTION

Fungal infections have emerged as major causes of human disease, especially among the immunocompromised patients and those hospitalized with serious underlying disease. As a consequence, the frequency of use of systemic antifungal agents has increased significantly and there is a growing concern about a shortage of effective antifungal agents. Although resistance rates to the clinically available antifungal agents remains low, reports of breakthrough infections and the increasing prevalence of uncommon fungal species that display elevated MIC values for existing agents is worrisome.

Biafungin (CD101, previously SP 3025) is a novel echinocandin that displays chemical stability and long-acting pharmacokinetics that is being developed for once-weekly or other intermittent administration (see posters #A-693 and A-694 for further information). In this study, we test biafungin and comparator agents against a collection of common *Candida* and *Aspergillus* species, including isolates resistant to azoles and echinocandins.

## MATERIALS AND METHODS

Organisms. A total of 106 *Candida* spp. and 67 *Aspergillus* spp. clinical isolates were collected from patients from hospitals participating in a global surveillance program during 2010. The collection included: *A. flavus* species complex (SC; 12), *A. fumigatus* SC (20), *A. terreus* SC (19), *A. niger* SC (16), *C. albicans* (25), *C. glabrata* (25), *C. tropicalis* (21), *C. parapsilosis* (15) and *C. krusei* (20). The collection contained 23 echinocandin-resistant *Candida* spp. strains and 12 itraconazole-resistant (MIC, ≥4 µg/ml) *Aspergillus* spp.

Susceptibility testing. Biafungin and comparator agents were tested using the CLSI and EUCAST broth microdilution reference methods. Stock solutions were prepared in DMSO and the final range of concentrations tested was 0.008-16 µg/ml. CLSI broth microdilution testing was performed as outlined in documents M27-A3 and M38-A2 by using RPMI 1640 medium with 0.2% glucose, inocula of $0.5x10^3$ to $2.5x10^3$ cells/ml and incubation at 35°C. MIC values were determined visually after 24-h (yeasts) and 48-h (moulds) of incubation. MIC/MEC endpoint criteria at both reading times include the lowest concentration of drug that caused a significant diminution (50% inhibition) of growth relative to that of the growth control for the echinocandins, including biafungin.

EUCAST broth microdilution testing was performed as outlined in document EDef. 7.1 by using RPMI 1640 with 2.0% glucose, inocula of $0.5x10^5$ to $2.5x10^5$ cells/ml and incubation at 35°C. MIC/MEC values were determined spectrophotometrically (at 530 nm) for yeasts and visually for moulds, after 24-h of incubation as the lowest concentration of drug that resulted in both 50% inhibition of growth relative to that of the growth control.

Quality control (QC) was ensured by testing *C. krusei* ATCC 6258 and *C. parapsilosis* ATCC 22019 as recommended by CLSI and EUCAST guidelines.

## RESULTS

- The investigational echinocandin biafungin ($MIC_{50/90}$, 0.06/0.5 µg/ml [CLSI results]; **Table 1**) was comparable to caspofungin and anidulafungin ($MIC_{50/90}$, 0.03/1 and 0.12/1 µg/ml [CLSI results], respectively) when tested against *C. albicans*.
- Biafungin ($MIC_{50/90}$, 0.12/1 µg/ml [CLSI results]; **Table 1**) displayed activity comparable to anidulafungin and caspofungin ($MIC_{50/90}$, 0.12/1 and 0.25/1 µg/ml, respectively) when tested against *C. glabrata* by CLSI method. Using the EUCAST method, biafungin ($MIC_{50}$, 0.06 µg/ml; **Table 2**) was eight-fold more active than caspofungin ($MIC_{50}$, 0.5 µg/ml).
- Against *C. tropicalis*, biafungin ($MIC_{50/90}$, 0.03/0.25 µg/ml; **Table 1**) showed activity comparable to anidulafungin ($MIC_{50/90}$, 0.03/0.5 µg/ml) and was four-fold more active than caspofungin ($MIC_{50/90}$, 0.12/1 µg/ml) when tested using the CLSI method. Similar results were noted using the EUCAST method (**Table 2**).
- *C. krusei* strains displayed low MIC values for biafungin ($MIC_{90}$ values of 0.06 µg/ml for CLSI and EUCAST methods; **Tables 1** and **2**). The activity of caspofungin was four- and 16-fold lower compared to biafungin using CLSI ($MIC_{90}$, 0.25 µg/ml) and EUCAST ($MIC_{90}$, 1 µg/ml) methods, respectively.
- The activity of biafungin against *C. parapsilosis* strains ($MIC_{50/90}$, 1/2 µg/ml; **Table 1**) was comparable to anidulafungin ($MIC_{50/90}$, 2/2 µg/ml) and both compounds were less active than caspofungin ($MIC_{50/90}$, 0.5/0.5 µg/ml) against this species according to the CLSI method results.
- The activity of biafungin ($MIC_{50/90}$, ≤0.008/0.015 µg/ml; **Table 1**) was very good for *A. fumigatus* when using 50% endpoint criteria at 48-h incubation and all strains were inhibited at ≤0.06 µg/ml. Identical values were noted for anidulafungin and caspofungin was slightly less active ($MIC_{50/90}$, 0.06/0.12 µg/ml). Similar results were noted using the EUCAST method (**Table 2**).
- Biafungin displayed good activity that was slightly greater than caspofungin ($MIC_{90}$ ranging from 0.06 to 0.12 µg/ml) and comparable to anidulafungin ($MIC_{90}$ ranging from ≤0.008 to 0.015 µg/ml) against *A. terreus* ($MIC_{50/90}$, 0.015/0.015 µg/ml), *A. niger* ($MIC_{50/90}$, ≤0.008/0.03 µg/ml) and *A. flavus* ($MIC_{50/90}$, ≤0.008/≤0.008 µg/ml) using the CLSI reference broth microdilution method.
- This investigational compound also displayed similar activity to other echinocandins when tested against echinocandin-resistant strains that harbor alterations on *FKS* and biafungin MIC values ranged from 0.06 to 2 µg/ml against these selected resistant isolates (**Table 3**).

**Table 3**. Biafungin, anidulafungin and caspofungin results against *Candida* spp. strains carrying *fks* mutations.

| | 1,3-β-D-glucan synthase aminoacid alterations[a]: | | | | MIC according to CLSI method (µg/ml): | | |
|---|---|---|---|---|---|---|---|
| Organism | *FKS1* HS1 | *FKS1* HS2 | *FKS2* HS1 | *FKS2* HS2 | BIAF | AND | CSP |
| *Candida albicans* | F641I | WT | NT | NT | 0.12 | 0.12 | 0.5 |
| *Candida albicans* | F641S | WT | NT | NT | 0.25 | 0.12 | 0.5 |
| *Candida albicans* | S645P | WT | NT | NT | 0.5 | 0.5 | 2 |
| *Candida albicans* | F641S | WT | NT | NT | 0.25 | 0.25 | 1 |
| *Candida albicans* | S645Y | WT | NT | NT | 1 | 2 | 1 |
| *Candida albicans* | S645F | WT | NT | NT | 0.5 | 1 | 1 |
| *Candida albicans* | D648Y | WT | NT | NT | 0.25 | 0.25 | 0.5 |
| *Candida albicans* | P649H | WT | NT | NT | 0.25 | 0.25 | 0.5 |
| *Candida albicans* | S645P | WT | NT | NT | 1 | 1 | 1 |
| *Candida glabrata* | WT | WT | F659V | WT | 1 | 1 | 0.5 |
| *Candida glabrata* | S629P | WT | WT | WT | 2 | 4 | 16 |
| *Candida glabrata* | D632Y | WT | WT | WT | 0.12 | 0.25 | 0.25 |
| *Candida glabrata* | L630I | WT | WT | WT | 0.06 | 0.06 | 0.25 |
| *Candida glabrata* | WT | WT | D648E | WT | 0.25 | 0.25 | 0.25 |
| *Candida glabrata* | F625Y | WT | WT | WT | 0.06 | 0.12 | 0.12 |
| *Candida glabrata* | F625S | WT | WT | WT | 0.5 | 1 | 2 |
| *Candida glabrata* | WT | WT | S663P | WT | 1 | 2 | 1 |
| *Candida glabrata* | WT | WT | P667T | WT | 0.25 | 0.25 | 0.5 |
| *Candida krusei* | WT | NT | NT | NT | 0.06 | 0.06 | 0.25 |
| *Candida krusei* | WT | R1361G | WT | WT | 1 | 2 | 8 |
| *Candida krusei* | F655C | WT | WT | WT | 0.25 | 0.5 | 1 |
| *Candida tropicalis* | S645P | WT | WT | WT | 0.5 | 1 | 2 |
| *Candida tropicalis* | F641S | WT | WT | WT | 0.25 | 0.25 | 0.25 |

Abbreviations: BIAF, Biafungin; AND, Anidulafungin; CSP, Caspofungin.
a. WT= wildtype; NT= not tested.

**Table 1**. Frequency distributions of biafungin and comparator echinocandin compounds when tested against 106 *Candida* spp. and 67 *Aspergillus* spp. isolates using the CLSI reference method.

| Organism (no. tested) | Number (cumulative %) of isolates inhibited at MIC/MEC (µg/ml)[a]: | | | | | | | | | | | | MIC/MEC | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Antifungal agent | ≤0.008 | 0.015 | 0.03 | 0.06 | 0.12 | 0.25 | 0.5 | 1 | 2 | 4 | 8 | ≥16 | 50% | 90% |
| *C. albicans* (25) | | | | | | | | | | | | | | |
| Biafungin | 1 (4.0) | 7 (32.0) | 3 (44.0) | 4 (60.0) | 1 (64.0) | 5 (84.0) | 2 (92.0) | 2 (100.0) | -- | -- | -- | -- | 0.06 | 0.5 |
| Anidulafungin | 4 (16.0) | 6 (40.0) | 5 (60.0) | 0 (60.0) | 2 (68.0) | 4 (84.0) | 1 (88.0) | 2 (96.0) | 1 (100.0) | -- | -- | -- | 0.03 | 1 |
| Caspofungin | -- | -- | 2 (8.0) | 5 (28.0) | 7 (56.0) | 1 (60.0) | 5 (80.0) | 4 (96.0) | 1 (100.0) | -- | -- | -- | 0.12 | 1 |
| *C. glabrata* (25) | | | | | | | | | | | | | | |
| Biafungin | -- | 1 (4.0) | 4 (20.0) | 10 (60.0) | 4 (76.0) | 2 (84.0) | 1 (88.0) | 2 (96.0) | 1 (100.0) | -- | -- | -- | 0.06 | 1 |
| Anidulafungin | 1 (4.0) | 0 (4.0) | 2 (12.0) | 8 (44.0) | 6 (68.0) | 4 (84.0) | 0 (84.0) | 2 (92.0) | 1 (96.0) | 1 (100.0) | -- | -- | 0.12 | 1 |
| Caspofungin | -- | -- | 1 (4.0) | 0 (4.0) | 11 (48.0) | 7 (76.0) | 3 (88.0) | 1 (92.0) | 1 (96.0) | 0 (96.0) | 0 (96.0) | 1 (100.0) | 0.25 | 1 |
| *C. tropicalis* (21) | | | | | | | | | | | | | | |
| Biafungin | 1 (4.8) | 6 (33.3) | 4 (52.4) | 4 (71.4) | 0 (71.4) | 4 (90.5) | 1 (95.2) | 1 (100.0) | -- | -- | -- | -- | 0.03 | 0.25 |
| Anidulafungin | 2 (9.5) | 5 (33.3) | 7 (66.7) | 1 (71.4) | 0 (71.4) | 3 (85.7) | 1 (90.5) | 2 (100.0) | -- | -- | -- | -- | 0.03 | 0.5 |
| Caspofungin | -- | -- | -- | 4 (19.0) | 9 (61.9) | 4 (81.0) | 1 (85.7) | 1 (90.5) | 2 (100.0) | -- | -- | -- | 0.12 | 1 |
| *C. krusei* (20) | | | | | | | | | | | | | | |
| Biafungin | -- | 1 (5.0) | 8 (45.0) | 9 (90.0) | 0 (90.0) | 1 (95.0) | 0 (95.0) | 1 (100.0) | -- | -- | -- | -- | 0.06 | 0.06 |
| Anidulafungin | -- | 1 (5.0) | 0 (5.0) | 14 (75.0) | 3 (90.0) | 0 (90.0) | 1 (95.0) | 0 (95.0) | 1 (100.0) | -- | -- | -- | 0.06 | 0.12 |
| Caspofungin | -- | -- | -- | -- | 2 (10.0) | 16 (90.0) | 0 (90.0) | 1 (95.0) | 0 (95.0) | 0 (95.0) | 1 (100.0) | -- | 0.25 | 0.25 |
| *C. parapsilosis* (15) | | | | | | | | | | | | | | |
| Biafungin | -- | -- | -- | -- | -- | -- | 5 (33.3) | 7 (80.0) | 3 (100.0) | -- | -- | -- | 1 | 2 |
| Anidulafungin | -- | -- | -- | -- | -- | -- | 2 (13.3) | 5 (46.7) | 8 (100.0) | -- | -- | -- | 2 | 2 |
| Caspofungin | -- | -- | -- | -- | 1 (6.7) | 3 (26.7) | 10 (93.3) | 1 (100.0) | -- | -- | -- | -- | 0.5 | 0.5 |
| *A. fumigatus* (20) | | | | | | | | | | | | | | |
| Biafungin | 15 (75.0) | 4 (95.0) | 0 (95.0) | 1 (100.0) | -- | -- | -- | -- | -- | -- | -- | -- | ≤0.008 | 0.015 |
| Anidulafungin | 15 (75.0) | 4 (95.0) | 0 (95.0) | 1 (100.0) | -- | -- | -- | -- | -- | -- | -- | -- | ≤0.008 | 0.015 |
| Caspofungin | -- | -- | 1 (5.0) | 11 (60.0) | 7 (95.0) | 0 (95.0) | 1 (100.0) | -- | -- | -- | -- | -- | 0.06 | 0.12 |
| *A. terreus* (19) | | | | | | | | | | | | | | |
| Biafungin | 8 (42.1) | 10 (94.7) | 1 (100.0) | -- | -- | -- | -- | -- | -- | -- | -- | -- | 0.015 | 0.015 |
| Anidulafungin | 11 (57.9) | 7 (94.7) | 1 (100.0) | -- | -- | -- | -- | -- | -- | -- | -- | -- | ≤0.008 | 0.015 |
| Caspofungin | -- | -- | -- | 11 (57.9) | 8 (100.0) | -- | -- | -- | -- | -- | -- | -- | 0.06 | 0.12 |
| *A. flavus* (12) | | | | | | | | | | | | | | |
| Biafungin | 11 (91.7) | 1 (100.0) | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | ≤0.008 | ≤0.008 |
| Anidulafungin | 11 (91.7) | 1 (100.0) | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | ≤0.008 | ≤0.008 |
| Caspofungin | -- | -- | 3 (25.0) | 8 (91.7) | 1 (100.0) | -- | -- | -- | -- | -- | -- | -- | 0.06 | 0.06 |
| *A. niger* (16) | | | | | | | | | | | | | | |
| Biafungin | 14 (87.5) | 0 (87.5) | 2 (100.0) | -- | -- | -- | -- | -- | -- | -- | -- | -- | ≤0.008 | 0.03 |
| Anidulafungin | 15 (93.8) | 1 (100.0) | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | ≤0.008 | ≤0.008 |
| Caspofungin | -- | -- | -- | 14 (87.5) | 2 (100.0) | -- | -- | -- | -- | -- | -- | -- | 0.06 | 0.12 |

**Table 2**. Frequency distributions of biafungin and comparator echinocandin compounds when tested against 106 *Candida* spp. and 67 *Aspergillus* spp. isolates using the EUCAST reference method.

| Organism (no. tested) | Number (cumulative %) of isolates inhibited at MIC/MEC (µg/ml)[a]: | | | | | | | | | | | | MIC/MEC | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Antifungal agent | ≤0.008 | 0.015 | 0.03 | 0.06 | 0.12 | 0.25 | 0.5 | 1 | 2 | 4 | 8 | ≥16 | 50% | 90% |
| *C. albicans* (25) | | | | | | | | | | | | | | |
| Biafungin | 12 (48.0) | 1 (52.0) | 2 (60.0) | 0 (60.0) | 5 (80.0) | 1 (84.0) | 3 (96.0) | 1 (100.0) | -- | -- | -- | -- | 0.015 | 0.5 |
| Anidulafungin | 15 (60.0) | 0 (60.0) | 3 (72.0) | 2 (80.0) | 1 (84.0) | 4 (100.0) | -- | -- | -- | -- | -- | -- | ≤0.008 | 0.25 |
| Caspofungin | -- | -- | -- | -- | 5 (20.0) | 10 (60.0) | 0 (60.0) | 5 (80.0) | 3 (92.0) | 2 (100.0) | -- | -- | 0.25 | 2 |
| *C. glabrata* (25) | | | | | | | | | | | | | | |
| Biafungin | 1 (4.0) | 0 (4.0) | 7 (32.0) | 9 (68.0) | 2 (76.0) | 3 (88.0) | 1 (92.0) | 1 (96.0) | 1 (100.0) | -- | -- | -- | 0.06 | 0.5 |
| Anidulafungin | 7 (28.0) | 2 (36.0) | 8 (68.0) | 2 (76.0) | 2 (84.0) | 2 (92.0) | 0 (92.0) | 1 (96.0) | 1 (100.0) | -- | -- | -- | 0.03 | 0.25 |
| Caspofungin | -- | -- | -- | -- | -- | 11 (44.0) | 8 (76.0) | 2 (84.0) | 2 (92.0) | 0 (92.0) | 1 (96.0) | 1 (100.0) | 0.5 | 2 |
| *C. tropicalis* (21) | | | | | | | | | | | | | | |
| Biafungin | 2 (9.5) | 0 (9.5) | 7 (42.9) | 5 (66.7) | 3 (81.0) | 1 (85.7) | 3 (100.0) | -- | -- | -- | -- | -- | 0.06 | 0.5 |
| Anidulafungin | 14 (66.7) | 0 (66.7) | 1 (71.4) | 2 (81.0) | 0 (81.0) | 3 (95.2) | 1 (100.0) | -- | -- | -- | -- | -- | ≤0.008 | 0.25 |
| Caspofungin | -- | -- | -- | -- | 3 (14.3) | 11 (66.7) | 2 (76.2) | 1 (81.0) | 4 (100.0) | -- | -- | -- | 0.25 | 2 |
| *C. krusei* (20) | | | | | | | | | | | | | | |
| Biafungin | -- | -- | 5 (25.0) | 13 (90.0) | 1 (95.0) | 0 (95.0) | 1 (100.0) | -- | -- | -- | -- | -- | 0.06 | 0.06 |
| Anidulafungin | 1 (5.0) | 0 (5.0) | 8 (45.0) | 9 (90.0) | 1 (95.0) | 0 (95.0) | 0 (95.0) | 1 (100.0) | -- | -- | -- | -- | 0.06 | 0.06 |
| Caspofungin | -- | -- | -- | -- | -- | 1 (5.0) | 10 (55.0) | 8 (95.0) | 0 (95.0) | 0 (95.0) | 0 (95.0) | 1 (100.0) | 0.5 | 1 |
| *C. parapsilosis* (15) | | | | | | | | | | | | | | |
| Biafungin | -- | -- | -- | -- | -- | -- | 5 (33.3) | 10 (100.0) | -- | -- | -- | -- | 1 | 1 |
| Anidulafungin | -- | -- | -- | -- | -- | 3 (20.0) | 6 (60.0) | 6 (100.0) | -- | -- | -- | -- | 0.5 | 1 |
| Caspofungin | -- | -- | -- | -- | -- | -- | 3 (20.0) | 12 (100.0) | -- | -- | -- | -- | 1 | 1 |
| *A. fumigatus* (20) | | | | | | | | | | | | | | |
| Biafungin | 6 (30.0) | 13 (95.0) | 1 (100.0) | -- | -- | -- | -- | -- | -- | -- | -- | -- | 0.015 | 0.015 |
| Anidulafungin | 7 (35.0) | 13 (100.0) | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | 0.015 | 0.015 |
| Caspofungin | -- | -- | -- | 1 (5.0) | 11 (60.0) | 8 (100.0) | -- | -- | -- | -- | -- | -- | 0.12 | 0.25 |
| *A. terreus* (19) | | | | | | | | | | | | | | |
| Biafungin | 14 (73.7) | 2 (84.2) | 3 (100.0) | -- | -- | -- | -- | -- | -- | -- | -- | -- | ≤0.008 | 0.03 |
| Anidulafungin | 15 (78.9) | 4 (100.0) | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | ≤0.008 | 0.015 |
| Caspofungin | -- | -- | -- | 1 (5.3) | 4 (26.3) | 13 (94.7) | 0 (94.7) | 1 (100.0) | -- | -- | -- | -- | 0.25 | 0.25 |
| *A. flavus* (12) | | | | | | | | | | | | | | |
| Biafungin | 7 (58.3) | 3 (83.3) | 2 (100.0) | -- | -- | -- | -- | -- | -- | -- | -- | -- | ≤0.008 | 0.03 |
| Anidulafungin | 6 (50.0) | 6 (100.0) | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | ≤0.008 | 0.015 |
| Caspofungin | -- | -- | -- | 1 (8.3) | 9 (83.3) | 2 (100.0) | -- | -- | -- | -- | -- | -- | 0.12 | 0.25 |
| *A. niger* (16) | | | | | | | | | | | | | | |
| Biafungin | 15 (93.8) | 0 (93.8) | 1 (100.0) | -- | -- | -- | -- | -- | -- | -- | -- | -- | ≤0.008 | ≤0.008 |
| Anidulafungin | 15 (93.8) | 1 (100.0) | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | ≤0.008 | ≤0.008 |
| Caspofungin | -- | -- | -- | -- | 9 (56.3) | 7 (100.0) | -- | -- | -- | -- | -- | -- | 0.12 | 0.25 |

## CONCLUSIONS

- Biafungin is a potent and broad-spectrum antifungal agent with excellent activity against wild-type and troublesome azole- and echinocandin-resistant strains of *Candida* spp. The activity of biafungin is comparable to anidulafungin.
- Biafungin was active against both wild-type and itraconazole-resistant strains of *Aspergillus* spp. from four different species.
- In vitro susceptibility testing of biafungin against isolates of *Candida* and *Aspergillus* may be accomplished by either CLSI or EUCAST broth microdilution methods each providing comparable results.
- The use of long-acting intravenous antifungal agents that could safely be given once a week to select patients is desirable and might decrease costs with long-term hospitalizations.

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