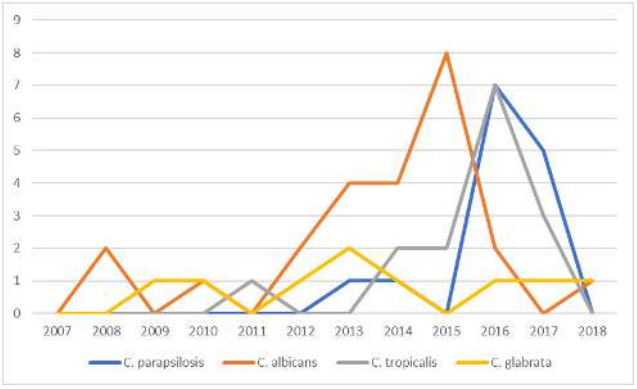


***Disclosures.*** **All authors:** No reported disclosures.

**2115. Activity of a Long-Acting Echinocandin Rezafungin and Comparator Antifungal Agents Tested against Contemporary Invasive Fungal Isolates: SENTRY 2018**

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***Background.*** Echinocandins are the first-line treatment of candidemia. We evaluated the activity of rezafungin (RZF), a novel long-acting echinocandin with front-loaded drug exposure and extensive distribution to sites of infection, and comparators using CLSI broth microdilution methods against 709 invasive fungal isolates collected worldwide during 2018.

***Methods.*** Susceptibility (S) tests on 663 *Candida* spp. (6 species), 21 *C. neoformans* (CNEO), and 25 *A. fumigatus* (ASF) were conducted for RZF, anidulafungin (ANF), caspofungin (CSF), micafungin (MCF), and azoles. CLSI clinical breakpoint (CBP) and epidemiological cutoff value (ECV) interpretive criteria were applied. Isolates displaying echinocandin MIC>ECV were sequenced for *fks* hot spot (HS) mutations.

***Results.*** RZF inhibited 99.7% of *C. albicans* (CA) isolates ($MIC_{50/90}$, 0.015/0.06 mg/L), 100.0% of *C. tropicalis* (CT) ($MIC_{50/90}$, 0.03/0.06 mg/L), 98.9% of *C. glabrata* (CG) ($MIC_{50/90}$, 0.03/0.06 mg/L), 100.0% of *C. krusei* (CK) ($MIC_{50/90}$, 0.015/0.12 mg/L), and 100.0% of *C. dubliniensis* (CD) ($MIC_{50/90}$, 0.03/0.06 mg/L) at ≤0.12 mg/L. All (104/104 [100.0%]) *C. parapsilosis* (CP) isolates ($MIC_{50/90}$,1/2 mg/L) were inhibited by RZF at ≤2 mg/L. Fluconazole resistance was detected among 9.0% of CG, 17.3% of CP, and 1.6% of CT. The activity of RZF against these 6 *Candida* spp. was similar to that of the other echinocandins, the vast majority of which were susceptible/wild type (WT) using CBP/ECV. A total of 5 isolates (3 CG, 1 CA, and 1 CT) displayed 1 or more non-WT or-resistant MIC values and were sequenced for *fks* HS mutations. Fluconazole and other azoles displayed good activity against CNEO whereas echinocandins including RZF displayed limited activity against CNEO isolates. Echinocandins displayed good activity against ASF, and RZF activity was similar to that of anidulafungin, caspofungin, and micafungin. All but 1 isolate (non-WT MIC for itraconazole, 2 mg/L) displayed WT MIC values for the mould-active azoles.

***Conclusion.*** Rezafungin was as active as other echinocandins against common organisms recovered from invasive fungal infections. These *in vitro* data contribute to accumulating research demonstrating rezafungin potential for prevention and treatment of invasive fungal infection.

| | MIC/MEC$_{50/90}$ (µg/mL) | | | |
|---|---|---|---|---|
| Organism (no. tested) | RZF | ANF | CSF | MCF |
| *C. albicans* (360) | 0.015/0.06 | 0.015/0.03 | 0.015/0.03 | 0.008/0.015 |
| *C. glabrata* (89) | 0.03/0.06 | 0.06/0.12 | 0.03/0.06 | 0.008/0.03 |
| *C. parapsilosis* (104) | 1/2 | 2/2 | 0.25/0.5 | 1/1 |
| *C. tropicalis* (62) | 0.03/0.06 | 0.015/0.03 | 0.015/0.06 | 0.03/0.06 |
| *C. krusei* (16) | 0.015/0.12 | 0.03/0.12 | 0.12/0.25 | 0.06/0.25 |
| *C. dubliniensis* (33) | 0.03/0.06 | 0.03/0.06 | 0.03/0.06 | 0.015/0.03 |
| *A. fumigatus* (25) | 0.015/0.03 | 0.015/0.015 | 0.03/0.06 | 0.008/0.015 |

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**2116. Comparative Effectiveness of Amphotericin B, Azoles, and Echinocandins in the Treatment of Candidemia and Invasive Candidiasis: A Systematic Review and Network Meta-Analysis**

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***Background.*** Current guidelines recommend the use of echinocandins, amphotericin B or fluconazole for the treatment of invasive candidiasis and candidemia. The objective of our study was to compare these agents through a systematic review of the literature and network meta-analysis of randomized controlled trials.

***Methods.*** Three electronic databases (Medline, PubMed, and the Cochrane Database of Systematic Reviews) were searched from database inception to January 1 2019. Randomized controlled trials that compared triazoles, echinocandins and/or amphotericin B (either in lipid formulation or deoxycholate form) for the treatment of invasive candidiasis or candidemia were included. Among included studies, treatment success was collected as the primary outcome and was assessed by a random effect network meta-analysis using Bayesian estimation methods. A sensitivity analysis was performed for all patients with candidemia.

***Results.*** Eleven randomized controlled trials met the study inclusion criteria. Of the 2,475 patients included from these trials, 684 received an echinocandin, 855 received amphotericin B and 936 received a triazole. Echinocandins were associated with the highest rate of treatment success when compared with amphotericin B (OR 1.40, 95% CI 1.02–1.93) and the triazoles (OR 1.80, 95% CI 1.32–2.51). Similarly, in the pre-specified analysis of candidemic patients, echinocandins were also more effective overall than amphotericin B (OR 1.25, 95% CI 0.84–1.87) and triazoles (OR 1.66, 95% CI 1.16–2.44). Patients treated with triazoles had a lower rate of treatment success than amphotericin B in the overall (OR 0.78, 95% CI 0.60–1.01) and candidemia sensitivity analyses (OR 0.76, 95% CI 0.56–1.01) Rank probability analysis favored echinocandins as the most effective treatment choice 98% of the time.

***Conclusion.*** In our meta-analysis comparing treatment strategies for severe *Candida* infections, the echinocandins had the highest rate of treatment success compared with both amphotericin B and triazoles. Echinocandins should be considered as first-line agents in the treatment of invasive candidiasis and candidemia. Further research is needed to determine the minimum duration of echinocandin treatment prior to using step-down therapy.

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**2117. Fluconazole vs. Echinocandins as Initial Therapy for Candidemia Caused by Fluconazole-Susceptible Species in the Era of Rapid Diagnostic Testing**

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***Background.*** Echinocandins (ECH) are recommended first-line for initial therapy (IT) of candidemia (CD) over fluconazole (FLU) due to their broad spectrum of activity. This recommendation was made prior to widespread implementation of rapid diagnostic testing (RDT), allowing prompt species identification and targeted therapy. The objective of this study was to compare clinical outcomes in patients with CD caused by FLU-susceptible species who received either FLU or ECH as IT.

***Methods.*** This was a multicenter, retrospective cohort study of adults with CD caused by *C. albicans*, *C. tropicalis*, or *C. parapsilosis*. Patients who received FLU or ECH as IT for at least 48 hours from May 2012 to October 2018 were included. Patients who died within 48 hours of first positive blood culture were excluded. The primary endpoint was the rate of clinical failure (persistent CD for >72 hours, recurrent infection within 30 days, change in therapy, and all-cause mortality within 30 days). Secondary endpoints included 90-day all-cause mortality and time to culture clearance. A subgroup analysis in critically ill patients was conducted.

***Results.*** Of the 371 patients evaluated, 128 met criteria for inclusion, 57 received FLU and 71 received ECH. Patients in the ECH group had a higher incidence of sepsis at the time of first positive blood culture (45.1% vs. 19.3%, $P = 0.002$). A line-associated source was more common in the ECH group (56.3%) vs. urinary source in the FLU group (21.1%). *C. albicans* was most common in both groups (63%). Clinical failure was similar in the FLU and ECH groups (38.6% vs. 35.2%, $P = 0.69$). 90-day mortality and time to culture clearance (1.6 vs. 1.5 days, $P = 0.63$) did not yield significant differences. In the subgroup analysis of critically ill patients, there was a trend suggesting higher rate of failure in patients who received FLU vs. an ECH (60.9% vs. 47.7%, $P = 0.31$), though underpowered to detect such a difference. Length of stay (LOS) was shorter in patients who received FLU (12 vs. 18 days, $P = 0.018$).

***Conclusion.*** FLU as IT for FLU-susceptible CD may be a reasonable option in non-critically ill patients in the setting of RDT. This may lead to shorter LOS given the availability of an oral formulation. Additional prospective studies are needed to validate these conclusions.

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**2118. Antifungal Susceptibility Testing of Clinical Isolates of *Aspergillus* in Mexico**

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