165. Outcomes Comparing Initial Short vs Long Course Echinocandin Therapy in Patients with Candidemia Caused by Fluconazole Susceptible Strains
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Background. Guidelines for candidemia (CAND) treatment recommend initial echinocandin (ECHINO) therapy with transition to fluconazole (FLUC) after 5–7 days in patients with clinical stability, FLUC-susceptibility, and negative cultures; however, optimal timing for transition in CAND due to routinely FLUC-susceptible species, as well as the impact of earlier transition in CAND due to routinely FLUC-susceptible species, is unknown. Methods. Retrospective study of adult patients at NewYork-Presbyterian Hospital from 2012 to 2014. Inclusion criteria included ≥1 blood culture with C. albi, C. tropicalis or C. parapsilosis, ≥1 dose ECHINO initial therapy, ≥3 days total treatment, and no prior episode of CAND within 30 days. Patients with polymicrobial bloodstream infection excluded. Patients de-escalated from ECHINO at ≤3 days (short course; SC-ECH) were compared with those who received ≥4 days of ECHINO (long course; LC-ECH). The primary outcome was 14-day complete response (CR), defined as survival with clinical improvement and sterilization of blood cultures. Secondary outcomes included day 7 microbiological success (MicroS) and 28-day survival (SURV). Results. 76 patients included: 21 in SC-ECH, 55 in LC-ECH groups. C. albicans (58%) most common species. Majority were male (59%) with median age 64 years (IQR 49–74), 62% were in ICU at time of Candida, 50% had recent surgery. No significant baseline differences between SC-ECH and LC-ECH groups, including in PITT bacteremia score ≥4 (43% vs. 42%; P = 0.6) or median APACHE (20 vs. 20; P = 0.684). There was no difference between SC-ECH vs. LC-ECH CR (52% vs. 49%; P = 1.0), early MicroS (81% vs. 87%; P = 0.484), or SURV (62% vs. 73%; P = 0.523). On multivariable analysis with duration of ECHINO therapy forced into the model, only PITT bacteremia score ≥4 remained an independent predictor of CR (OR 6.1, 95% CI 2.1–17.9; P = 0.001). Conclusion. In adult patients with CAND due to routinely FLUC-susceptible species, early de-escalation from ECHINO was associated with similar outcomes, including day 7 MicroS. Early de-escalation based on early species identification has the potential to be a target for ASPs to optimize antifungal therapy without compromising clinical outcomes.

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166. Breakthrough Invasive Candidiasis in Children
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Background. Breakthrough invasive candidiasis (bIC) has been described in adults, but the epidemiology and outcomes in children are unknown. Methods. Retrospective cohort analysis of children diagnosed with IC from 9/1/09 to 1/30/17. bIC was defined as isolation of Candida spp. from sterile site des- pite receiving ≥3 doses of antifungal (AF) to which isolate is susceptible. Clinical and microbiological data, management, and outcomes were collected. Non-parametric and logistic regression statistics were applied.
Results. There were 92 patients with IC, 23 of which were bIC (Table 1). Underlying conditions included GI (n = 26), hem/onc (n = 17), prematurity (n = 16), cardiac (n = 15), HCT (n = 4), SOT (n = 5), and other (n = 9). Patients received an azole (n = 17), micafungin (n = 5), or amphotericin B (n = 1) for median of 20 days [3–522] before bIC vs. prophylaxis (n = 8), targeted therapy (n = 5), or empiric fever driven therapy (n = 10). bIC was caused by non-albinic Candida in 16/23 (70%) cases. Compared with IC controls, children with bIC had increased ICU admission, vasopressor use, mechanical ventilation, and renal failure (all with P < 0.01). In multivariate analysis, immunosuppression was an independent risk factor for bIC (OR 39.4, 95% CI 7.5–205). Death attributable to IC occurred in bIC group (n = 3, P = 0.04).
Conclusion. bIC in our cohort was caused most frequently by non-albic Candida spp. and associated with significantly worse outcomes, including mortality.

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167. Comparing Diagnostic-Driven Approaches to Empiric Therapy in the Treatment of Invasive Aspergillosis in Patients with Hematologic Malignancy
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Background. Early antifungal therapy of invasive aspergillosis (IA) has been shown to be associated with improved outcome. Given the difficulty to establish the diagnosis of IA based on conventional methods, early initiation of empiric antifungal therapy has been used in patients with clinically suspected IA. Diagnostic-driven approach (DDA) relies on using novel diagnostic methods (e.g., early galactomannan testing). In this current study, we compared the outcomes of hematological malignancy (HM) patients with IA who were treated with Voriconazole using the DDA (DDA-Vori) vs. empiric therapy with a non-Voriconazole containing regimen (EMP-non-Vori) or empiric therapy with Voriconazole (EMP-Vori).

Methods. We retrospectively reviewed the medical records of 604 HM patients with documented, proven or probable IA (according to EORTC/MSG criteria) diagnosed between November 1993 and February, 2016 at our center. We included 346 patients with underlying host factors, a suggestive CT findings of IA, and positive biopsy, fungal culture or galactomannan indicative of IA, and who received at least 7 days of DDA-Vori, EMP-Vori, or EMP-non-Vori. Outcome assessment included response to therapy (clinical and radiographic), all causing mortality and IA attributable mortality.

Results. The patients’ median age was 54 years and 59% were males. By multivariate analysis, factors that were predictive of a favorable response included: localized/sinus IA vs. disseminated/pulmonary IA (P = 0.0001), not receiving WBC transfusion (P = 0.01), and DDA-Vori vs. EMP-non-Vori (P = 0.0001). On the other hand, predictors of mortality within 6 weeks of initiation of IA therapy included disseminated/pulmonary infection vs. localized/sinus IA (P < 0.01), not having stem-cell transplant within 1 year prior of IA (P = 0.01) and EMP-non-Vori vs. DDA-Vori (P < 0.001).

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Conclusion. DDA-Vori is associated with a better outcome (response and survival) when compared with EMF-norf-Vori and equivalent outcome to EMP-Vori. The superior to equivalent outcome associated with the DDA approach could also reduce unnecessary costs and adverse events associated with widespread use of empiric therapy.

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168. In Vitro Interactions of Echinocandins with Triazoles Against Multidrug-Resistant Candida auris
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Background. Blood stream infections due to Candida auris are related to a high mortality rate and treatment failure attributed to resistance to fluconazole, voriconazole, amphotericin B, and caspofungin. Thus, the precise identification of agents and in vitro antifungal susceptibility testing is highly recommended. Novel therapeutic strategies, such as combination therapy, are essential for increasing the efficacy and reducing the toxicity of antifungal agents. Therefore, we investigated the in vitro combination of micafungin plus voriconazole against multidrug-resistant C. auris isolated from cases of candidemia.

Methods. The in vitro interactions between echinocandins and azoles were determined against ten multidrug-resistant Candida auris strains by using a microdilution checkerboard technique.

Results. Results revealed that MICs range for voriconazole and micafungin were 0.5–8.0 and 0.25–8.0 µg/mL, respectively. The checkerboard analysis revealed that the combination of micafungin with voriconazole exhibited synergistic activity against all 10 multidrug-resistant C. auris isolates (FICI range: 0.15–0.5). Overall, no antagonistic effects were observed in these experiments.

Conclusion. In vitro studies have previously suggested that among azoles, isavuconazole and posaconazole are more active drugs against C. auris. In addition, the majority of isolates reported are resistant to fluconazole. Remarkably, unsuccessful treatment of C. auris infections with fluconazole, voriconazole, amphotericin B, caspofungin, and anidulafungin has been already on record. Here in we demonstrate that interaction between micafungin with voriconazole exhibited synergistic activity against multidrug-resistant C. auris isolates. It seems that lower concentrations of drugs cause fewer side-effects and improve the treatment outcomes. However, in vivo studies with suitable animal models of C. auris infection is highly recommended.

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169. Disseminated Coccidioidomycosis Among Children in Central California: A Retrospective Review
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Background. The burden of coccidioidomycosis in central California is significant among children. Yet, the literature on such infection is limited, particularly on disseminated coccidioidomycosis (DC) in children.

Objectives. Review the natural history, treatment and outcomes of DC in a tertiary children's hospital.

Methods. Retrospective review of patients ≤21 years old with DC seen at our facility during 1/1/07–12/31/16.

Results. Eighty cases were identified. Median age was 8.5 years (IQR 4.3–14.6); majority was Hispanic (66%) and without comorbid conditions (85%). Pulmonary disease with other organ involvement occurred in 69%; 19% had meningitis. Overall, 82% were hospitalized and/or stable disease (RS), whereas 14% experienced relapse and/or progressive disease (RP). Meningitis more commonly seen in older age group (14.3 vs. 6.9 years, P = 0.04) and had low eosinophil's (0.8 vs. 2.1%, P < 0.01). More organ involvement (64% vs. 35%, P = 0.03) and RP disease (22% vs. 5%, P = 0.04) commonly seen in children 10 years or older. Non-Hispanics also found to be older (14.3 vs. 6.9 years, P = 0.07), coccidioidal complement fixation (CF) titers ≥ 1 (32% vs. 73%, P = 0.07), and RP disease (24% vs. 7%, P = 0.06) than Hispanics. No significant association was found between gender and age, CF titers, and/or outcome. Isavuconazole (ISV) is a new triazole approved for treatment of mucormycosis and aspergillosis. In addition, it is highly recommended. Novel therapeutic strategies, such as combination therapy, are essential for increasing the efficacy and reducing the toxicity of antifungal agents. Therefore, we investigated the in vitro combination of micafungin with voriconazole exhibited synergistic activity against all ten multidrug-resistant C. auris isolates (FICI range: 0.15–0.5). Overall, no antagonistic effects were observed in these experiments.

Conclusion. To our knowledge, this is the first study to assess a real-world setting and a heterogeneous population with previous triazole prophylaxis or treatment. Our work provides important information (45%) that compares favorably to published trials (35% Aspergillus; 11% Mucorales). Mortality in our study (36%) is similar to comparable trial results (19% Aspergillus; 35% Mucorales). No major safety signal was observed. Largely children are needed to describe additional real-world ISV use and determine associations with patient outcomes.

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170. Real-World Use – Isavuconazole at a Large Academic Medical Center
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Background. Invasive fungal infections cause significant mortality and morbidity. Isavuconazole (ISV) is a new triazole approved for treatment of mucormycosis and aspergillosis. Data on its effectiveness outside clinical trials and in patients receiving prior triazole prophylaxis are lacking.

Methods. We conducted a retrospective cohort study on all patients at the Cleveland Clinic 6/1/2015–1/31/2017 who received ISV to determine 6-week response in a population with varying underlying diseases, and previous triazole prophylaxis or treatment. Descriptive statistics and univariate associations were calculated.

Results. Thirty-three patients were identified including organ transplant recipients (5), hematopoietic cell transplant recipients (7), and acute leukemia (18). Twenty-five had lung involvement while 13 had rhino-orbital-cerebral disease. In 13 cases, a fungal pathogen was identified: Mucorales (7) and Aspergillus (6). Fifteen received triazole prophylaxis prior to initiating ISV. Twenty-four received antifungal therapy immediately prior to switching to ISV: amphotericin B (1), fluconazole (1), voriconazole (16), posaconazole (4), and micafungin (2). Switching was often to broaden empiric coverage (18). Six-week response according to subgroups is presented in Figure 1. Complete or partial response was 36% (11/30) of the patients with mortality was 36% (11/30). No ISV-related adverse effects were reported.

Conclusion. To our knowledge, this is the first study to assess a real-world setting and a heterogeneous population with previous triazole prophylaxis or treatment. Our work provides important information (45%) that compares favorably to published trials (35% Aspergillus; 11% Mucorales). Mortality in our study (36%) is similar to comparable trial results (19% Aspergillus; 35% Mucorales). No major safety signal was observed. Larger cohorts are needed to describe additional real-world ISV use and determine associations with patient outcomes.

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