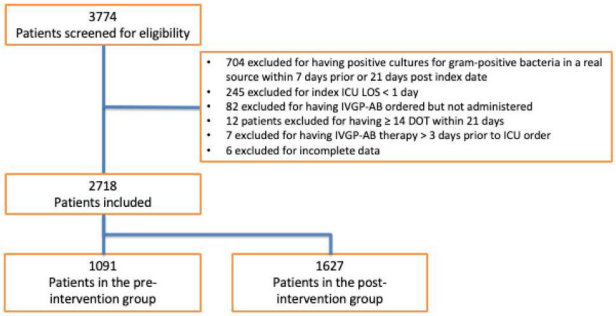
(ICU). This retrospective, single-center, pre- post-intervention study looked at eight ICUs at our institution from two equal periods. Adults (age ≥ 18 years) were included who received an IV gram-positive antibiotic (IVGP-AB), specifically linezolid or vancomycin, used for empiric therapy and were admitted to the ICU. The primary outcome was antimicrobial consumption of IVGP-AB defined as days of therapy (DOT) per patient. Secondary outcomes included in-hospital length of stay (LOS), ICU LOS, in-hospital mortality, 30-day readmission, and incidence of acute kidney injury (AKI).

Figure 1. Flowchart of patient inclusion into the study




***Results:*** 2718 patients met criteria for inclusion in the study. 1091 patients were included in the pre-intervention group and 1627 patients were included in the post-intervention group. Baseline characteristics between the two groups were similar, with ID consults being higher in the pre-intervention group. Total mean DOT of IVGP-AB in pre- and- post-intervention groups was 4.97 days vs. 4.36 days, p< 0.01. Secondary outcomes of in-hospital LOS, ICU LOS, and in-hospital mortality did not vary significantly between groups. Thirty-day readmission was lower in the post-intervention group (12.9% vs. 3.9%, p< 0.01). AKI did not differ significantly between groups, however the need for renal replacement therapy was higher in the pre-intervention group (1.2% vs. 0.2%, p< 0.01).

Table 1. Baseline Characteristics of Study Participants

| Characteristic | Pre-Intervention Group (N=1091) | Post-Intervention Group (N=1627) | P Value |
|---|---|---|---|
| Age – Mean (SD), years | 58.6 (± 16.2) | 59.4 (± 16.2) | 0.23 |
| Male sex – no. (%) | 668 (61.2) | 956 (58.8) | 0.20 |
| White race – no. (%) | 806 (73.9) | 1182 (72.7) | 0.51 |
| ID Consult – no. (%) | 385 (35.3) | 513 (31.5) | 0.04 |
| Time from ICU admission to antibiotic order - Median (IQR), days | 0.731 (2.75) | 0.523 (2.18) | 0.20 |
| Ventilator- no. (%) | 347 (31.8) | 571 (35.1) | 0.08 |

Abbreviations: ID, infectious diseases; ICU, intensive care unit

Table 2. Primary and Secondary Outcomes

| Outcome | Pre-Intervention Group (N=1091) | Post-Intervention Group (N=1627) | P Value |
|---|---|---|---|
| Total DOT IVGP-AB- Mean (SD), days | 4.97 (± 4.31) | 4.36 (± 3.38) | <0.01 |
| DOT Vancomycin- Mean (SD), days | 4.93 (± 4.31) | 3.87 (± 3.39) | <0.01 |
| DOT Linezolid- Mean (SD), days | 0.05 (± 0.55) | 0.49 (± 1.51) | <0.01 |
| In-hospital LOS- Mean (SD), days | 19.0 (± 17.7) | 18.4 (±21.9) | 0.46 |
| ICU LOS- Mean (SD), days | 11.9 (± 14.3) | 11.0 (± 15.6) | 0.10 |
| 30-day readmission – no. (%) | 141 (12.9) | 63 (3.9) | <0.01 |
| In-hospital mortality – no. (%) | 35 (3.2) | 36 (2.2) | 0.11 |
| AKI – no. (%) | 0 (0) | 3 (0.2) | 0.28 |
| RRT - no. (%) | 13 (1.2) | 3 (0.2) | <0.01 |

Abbreviations: DOT, days of therapy

Table 3: Multivariate Analysis Evaluating Impact of Baseline Characteristics on the Primary Outcome

| Term | Estimate | P Value |
|---|---|---|
| Post-intervention vs. pre-intervention | - 0.24 | <0.01 |
| Female sex | - 0.16 | 0.02 |
| Age at encounter | - 0.01 | <0.01 |
| Time from ICU admission to antibiotic order | + 0.04 | <0.01 |
| ID consult | + 1.53 | <0.01 |

***Conclusion:*** This study assessed the impact of an ATO policy allowing 72 hours of empiric linezolid in the ICU. We found a statistically significant reduction in days of therapy of IVGP-AB without increases in LOS, mortality, readmission, and AKI.

***Disclosures:*** **All Authors**: No reported disclosures

**144. MSG-15: Pharmacokinetic (PK), Adverse Events (AEs), and Tolerability Data from an Open Label Randomized Clinical Trial (RCT) Comparing Oral Suba-itraconazole (SUBA-ITC) to Conventional Itraconazole (C-ITC) for Treatment of Endemic Mycosis (EM)**

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***Background:*** C-ITC is a drug of choice for non-life-threatening, non-CNS histoplasmosis, blastomycosis, sporotrichosis, coccidioidomycosis and other EM. Oral C-ITC is problematic due to inconsistent absorption often leading to sub-therapeutic serum levels. SUBA-ITC is an FDA approved formulation which utilizes nanotechnology to provide more consistent absorption when compared to C-ITC. We performed an open-label RCT comparing SUBA-ITC to C-ITC for non-life-threatening non-CNS EM, and is the first US based RCT examining SUBA-ITC. Herein we report the PK during the first 6 wks of study therapy (rx) and drug-related AEs and tolerability throughout the course of rx.

***Methods:*** Subjects with a proven or probable EM, who had received <14 days prior antifungal tx, and were able to take po meds were eligible. Those with life-threatening and CNS disease or prohibited meds were excluded. Subjects were randomized to SUBA-ITC 130 mg or C-ITC 200mg, both PO BID, for up to 6 mo. All subjects received loading doses x 3d. Clinical assessment was performed on d 7, 14, 28, 42, 84, and 180. PK and safety evaluations were performed on d 7, 14 and 42. Serum levels and AUC were calculated and demonstrated using combined ITC and hydroxy-ITC measurements. Tolerability was based on subject ability to remain on rx.

***Results:*** 62 subjects are included in this analysis (31 each in SUBA-ITC and C-ITC, respectively). Median serum levels of ITC + hydroxy-ITC at d 7, 14 and 42 were consistently higher in the SUBA-ITC arm (Fig 1, p=0.8, NS). Combined AUC (ITC+hydroxy-ITC) were 2951 and 2845 for SUBA-ITC and C-ITC, respectively (NS). 4 subjects in each arm had sub-therapeutic d 7 levels (< 1000ng/ml). Drug-related AEs and tolerability were similar in both arms (Table 1). Lower extremity edema, hypertension, nausea, and anorexia were the most common AEs. Premature study withdrawal was seen in 12 (19%) subjects overall (5 and 7 subjects, respectively on SUBA-ITC and C-ITC).

Figure 1

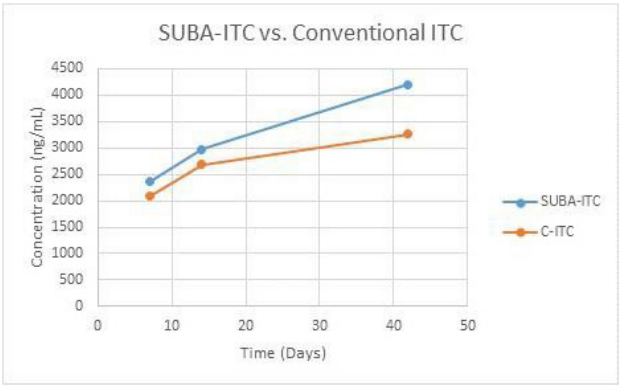


***Table 1 Drug-Related Adverse Events (definite and probable) and withdrawals (tolerability)***

| Drug-related AEs | SUBA-ITC | Conventional ITC |
|---|---|---|
| Cardiovascular (edema, HBP, CHF, dyspnea) | 9 (29%) | 9 (29%) |
| Gastrointestinal (nausea, vomiting, abd pain) | 4 (13%) | 8 (26%) |
| Abnormal LFTs | 1 (3%) | 1 (3%) |
| Skin (alopecia) | 0 (0%) | 1 (3%) |
| Musculoskeletal | 1 (3%) | 0 (0%) |
| | | |
| **Early Withdrawals** | 5 (16%) | 7 (23%) |
| Adverse event | 3 | 3 |
| Lack of efficacy | 0 | 2 |
| Pregnancy | 0 | 1 |
| LTFU | 1 | 0 |
| Withdrew consent | 0 | 1 |
| Unrelated death | 1 | 0 |

***Conclusion:*** SUBA-ITC dosed at 130 mg BID PO is safe, well-tolerated, and consistently leads to combined serum ITC/hydroxy-ITC levels and AUC that are higher (NS) when compared to C-ITC 200 mg BID. Moreover, compared to C-ITC, SUBA-ITC achieves these serum levels when administered at substantially lower daily doses (130mg BID vs 200 mg BID).

***Disclosures:*** **Peter G. Pappas, MD**, **Mayne Pharma** (Scientific Research Study Investigator) **Andrej Spec, MD, MSCI**, **Mayne** (Consultant, Grant/Research Support) **Marisa H. Miceli, MD, FIDSA**, **SCYNEXIS, Inc.** (Advisor or Review Panel member)

**Laurie Proia, MD**, **Mayne Pharma** (Scientific Research Study Investigator) **Ana Belen Arauz, MD**, **Mayne Pharma** (Scientific Research Study Investigator) **Justin Hayes, MD**, **Mayne Pharma** (Grant/Research Support) **Alisa Peinhardt, MAIS, BSN**, **Mycoses Study Group Education and Research Consortium** (Consultant)

### 145. the Efficacy and Safety of Low Dose Trimethoprim-sulfamethoxazole for the Treatment of Pneumocystis Pneumonia: A Systematic Review and Meta-analysis

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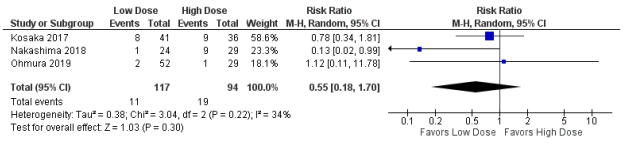
***Background:*** *Pneumocystis jirovecii* pneumonia (PJP) is an opportunistic fungal infection causing significant morbidity and mortality in immunocompromised patients. The conventional treatment of PJP is sulfamethoxazole-trimethoprim (SMX-TMP) dosed at 15–20 mg/kg/day of the trimethoprim component. This high-dose regimen is associated with severe adverse reactions that result in patient harm or treatment discontinuation. Studies have suggested similar mortality and an improved adverse effect profile using lower dose (< 15 mg/kg/day) SMX-TMP. Our objective of this meta-analysis was to evaluate the safety and efficacy of lower dose SMX-TMP for PJP pneumonia.

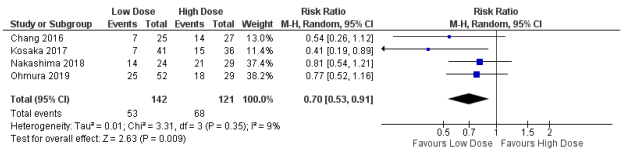
***Methods:*** We conducted a systematic review and meta-analysis according to PRISMA guidelines. Pubmed and Embase databases were searched from inception to January 15, 2020, for studies in English evaluating low-dose SMX-TMP (< 15 mg/kg/day) compared with conventional dosing for the treatment of PJP. Additionally, conference proceedings were reviewed to address potential publication bias. Outcomes evaluated in our meta-analysis include survival and adverse reactions. We performed a sensitivity analysis using E-values to determine the robustness of our results.

***Results:*** After excluding studies that did not meet our inclusion criteria, four studies were analyzed for adverse reaction rates and three for mortality rates. Overall, there was no significant difference in mortality between low-dose and conventional-dose SMX-TMP groups (relative risk [RR]: 0.55, 95% confidence interval [CI], 0.18 -1.70). There was a significant decrease in the rate of adverse reactions for the low-dose group compared with the conventional-dose group (RR: 0.70, 95% CI, 0.53 - 0.91). Sensitivity analyses using E-Values reflect a confounder with RR 2.2 or greater could explain away the estimate on adverse events leading to no difference while mortality would require RR 5.6 to reflect worse outcomes with low dose.

Mortality Forest Plot




Adverse Effects Forest Plot




***Conclusion:*** This meta-analysis shows a significant decrease in adverse reactions and similar mortality rates with lower-dose SMX-TMP compared with conventional dosing. A low-dose SMX-TMP regimen in the treatment of PJP should be considered a viable option with the potential to decrease treatment discontinuation and reduce harm.

***Disclosures:*** **All Authors**: No reported disclosures

### 146. antifungal Susceptibility Patterns of candida Parapsilosis Bloodstream Isolates in the US, 2008–2018

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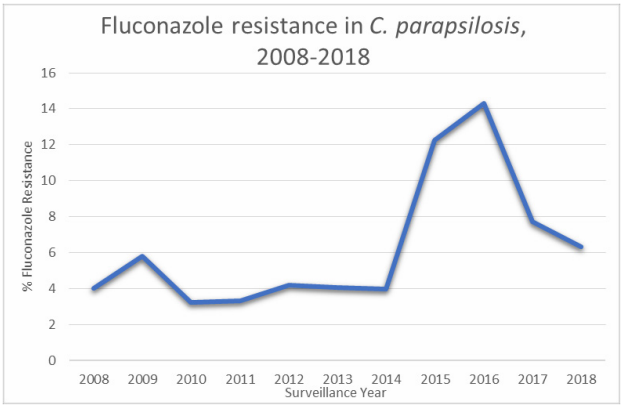
***Background:*** Multidrug resistant *Candida* is an increasing concern. *C. parapsilosis* in particular has decreased *in vitro* susceptibility to echinocandins. As a result, fluconazole had been favored for *C. parapsilosis* treatment. However, there is growing concern about increasing azole resistance among *Candida* species. We report on antifungal susceptibility patterns of *C. parapsilosis* in the US from 2008 through 2018.

***Methods:*** Active, population-based surveillance for candidemia through the Centers for Disease Control and Prevention's (CDC) Emerging Infections Program was conducted between 2008–2018, eventually encompassing 9 states (GA, MD,OR, TN, NY, CA, CO, MN, NM). Each incident isolate was sent to the CDC for species confirmation and antifungal susceptibility testing (AFST). Frequency of resistance was calculated and stratified by year and state using SAS 9.4

***Results:*** Of the 8,704 incident candidemia isolates identified, 1,471 (15%) were *C. parapsilosis*; the third most common species after *C. albicans* and *C. glabrata*. AFST results were available for 1,340 *C. parapsilosis* isolates. No resistance was detected to caspofungin ($MIC_{50}$ 0.25) or micafungin ($MIC_{50}$ 1.00) with only one (< 1%) isolate resistant to anidulafungin ($MIC_{50}$ 1.00). In contrast, 84 (6.3%) isolates were resistant to fluconazole and another 44 (3.3%) isolates had dose-dependent susceptibility to fluconazole ($MIC_{50}$ 1.00). Fluconazole resistance increased sharply from an average of 4% during 2008–2014 to a peak of 14% in 2016 with a subsequent decline to 6% in 2018 (see figure). Regional variation is also observed with fluconazole resistance ranging from 0% (CO, MN, NM) to 42% (NY) of isolates by site.




***Conclusion:*** The recent marked increase in fluconazole resistance among *C. parapsilosis* highlights this pathogen as an emerging drug resistant pathogen of concern and the need for ongoing antifungal resistance surveillance among *Candida* species. Our data support the empiric use of echinocandins for *C. parapsilosis* bloodstream infections and underscore the need to obtain AFST prior to fluconazole treatment. Furthermore, regional variation in fluconazole resistance emphasizes the importance of understanding local *Candida* susceptibility patterns.

***Disclosures:*** **Lee Harrison, MD**, **GSK** (Consultant)**Merck** (Consultant)**Pfizer** (Consultant)**Sanofi Pasteur** (Consultant)

### 147. Clinical Safety and Efficacy of Novel Antifungal, Fosmanogepix, in the Treatment of Candidemia: Results from a Phase 2 Proof of Concept Trial

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***Background:*** Fosmanogepix (FMGX) is a first-in-class antifungal agent, with a unique MOA targeting the fungal enzyme Gwt1, that has broad-spectrum activity against both yeasts, molds, and dimorphic fungi, including fungi resistant to other antifungal agents. FMGX has a favorable safety profile, reduced potential for clinically significant drug-drug interactions, and is formulated for IV and oral administration.

***Methods:*** This global, multicenter, open-label, non-comparative study evaluated the safety and efficacy of FMGX for first-line treatment of candidemia. Patients with a recent diagnosis of candidemia defined as positive blood culture for *Candida* spp. within 96 hrs prior to study entry, with ≤2 days of prior antifungal treatment were eligible. Patients with neutropenia, *C. krusei* infection, or deep-seated *Candida* infections were excluded. Patients were treated with FMGX for up to 14 days: 1000 mg IV BID for 1 day, then 600 mg IV QD for at least 2 days, followed by either 600 mg IV QD or 700 mg PO QD. Short-term fluconazole (or appropriate alternative) could follow if treatment was required beyond 14 days. Patients with a diagnosis of candidemia