profile, and oral bioavailability makes it an attractive antifungal option. In July 2017, isavuconazole was added to our hospital formulary as a restricted antimicrobial. Since then, we have seen increased use for both prophylaxis and treatment of invasive fungal infections.

Methods. A single-center, retrospective chart review was conducted on adult patients who received at least 1 dose of isavuconazole at The Mount Sinai Hospital between July 1, 2017 and December 31, 2018. The electronic medical record was utilized to collect information on therapeutic indication, dosing, formulation, duration, reasons for switching to isavuconazole, prior antifungals, and proven or probable breakthrough invasive fungal infections (bIFIs) based on EORTG/MTG definitions.

Results. 54 patients received 61 courses of isavuconazole. Reasons for switching to isavuconazole are described in Table 1. Eleven patients received inappropriate intravenous formulations and 14% of orders were prescribed isavuconazole without a loading dose (Table 2). We identified 4 proven/probable bIFIs, representing 7.4% of patients and 6.6% of courses (Table 3). All patients died within 60 days of bIFI onset.

Conclusion. Since its addition to hospital formulary, we have observed varying isavuconazole prescribing practices, highlighting the need for improved antifungal stewardship. Rates of bIFIs on isavuconazole were lower than previously reported studies. Additional studies are needed to provide guidance on isavuconazole use and determine its role as prophylaxis therapy.

Table 1.

Reasons for switching to isavuconazole	Prophylaxis	Treatment
QTc prolongation, n (%)	6	3
Acute kidney injury, n (%)	0	8
Broader spectrum of activity	4	3
Concern for breakthrough infection on prophylaxis therapy	N/A	7
Drug interactions, n (%)	3	2
Oral option for discharge, n (%)	1	4
Transaminitis, n (%)	4	0
Poor oral intake/absorption, n (%)	4	0
Subtherapeutic prior azole levels, n (%)	1	3
Altered mental status secondary to voriconazole, n (%)	2	1
Other, n (%)		
- Good CNS & bone penetration	1	0
- Pill burden	1	0
- Allergic reaction to liposomal amphotericin B	0	1

Table 2.

Isavuconazole prescribing patterns	
Formulation, n (%)	
- Oral	112 (68)
- Intravenous	53 (32)
Reasons for intravenous formulation, n (%)	
- Not tolerating oral intake	12 (22)
- Malabsorption due to GVHD	11 (21)
- Severe disease	19 (36)
- None	11 (21)
Initiated on appropriate dose with loading dose, n (%)	89 (86)

Table 3.

Age	Sex	Disease	Description
59	M	AML	Probable invasive pulmonary aspergillosis on isavuconazole prophylaxis
24	M	Allogeneic SCT	Proven Candida tropicalis bacteremia on isavuconazole prophylaxis
66	F	Cardiac transplant	Proven pulmonary mucormycosis on isavuconazole treatment for probable pulmonary *Aspergillus fumigatus*
39	M	ALL	Probable invasive pulmonary aspergillosis on isavuconazole treatment for prior possible invasive fungal infection

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2107. Azole Therapeutic Drug Monitoring (TDM) in a Multiracial Cohort with Varied Pharmacogenetics

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Background. Voriconazole (VOR) and posaconazole (POS) exhibit wide pharmacokinetic variability. Various factors including race and genetic polymorphisms are at play and this may affect treatment response. We aim to evaluate the utility of VOR/POS TDM among Southeast Asians that are predominantly intermediate/poor VOR metabolizers.

Methods. All adults with VOR/POS TDM performed at our institution from 2015 to 2018 were included. We determined proportion of patients and doses required to achieve TDM targets [(2 – 5.5 mg/L (VOR) or ≥ 0.7 and ≥ 1.0 mg/L (POS prophylaxis and treatment respectively)], and correlate levels with treatment efficacy and safety.

Results. VOR/POS TDM was performed mostly among patients with hematological malignancy or solid-organ transplant (146/174, 83.9%). Less than half (32/70, 45.7%) of patients on VOR achieved target—18 (25.7%) were < 2 mg/L while 20 (28.5%) had levels > 5.5 mg/L. Doses required to achieve TDM target ranged from 1.9–11.4 mg/kg/day. Drug interactions, critically ill state and change in drug formulation were major causes of intra-patient variability. One-fifth (n = 14) experienced transaminitis; corresponding VOR trough levels were 0.5–> 7.5 mg/L. Neurotoxicity was also seen in 3 (4.3%) patients—all 3 had VOR trough ≥ 6.7 mg/L and saw symptom resolution upon dose reduction. There appears to be no association between the achievement of TDM targets and response rates. Majority (81/104, 77.9%) of patients on POS achieved TDM targets. Patients prescribed POS tablet were significantly more likely to attain targets compared with suspension 600 mg/day [19/26 (73.0%) vs. 27/62 (43.5%), P < 0.05] and 800 mg/day [17/26 (65.3%) vs. 4/16 (25.0%), P < 0.05)]. Of 23 with sub-therapeutic levels, 19 (82.6%) responded to dose increase and/or change in acid-reducing agents. Breakthrough infection occurred despite troughs ≥ 0.7 mg/L [5/42 (11.9%) vs. 2/40 (5.0%) when < 0.7 mg/L (P = 0.3)]. Treatment failure was observed in 2 patients (troughs > 1.0 mg/L).

Conclusion. VOR/POS TDM should be implemented in Southeast Asians due to significant unpredictability in dose exposure and potential to avoid need for switch to alternative anti-fungals due to intolerability. Higher POS trough cutoff may be required for effective anti-fungal prophylaxis.

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2108. Comparison of Voriconazole vs. Itraconazole in the Treatment of Histoplasmosis – A Retrospective Analysis

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Background. The guideline-preferred azole for histoplasmosis (HP) is itraconazole (IC). While voriconazole (VC) has shown success in in-vitro and in retrospective analyses, there has not been enough data to include newer generation azoles as first-line treatment for infections with *Histoplasma capsulatum*.

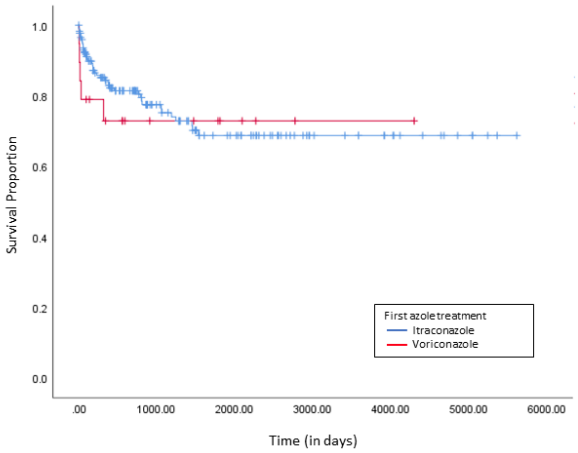
Methods. We conducted a single-center retrospective cohort study of adult patients diagnosed with HP from 2002 through 2017. Data included demographics, clinical features and sites of infection, immune status, treatments, and mortality. Patients were categorized into two groups based on initial choice of azole (IC or VC) and mortality was compared between these two groups. The treatment groups were defined based on the first azole received, either IC or VC, as initial or as step-down therapy from amphotericin. Patients initiated on other azoles were excluded.

Results. We identified 263 cases of HP from 2002 to 2017. After excluding patients initiated on other azoles, 194 patients remained. 175 (90%) patients were started on IC and 19 (10%) were started on VC, either as stepdown or initial choice of antifungal. There were no significant demographic differences between patients receiving IC compared with VC as their initial azole treatment. Patients with hematologic malignancies tended to be prescribed VC more frequently but this was not statistically significant (OR 3.1 [0.77–12.4]). Death occurred in 40 (23%) patients from the IC and 5 (26%) patients from the VC group. The hazard ratio for mortality with the use of VC was 1.21 (CI 0.4–3.6, P = 0.73).

Conclusion. IC is the mainstay in the treatment for HP. It appears that VC has comparable outcomes to IC and can be considered an alternative treatment option for HP, at least for patients with contraindications to IC treatment.

		Itraconazole	Voriconazole	Total	OR (95% CI)	p-value
Race						0.304
White		90.3% (n=131)	9.7% (n=14)	74.7% (n=145)		
African American		92.1% (n=35)	7.9% (n=3)	19.6% (n=38)		
Asian/Pacific Islander		50.0% (n=1)	50.0% (n=1)	1.0% (n=2)		
Hispanic		100.0% (n-4)	0.0% (n=0)	2.1% (n=4)		
Other		80.0% (n=4)	20.0% (1)	2.6% (n=5)		
Gender					0.99 (0.38-2.59)	0.988
Male (1)		90.2% (n=101)	9.8% (n=11)	57.7% (n=112)		
Female (2)		90.2% (n=74)	9.8% (n=8)	42.3% (n=82)		
Age						
≤25		95.0% (n=19)	5.0% (n=1)	11.2% (n=20)		0.624
26-45		91.5% (n=54)	8.5% (n=5)	33.1% (n=59)		
46-65		88.9% (n=64)	11.1% (n=8)	40.4% (n=72)		
>65		96.3% (n=26)	3.7% (n=1)	15.2% (n=27)		
Disseminated disease	Yes	88.5% (n=85)	11.5% (n=11)	50.5% (n=96)	1.39 (0.53-3.63)	0.498
	No	91.5% (n=86)	8.5% (n=8)	49.5% (n=94)		
Comorbidities						
Immunocompromised	Yes	88.7% (n=102)	11.3% (n=13)	59.3% (n=115)	1.55 (0.6-4.3)	0.393
	No	92.4% (n=73)	7.6% (n=6)	40.7% (n=79)		
Cancer, solid	Yes	93.8% (n=15)	6.3% (n=1)	8.2% (n=16)	0.59 (0.07-4.8)	0.619
	No	89.9% (n=160)	10.1% (n=18)	91.8% (n=178)		
Cancer, hematologic	Yes	76.9% (n=10)	23.1% (n=3)	6.7% (n=13)	3.1 (0.77-12.4)	0.095
	No	91.2% (n=165)	8.8% (n=16)	93.3% (n=181)		
Chemotherapy	Yes	76.9% (n=10)	23.1% (n=3)	6.7% (n=13)	3.1 (0.77-12.4)	0.095
	No	91.2% (n=165)	8.8% (n=16)	93.3% (n=181)		
Any transplant	Yes	90.5% (n=19)	9.5% (n=2)	10.8% (n=21)	0.97 (0.21-4.51)	0.965
	No	90.2% (n=156)	9.8% (n=17)	89.2% (n=173)		
HIV	Yes	91.7% (n=44)	8.3% (n=4)	24.9% (n=48)	0.79 (0.25-2.5)	0.685
	No	89.7% (n=130)	10.3% (n=15)	75.1% (n=145)		

Figure 1: Survival probability of patients receiving Itraconazole versus Voriconazole for first azole treatment



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2109. Liposomal Amphotericin B-associated Nephrotoxicity in Obese and Non-obese Patients

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Background. Liposomal amphotericin B (L-amb) is an important antifungal agent which exhibits significant rates of dose-dependent nephrotoxicity. Animal studies demonstrate only small amounts of L-amb distribute into adipose tissue and obese animals show greater risk of nephrotoxicity with L-amb administration. This study aims to determine whether obese patients are at a higher risk of nephrotoxicity with weight-based doses of L-amb.

Methods. We performed a multi-center, retrospective cohort study of nephrotoxicity with L-amb in obese (BMI > 30) and non-obese adult patients at University of Utah Health and Intermountain Healthcare from January 1, 2014 through December 31, 2018. Our primary outcome was the rate of nephrotoxicity as determined by AKIN criteria. Patients receiving at least one dose of L-amb were identified for inclusion. Patients were excluded if they were already on a renal replacement at the time of L-amb initiation or they received L-amb prior to admission.

Results. We included 221 patients, 47 (21%) were obese and 174 (79%) were non-obese. Median total body weight was 109 kg in obese patients compared with 70 kg in non-obese patients. Dosage based on ideal body weight was higher in the obese group (median 6.9 mg/kg vs. 4.9 mg/kg). Obese patients were significantly more likely to experience acute kidney injury (AKI) than non-obese patients (55% vs. 37%, $P = 0.03$). Patients who experienced nephrotoxicity received a higher average daily dose than those who did not (365 mg vs. 333 mg, $P = 0.03$), had a higher median cumulative dose (3,130 mg vs. 1,700 mg, $P < 0.001$), and had a higher median total body weight (79.6 kg vs. 71.9 kg, $P = 0.04$.). Additionally, daily dose normalized to total body weight was not associated with AKI (median 4.7 mg/kg in patients with AKI vs. 4.8 mg/kg in patients without AKI, $P = 0.86$). However, daily dose normalized to ideal body weight was associated with AKI (median 5.5 mg/kg in patients with AKI vs. 4.9 mg/kg in patients without AKI, $P = 0.02$).

Conclusion. We identified a higher rate of nephrotoxicity among obese patients receiving L-amb compared with non-obese patients. These data suggest that dosing L-amb based on total body weight places obese patients at a higher risk of nephrotoxicity. This should be considered when assessing the risks and benefits of this dosing strategy in obese patients.

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2110. Treatment of Coccidioidomycosis with Isavuconazole

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Background. There are limited prospective data available to guide the management of severe coccidioidomycosis. In particular, the treatment of disseminated coccidioidomycosis often requires extended courses of antifungal therapy, for which there are often intolerable side-effects, toxicities, and failures. In recent years, newer oral triazole antifungals with *in vitro* activity against *Coccidioides* have become available, but data are lacking on their efficacy in coccidioidomycosis. Isavuconazole lacks many of the toxicities of older triazole antifungals, such as QT prolongation and certain key drug interactions, making it an appealing option in selected patients.

Methods. Based on pharmacy prescription history at two federal facilities in southern California, we identified adult patients with coccidioidomycosis who received isavuconazole from 2017 to 2019. Patient records were reviewed to identify age, sex, ethnicity, sites of infection, prior antifungal therapy, indication for switch to isavuconazole, duration of follow-up, and outcomes.

Results. 12 patients were identified between the ages of 36 and 86 years; 3 were women. 6 were of Pacific Islander descent, 4 were African American, 1 European-American, and 1 Latino. 6 (50%) had significant pre-infection comorbidities. 8 (67%) had evidence of extrapulmonary dissemination, including 1 patient with meningitis. All but one had received prior treatment with other azoles; two had previously been treated with amphotericin B. Six (50%) were switched to isavuconazole due failure or progression of disease on prior therapy; 3 (25%) due to drug toxicity; and 2 (17%) due to drug interactions. Seven (58%) patients improved on isavuconazole; 4/12 (33%) were stable; one developed hepatotoxicity but improved on posaconazole, and one patient deteriorated.

Conclusion. Isavuconazole appears to be a promising agent for the treatment of coccidioidomycosis. Long-term follow-up will be required to assess the risks of toxicity, disease progression, or relapse. For patients who are clinically stable but with an extensive disease burden or toxicity from older agents, isavuconazole may present an amphotericin-sparing option.

AGE/ GENDER	ETHNICITY	COMORBIDITY	SITE OF INFECTION	PRIOR THERAPY	CF	FOLLOW-UP MONTHS	INDICATION FOR SWITCH	OUTCOME
67/F	API	DM, asthma	Cavitary pulmonary	F, P	32	2	progression of disease	stable
65/M	C	None	Cavitary pulmonary	F	4	8	hepatotoxicity	improved
81/M	AA	CAD	Prostate	F	8	15	torsades de pointes	improved
67/M	API	DM, CKD	Pulmonary, retinal, fungemia	F	16	1	drug interactions	stable
81/F	API	HCV	Pulmonary, bone	F, V	16	3	progression of disease	stable
86/F	API	DM, CAD	Pulmonary	F	<2	10	drug interactions	improved
39/M	AA	None	Pulmonary	F	4	1	failure to improve	stable
48/M	AA	None	Pulmonary, spine, deep soft tissue	F, I, V, P	1024	26	failure to improve	improved
38/M	API	DM, asthma	Pulmonary, empyema	F	<2	17	Qtc >500	improved
36/M	AA	None	Pulmonary, knee joint	None	512	3	n/a (initial therapy)	hepatotoxicity
74/M	API	None	Knee joint	A, F	16	4	failure to improve	improved
39/M	L	None	Pulmonary, meningeal	A, F	64	2	progression of disease	worse

Table 1. Description of patients with coccidioidomycosis receiving therapy with isavuconazole.
CF = anti-*Coccidioides* complement fixation titer prior to isavuconazole switch
API = Asian/Pacific Islander, C= Caucasian, AA=African-American, L=Latino.
DM=diabetes mellitus, CAD=coronary artery disease, CKD=chronic kidney disease, HCV=chronic hepatitis C infection
F=fluconazole, P=posaconazole, V=voriconazole, I=itraconazole, A=liposomal amphotericin B

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2111. Anidulafungin vs. Micafungin Treatment in Adult Patients with Candidemia: A Retrospective Study of Single-Center Experience

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Background. Candidemia is one of the fatal causes of nosocomial infection, requiring prompt recognition and treatment. Echinocandins are recommended for the treatment of invasive candidiasis and candidemia. Although similar clinical efficacy and safety are well known between caspofungin and micafungin, there are few studies comparing micafungin and anidulafungin. The objective of this study was to evaluate the clinical efficacy and safety between micafungin and anidulafungin treatment for adult patients with candidemia.

Methods. This retrospective cohort study was performed on adult candidemia patients diagnosed from January 2006 through December 2018 at a tertiary medical center, Seoul, South Korea. The study subjects included adult patients ≥19 years with candidemia who were only treated with micafungin or anidulafungin for more than 3 days. Baseline and clinical characteristics were reviewed through electrical medical records. Liver function was assessed according to Common Terminology Criteria for Adverse Events (CTCAE) Version 5.0. Hepatotoxicity was defined as the elevation of more than CTCAE grade 1 and severe hepatotoxicity was defined as the CTCAE grade 3 or higher elevations.

Results. A total of 98 patients with candidemia was treated with micafungin ($n = 46$, 46.9%) or anidulafungin ($n = 52$, 53.1%). In the univariate analysis, there were no significant differences in age, sex, source of candidemia, and comorbidities between the micafungin and anidulafungin groups. Although the clearance time of candidemia after echinocandin treatment was shorter in the anidulafungin than in the micafungin (5.64 ± 2.79 vs. 8.06 ± 5.30 days, $P = 0.009$) group, there was no significant difference in terms of clinical response (51.9% vs. 46.7%), mycological response (76.9% vs. 67.4%), and mortality (54.3% vs. 55.8%) between these two groups. The overall incidence of hepatotoxicity was similar. Also, there was no difference in the development of hepatotoxicity or severe hepatotoxicity between micafungin and anidulafungin groups for patients with normal baseline liver function test(LFT) and abnormal baseline LFT.

Conclusion. Our results suggest that clinical efficacy and hepatotoxicity may be similar between micafungin and anidulafungin treatment for adult patients with candidemia.