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)		