1172. Mucormycosis Treated with Isavuconazole: A matched-Pair Analysis from the FungiScope® Registry

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Session: P-52. Medical Mycology

Background. Isavuconazole (ISAV) is a novel, broad-spectrum triazole antifungal, available in both intravenous and oral formulations, for the treatment of adult patients with invasive aspergillosis or mucormycosis. In this retrospective case collection study, we compared outcomes for patients with invasive mucormycosis treated with ISAV versus other systemic antifungal therapies, in order to evaluate the real-world effectiveness of ISAV.

Methods. Proven and probable invasive mucormycosis cases treated with ISAV for a minimum of four consecutive days between 2016 and 2019 were identified from the FungiScope® registry. Matched controls were defined as patients treated with lipid formulations of amphotericin B (lipid-AMB), posaconazole, or a combination of both, as first-line therapy between 2011 and 2019. Case-matching criteria included disease severity, presence of hematological malignancy or allogeneic stem cell transplantation, and surgery for fungal disease. Baseline patient characteristics and clinical outcomes were compared descriptively.

Results. Each of 30 ISAV cases was matched to 1–3 controls, including 25 ISAV cases each matched to 2 or 3 controls, which resulted in a total of 69 control cases. In 70.0% of ISAV cases (n=21), ISAV was administered as a treatment for invasive mucormycosis in patients who had received prior lipid-AMB. In the remaining cases, ISAV was administered after prior voriconazole treatment (n=3) or as first-line therapy (n=6). All control patients received either lipid-AMB, posaconazole, or a combination of both.

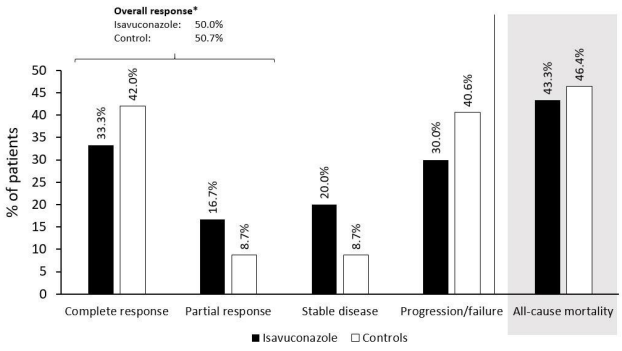
Baseline demographic and clinical characteristics and causative pathogens were similar between ISAV cases and controls (Table). Overall response rates (defined as achieving a complete or partial response) at the final assessment were 50.0% (15/30) for ISAV cases and 50.7% (35/69) for controls. All-cause mortality was 43.3% (13/30) in ISAV cases as compared to 46.4% (32/69) in controls (Figure).

Table. Demographic and clinical characteristics of 30 isavuconazole cases and 69 control cases

	Isavuconazole N=30		Control N=69		*P*-value*
Male sex, n (%)	22	73.3	42	60.9	0.261
EORTC/MSG disease classification					0.812
Proven	22	73.3	48	69.6	
Probable	8	26.7	21	30.4	
Hematological disease, n (%)	17	56.7	44	63.8	0.510
Allogeneic HSCT	4	13.3	10	14.5	
Solid organ transplantation†, n (%)	4	13.3	3	4.3	0.194
Sites of infection, n (%)					0.909
Disseminated or central nervous system	12	40.0	26	37.7	
Pulmonary only	15	50.0	34	49.3	
Other (localized, not central nervous system)	3	10.0	9	13.0	
Surgical intervention, n (%)	21	70.0	34	49.3	0.078
Causative fungal pathogen, n (%)					0.220
Rhizopus spp.	13	43.3	28	40.6	
Mucor spp.	7	23.3	15	21.7	
Lichtheimia spp.	4	13.3	12	17.4	
Rhizomucor spp.	4	13.3	2	2.9	
Other‡	2	6.7	12	17.4	

HSCT = hematopoietic stem cell transplantation
*Fisher's exact test or Pearson Chi-squared test
†Isavuconazole cases: kidney 2, lung 2; control cases: liver 3
‡Includes Mucorales not otherwise specified; isavuconazole cases: 1; control cases: 9

Figure. Clinical response at final assessment and all cause mortality for 30 isavuconazole cases and 69 control cases



*Overall response defined as proportion of patients achieving a complete or partial response at the final assessment

Conclusion. In this retrospective analysis of cases from the FungiScope® registry, patients with invasive mucormycosis showed similar overall treatment response and all-cause mortality rates with ISAV compared to treatment with lipid-AMB and/or posaconazole. These data support the effectiveness of isavuconazole in clinical practice.

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1173. Ocular Candidiasis in Patients with Candidemia Diagnosed by Blood Culture Versus T2Candida® Assay

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Session: P-52. Medical Mycology

Background. Ocular candidiasis (OC) is a serious complication of candidemia. Current guidelines recommend dilated fundoscopic exam (DFE) in all patients with candidemia. In this study, we examined characteristics and outcomes of patients at UAB Medical Center with candidemia diagnosed by blood culture (BC) or T2Candida® rapid diagnostic assay (T2C) who were found to have evidence of fungal disease on ophthalmologic exam.

Methods. Patients from 2016-2019 with either 1) at least one positive BC for *Candida* species or 2) positive T2C assay and negative or no paired BC were identified and retrospectively reviewed. Patients with additional positive BC or T2C within 60 days were excluded from the analysis. Data collected included risk factors for candidemia, causative *Candida* species, and whether DFE was performed after diagnosis. Patients with evidence of OC by exam were compared by type of ocular involvement (chorioretinitis vs. vitritis), whether visual symptoms were present, and whether intravitreal injection was performed.

Results. A total of 360 episodes of candidemia diagnosed by BC and 288 by T2C alone were included. Of those who underwent DFE, 33 BC patients (12.9%) had findings concerning for OC compared to 18 (8.9%) T2C patients (p=0.177) (Table 2). T2C patients with OC were younger, were more likely to have a prolonged ICU stay and to be mechanically ventilated, and were less likely to be on TPN compared to the BC group. Identification of *C. parapsilosis* was significantly more common in T2C patients (Table 1). There were no significant differences in presence of visual symptoms, type of ocular involvement, need for intravitreal injection, or 30-day mortality (Table 3).

Table 1. Demographics and risk factors

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	T2C+ (n=18)	BC+ (n=33)	P-value
Age – yr.			
Mean (Range)	46.4 (27 – 70)	56.3 (22 – 86)	**.0347**
Median	47.5	60	
Gender – no. (%)			
Male	7 (38.9)	15 (45.5)	.682
Race or ethnic group			
White	10 (55.6)	20 (60.6)	.731
Black	8 (44.5)	12 (36.4)	.888
Hispanic	0 (0)	1 (3)	.673
Location at time of collection			
ICU	11 (61.1)	12 (36.4)	.089
Floor	6 (33.3)	12 (36.4)	.832
ED	1 (5.6)	9 (27.3)	.074
Risk factors			
Broad-spectrum antibiotics	15 (83.3)	24 (72.7)	.425
CVL	13 (72.2)	24 (72.7)	.940
Removed if present	12 (92.3)	19 (79.2)	.315
ICU >72 hrs.	12 (66.7)	9 (27.3)	**.006**
Immunosuppression or steroids	7 (38.9)	11 (33.3)	.671
Mechanical ventilation	5 (27.8)	2 (6)	**.031**
Dialysis	3 (16.7)	4 (12.1)	.624
Total parenteral nutrition	1 (5.6)	10 (30.3)	**.049**
Intra-abdominal surgery	1 (5.6)	4 (12.1)	.497
Necrotizing pancreatitis	0 (0)	1 (3)	.463
***Candida* species**			
C. albicans or *tropicalis*	7 (38.9)	21 (63.6)	.094
C. glabrata or *krusei*	1 (5.6)	7 (21.2)	.147
C. parapsilosis	9 (50)	2 (6)	**.0003**
Other	N/A	2 (6)	.294
Polyfungemia	1 (5.6)	1 (3)	.651

Table 2. Episodes of candidemia and ocular candidiasis by year

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	2016	2017	2018	2019	Total
Total BC	103	74	83	100	360
DFE performed (%)	62 (60.2)	48 (64.9)	64 (77.1)	81 (81)	255 (70.8)
Total BC with OC (%)	8 (12.9)	6 (12.5)	8 (12.5)	11 (13.6)	33 (12.9)
Total T2C	27	60	80	121	288
DFE performed (%)	10 (37)	42 (70)	60 (75)	91 (75.2)	203 (70.5)
Total T2 with OC (%)	0 (0)	2 (4.8)	3 (5)	13 (14.3)	18 (8.9)

Table 3. Ocular findings and outcomes

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	T2C+	BC+	P-value
Visual symptoms – no. (%)			
Asymptomatic	10 (55.6)	17 (51.5)	.786
Unknown/unable to obtain	5 (27.8)	10 (30.3)	.882
Symptomatic	3 (16.7)	6 (18.2)	.929
Exam findings			
Chorioretinitis only	15 (83.3)	30 (90.9)	.403
Vitritis	3 (16.7)	3 (9.1)	.403
Outcomes			
Intravitreal injection performed	4 (22.2)	3 (9.1)	.200
30-day mortality	4 (22.2)	8 (24.2)	.873

Conclusion. The frequency of ocular disease was similar between groups. Significantly more T2C patients had candidemia due to *C. parapsilosis*, and the groups differed in terms of risk factors for candidemia. There were no differences in frequency of intravitreal injection, severity of eye disease, or mortality. Despite recent concerns about the necessity of DFE in asymptomatic patients with candidemia, we believe these results emphasize the importance of performing DFE in candidemic patients and also support the practice of doing so in patients with positive T2C even in the absence of positive blood cultures.

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1174. Phase 2 STRIVE Clinical Trial of Rezafungin for Treatment of Candidemia and/or Invasive Candidiasis Demonstrates Consistent Trough Concentrations Across Diverse Patient Populations

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Session: P-52. Medical Mycology

Background. Rezafungin is a novel echinocandin antifungal in development for treatment as well as prevention (prophylaxis) of invasive fungal infections. STRIVE (NCT02734862) is a global, randomized, double-blind, placebo-controlled, Phase 2 trial evaluating safety and efficacy of IV rezafungin once weekly (QWk) for treatment of candidemia and/or invasive candidiasis compared with standard-of-care (IV caspofungin once daily with optional oral stepdown). Here we report pharmacokinetic (PK) data from the completed STRIVE trial analyzed by patient demographics at baseline.

Methods. Rezafungin Day 8 trough (C_{min}) concentrations from patients treated with rezafungin were summarized categorically by race (black or white), sex (male or female), and geographic region (North America [NA], or Europe [EU]), or plotted versus continuous variables of age, body weight, body mass index (BMI), and body surface area (BSA). As the first dose of rezafungin was 400 mg for all rezafungin-treated patients, data from both dose groups (Group 1: 400 mg QWk; Group 2: 400 mg in Week 1 followed by 200 mg QWk) were combined in this analysis.

Results. Rezafungin mean C_{min} (SD) values were 1.8 (0.7) and 2.3 (1.2) in black and white patients, 1.9 (1.0) and 2.6 (1.2) in males and females, and 1.9 (0.6) and 2.4 (1.3) in patients from NA and EU. There were small differences in point estimates between the groups, but there was a great deal of overlap and the differences are not expected to be clinically meaningful (Figure). Similarly, no trends in C_{min} values were observed across a range of ages (20-80 years), weights (~40-155 kg), BMI (~15-65 kg/m^2), and BSA (~1.4-2.4 m^2).

Figure

Figure: Mean (SD) Rezafungin Trough Concentrations Across Various Subpopulations