1733. Voriconazole Prophylaxis Following Allogeneic Hematopoietic Stem Cell Transplant: How Much Is Enough, Are Low Voriconazole Levels Associated With Opportunistic Infections, and What Are the Reasons for Discontinuation?

Giorgos Hadjivassiliou, MBBS[1]; Claire Rummage, PharmD[2]; Craig Hoesley, MD[1]; Matthew L. Brown, PharmD[2]; [1]University of Alabama at Birmingham, Birmingham, Alabama; [2]University of Alabama in Birmingham Hospital, Birmingham, Alabama

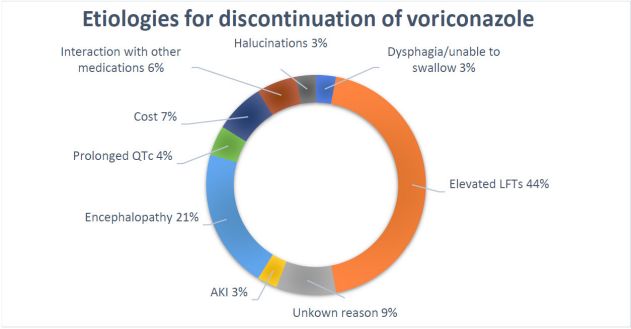
Session: 166. Transplant ID: Fungal
Friday, October 4, 2019: 12:15 PM

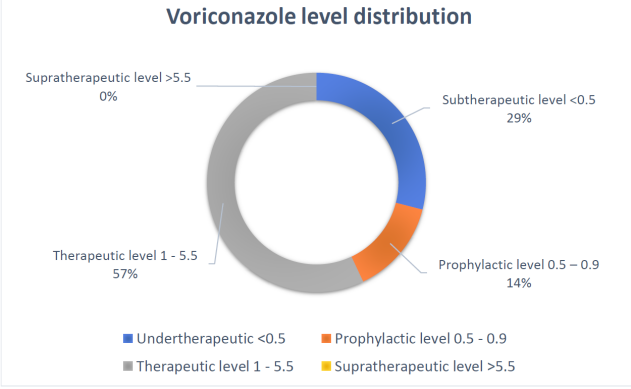
Background. Patients who undergo allogeneic hematopoietic stem cell transplantation (alloHSCT) are at increased risk for invasive fungal infections with associated high morbidity and mortality that necessitates the use of prophylactic antifungals. Voriconazole is commonly used for prophylaxis, but there are no recommendations for therapeutic drug monitoring. The purpose of this study was to characterize voriconazole therapeutic drug monitoring and associated outcomes in this patient population.

Methods. AlloHSCT patients receiving voriconazole prophylaxis at the University of Alabama at Birmingham Hospital between March 2015 and March 2018 were included in the analysis. Serum voriconazole levels (SVL) were evaluated to determine what percentage of patients achieved prophylactic or therapeutic concentrations. Incidence of invasive fungal infections (IFI) and voriconazole discontinuation was also assessed.

Results. Voriconazole prophylaxis was used in 151 of 162 alloHSCT patients, and 120 patients (79%) had SVL drawn correctly (≥4 days after initiation of course). We found that 35 (29%) patients achieved a subtherapeutic level (<0.5 μg/mL), 17 (14%) prophylactic level (0.5 to 1 μg/mL), 68 (57%) therapeutic level (1 to 5.5 μg/mL), and no patients achieved a supratherapeutic level (level ≥5.5 μg/mL). Voriconazole prophylaxis was discontinued early in 60 of 151 patients. Most common etiologies for discontinuation included liver function test abnormalities (44%) and encephalopathy (21%). The average SVL was 1.2 μg/mL in those requiring discontinuation. Four patients (3%) developed an IFI while receiving prophylactic voriconazole, of which only 1 had subtherapeutic level.

Conclusion. Even though approximately one-third of patients achieved a subtherapeutic SVL, there was no correlation with breakthrough IFI. There was also no linear correlation between SVL and risk of adverse effects requiring discontinuation. Our observational data do not support a need for therapeutic drug monitoring in alloHSCT patients receiving prophylactic voriconazole.





Disclosures. **All authors:** No reported disclosures.

1734. Antifungal Prophylaxis in Allogeneic Hematopoietic Stem Cell Transplantation: A Single-Center Experience in Colombia

Mayra Estacio, MD; Joaquin Rosales, MD; Francisco Jaramillo, MD; Ana-Maria Sanz, MD; Juan D. Vélez, MD; Pablo A. Moncada, MD; Fernando Rosso, MD, MSc; Fundación Valle del Lili, Cali, Valle del Cauca, Colombia

Session: 166. Transplant ID: Fungal
Friday, October 4, 2019: 12:15 PM

Background. Invasive fungal infections (IFI) are significant causes of morbidity and mortality among patients with hematopoietic stem cell transplantation (HSCT). Primary antifungal prophylaxis has lowered the IFI cases however there is no clear guidance regarding which mold active agent is most useful if mold-active prophylaxis. We aim to present the incidence of IFI in patients with allogeneic HSCT, and the impact of primary antifungal prophylaxis regimen.

Methods. Retrospective cohort study. We included patients older than 18 years, with allogeneic HSCT from Fundación Valle del Lili, between January 2008 and April 2017. The patients received antifungal prophylaxis with fluconazole, itraconazole, or posaconazole from conditioning day to +100 post-transplant day. The prophylactic antifungal agent was selected according to the initial diagnosis, transplant type, conditioning regimen and the risk of developing GVHD. All patients received myeloablative conditioning regimens and were hospitalized in laminar airflow rooms during their period with neutropenia. The cases were defined according to the EORTC/MSG Consensus Group. We analyzed patients with probable or confirmed IFI, in the first 120 post-transplant days.

Results. We enrolled a total of 101 patients who received HSCT over the course of the study. The median age was 32 (23–43). Posaconazole prophylaxis was used in 73%, fluconazole in 18% and itraconazole 10% of the patients. The IFI incidence was 3.9% (4 cases) and the median time from HSCT to the diagnosis of IFI was 60 days. The percentages of patients who experienced probable IFI in the itraconazole arm was 22% (2/9 patients) and in the fluconazole arm 11.1% (2/18), there was no infection in the posaconazole group ($P = 0.001$). Donor sources were HLA-matched sibling (42%), Haploidentical (48%), and cord blood (10%). The cumulative incidence of grade I–IV aGVHD was 63.4% and that of grade III–IV aGVHD was 37.5%.

Conclusion. In patients undergoing HSCT posaconazole prevented invasive fungal infections more effectively than did either fluconazole or itraconazole.

Variable	Total	Itraconazole	Fluconazole	Posaconazole	p
	n=101	n=9	n=18	n=74	
Age, median (IQR)	32 (23-43) 17-62	37 (24-46) 22-58	29 (22-42) 18-62	31.5 (23-43) 17-60	0,709
Male, n(%)	52 (51)	6 (66)	5 (27)	41 (55)	0.069
Diagnosis					0,010
ALL	40 (39,6)	2 (22,2)	11 (61,1)	27 (36,5)	
AML	37 (36,6)	1(11,1)	4 (22,2)	32 (43,2)	
NHL	2 (2)	2 (22,2)	0	0	
Medullary failure	13 (13)	2 (22,2)	3 (16,7)	8 (10,8)	
CML	3 (3)	0	0	3 (4,1)	
MDS	1 (1)	0	0	1 (1.4)	
other*	5(5)	2 (22,2)	0	3 (4,1)	
Transplant					0,092
Identical	43 (42,6)	7 (77,7)	6(33,3)	30 (40,5)	
Haploidentical	48 (47,5)	1(11,1)	9 (50)	38 (51,3)	
Cord	10 (9,9)	1(11,1)	3 (16,7)	6 (8,1)	
Accute GVHD	64 (63,4)	6 (66,7)	13 (72,2)	45 (60,8)	0,698
GVHDa grado III-IV	24 (37,5)	5 (83,3)	1 (7,7)	18 (40)	0,006
CMV reactivation	62 (61,4)	4 (44,4)	11 (61,1)	47 (63,5)	0,526
IFI	4	2 (22.2)	2 (11.1)	0	0,001

Disclosures. **All authors:** No reported disclosures.

1735. Epidemiology of Invasive Fungal Infections During Induction Chemotherapy in Adults With Newly Diagnosed Acute Myeloid Leukemia Without Antifungal Prophylaxis: A Retrospective Cohort Study

Eugenia Miranti, MD; Kyle Enriquez; Bruno Medeiros, MD; Aruna Subramanian, MD; Dora Ho, MD, PhD; David J. Epstein, MD; Stanford Medicine, Stanford, California

Session: 166. Transplant ID: Fungal
Friday, October 4, 2019: 12:15 PM

Background. While invasive fungal infections (IFIs) are common in patients with acute myeloid leukemia (AML) undergoing induction chemotherapy, little current data exist on the epidemiology of IFIs in this patient population given widespread use of antifungal prophylaxis. Because our institution does not administer antifungal prophylaxis, we are in a unique position to study the natural history of IFIs in these patients.

Methods. We evaluated the incidence of IFIs using established definitions in adults with AML undergoing induction chemotherapy at Stanford Health Care from 2012 to 2017. We also analyzed incidence of antifungal treatment, impact of IFI diagnosis on survival, and risk factors for IFI development. Patients were followed for up to 12 weeks after beginning induction chemotherapy.

Results. Of 488 patients analyzed, 243 were eligible for inclusion. The median age was 57 (interquartile range 45–65). Men composed 134 (55%) of the patients and 157 (65%) where white. Fifty-four (22%) had antecedent myelodysplastic syndrome; most received a "7 + 3" regimen involving cytarabine and an anthracycline. Thirty-one (13%) developed a proven or probable IFI; 104 (43%) developed a proven, probable, or possible IFI. Most IFIs were due to lower respiratory tract disease. Eighteen identified organisms were Candida, including six *C. albicans*. Eight organisms were mold, including four Aspergillus isolates (all but one *A. fumigatus*) and one isolate each of *Fusarium solani*, *Rhizomucor*, *Rhizopus*, and *Scedosporium apiospermum*/*Pseudallescheria boydii*. One hundred ninety patients (78%) received antifungals during their initial admission and 99 (46%) of patients surviving their initial admission were discharged on

antifungals. Only 66.7% of patients with a proven or probable IFI survived through 12 weeks, compared with 92.2% of those without ($P = 0.007$). Baseline absolute neutrophil count ≤500 cells/μL and longer duration of neutropenia were significantly associated with development of proven or probable IFIs.

Conclusion. Among patients receiving induction chemotherapy for AML, IFIs due to Candida and mold remain frequent absent antifungal prophylaxis and are associated with worse survival. Our findings support the use of antifungal prophylaxis in this patient population.

Disclosures. **All authors:** No reported disclosures.

1736. Evaluation of Targeted vs. Universal Antifungal Prophylaxis (AP) for Invasive Fungal Infections (IFI) After Lung Transplant (LTx)

Kathleen A. Linder, MD[1]; Twisha S. Patel, PharmD, BCPS, BCIDP[2]; Carol A. Kauffman, MD, FIDSA, FSHEA[3]; Linda J. Fitzgerald, PharmD[4]; Marisa H. Miceli, MD, FIDSA[1]; Marisa H. Miceli, MD, FIDSA[1]; [1]University of Michigan, Ann Arbor, Michigan; [2]Michigan Medicine, Ann Arbor, Michigan; [3]Ann Arbor VA Healthcare System, Ann Arbor, Michigan; [4]Division of Pharmacy, Ann Arbor, Michigan

Session: 166. Transplant ID: Fungal
Friday, October 4, 2019: 12:15 PM

Background. LTx patients (pt) are at increased risk for IFI. Systemic AP is widely used, but the optimal strategy remains unclear. Our LTx program changed from universal to targeted AP in July 2016; we compared outcomes between the 2 strategies.

Methods. All adult pt who underwent LTx at U. Michigan from July 1, 2014 to December 31, 2017 were studied for 18 mo post-LTx. Universal AP consisted of itraconazole (itra) ± inhaled liposomal amphotericin-B (iAmB) for 6 months. Pt received targeted AP with voriconazole for 3 months if they had a history of pre-LTx *Aspergillus* colonization or invasive pulmonary aspergillosis (IPA); 14 days of a yeast-active azole was given if donor or recipient had *Candida* colonization at the time of LTx. All other pt received no AP. Demographics, LTx characteristics, occurrence of proven/probable IFI defined by EORTC/MSG criteria, and mortality data were recorded.

Results. Of 105 LTx patients, 73 (70%) were men and 84 (80%) received a double LTx. The most common indication for LTx was idiopathic pulmonary fibrosis (38, 36%). Of 59 pt receiving universal AP, 36 (61%) received itra, and 23 (39%) received itra+iAmB; outcomes did not differ between these 2 regimens. Of 46 patients in the targeted AP cohort, 10 (22%) received antifungals based on predefined criteria. Overall, 19 proven/probable IFI occurred: 14 IPA, 3 invasive *Candida* infections, 1 *Cryptococcus* pneumonia, and 1 mold wound infection. IFI occurred in 5 patients (8%) in universal AP group vs. 13 patients (28%) in targeted AP group, $P = .008$. All but 1 IFI in the targeted AP group occurred among pt for whom antifungals were not recommended or given. IPA occurred in 4 patients (7%) in universal AP group and 9 patients (20%) in targeted AP group, $P = 0.05$; *Candida* infections occurred only among patients in the targeted AP cohort. Time to IFI was similar between the 2 AP strategies with the majority occurring <180 days post-LTx (median 109 days). Death occurred in 11 patients (8 in the universal AP cohort and 3 in the targeted AP cohort, $P = .34$); no deaths were related to IFI.

Conclusion. When compared with universal AP, targeted AP strategy was associated with a significant increase in IFI post-LTx. Universal AP for 6 months appears to be more effective than our targeted AP strategy for prevention of IFI post-LTx.

Disclosures: Marisa H. Miceli, MD, FIDSA, Astellas: Advisory Board, Research Grant; Scynexis: Research Grant.

1737. Impact of Therapeutic Drug Monitoring (TDM) of Azole Prophylaxis in Lung Transplant Recipients on the Development of Positive Fungal Events

Anooj Shah, PharmD[1]; Carly D'Agostino, PharmD[1]; Kathleen Cunningham, PharmD[1]; Clare Kane, PharmD[1]; Michael G. Ison, MD[2]; Jamie Schulte, PharmD[1]; [1]Northwestern Memorial Hospital, Chicago, Illinois; [2]Northwestern University, Chicago, Illinois

Session: 166. Transplant ID: Fungal
Friday, October 4, 2019: 12:15 PM

Background. The utility and clinical impact of therapeutic drug monitoring (TDM) of prophylactic azole antifungals in lung transplant recipients is not well described. The objective of this study was to investigate the impact of TDM of azole prophylaxis in lung transplant recipients on the development of positive fungal events.

Methods. A retrospective analysis was performed on 47 lung transplant recipients between 2013 and 2018 at Northwestern Memorial Hospital. A positive fungal event was defined as fungal species on BAL culture and/or positive BAL *Aspergillus* galactomannan (GM) with an index value ≥1.0. Study groups were defined based on attainment of therapeutic trough levels after initiation of oral therapy (therapeutic if posaconazole level ≥0.7 μg/mL or voriconazole ≥1–5.5 μg/mL, subtherapeutic if ≥2 consecutive levels of posaconazole <0.7 μg/mL or voriconazole <1 μg/mL after initial dose increase).

Results. There were no differences in baseline characteristics (Figure 1). There were a total of 11 fungal events with 3 (12.0%) occurring in the therapeutic cohort and 8 (36.4%) in those subtherapeutic ($P = 0.08$). In the 5 patients with a positive GM, the mean index was 2.02 ± 0.95. 7/30 (23.3%) of patients on posaconazole had a fungal event, with 2/7 (28.6%) requiring treatment at the time of event. For patients on voriconazole, 4/17 (23.5%) had a fungal event, with 1/4 (25.0%) requiring treatment. Mean time to fungal event was 164.5 ± 8.9 days vs. 135.9 ± 13.7 days in the therapeutic and subtherapeutic group, respectively ($P = 0.05$).

All patients on posaconazole suspension who experienced a fungal event were subtherapeutic (3/3, 100%) compared with the majority of patients on posaconazole delayed release (DR) tablets who achieved therapeutic levels (17/22, 77.3%). Mean posaconazole trough level observed in the patients receiving DR tablet was 2.15 ± 0.95 μg/mL.

Conclusion. There was an association between two consecutive subtherapeutic azole prophylaxis levels and positive fungal events indicating a role for TDM in lung transplant recipients. Time to fungal event post-transplant was shorter in subtherapeutic patients. As anticipated, the use of posaconazole suspension resulted in subtherapeutic levels. This study presents an opportunity for further research of the impact of TDM on clinical outcomes to optimize patient care.

	Therapeutic (n= 25)	Subtherapeutic (n= 22)
Age, years (mean ± SD)	57.9 ± 11.7	57.3 ± 12.6
Male (n, %)	15 (60.0%)	8 (36.4%)
Underlying lung disease (n, %)		
COPD	7 (28.0%)	7 (31.8%)
CF	3 (12.0%)	1 (4.5%)
Interstitial Lung Disease	6 (24.0%)	9 (40.9%)
Emphysema	1 (4.0%)	0 (0%)
PAH	2 (8.0%)	2 (9.1%)
Other	6 (24.0%)	3 (13.6%)
Type of lung transplant (n, %)		
Single Lung	9 (36.0%)	9 (40.9%)
Double Lung	16 (64.0%)	13 (59.1%)
Induction therapy (n, %)		
Basiliximab with methylprednisolone	19 (76.0%)	18 (81.8%)
Methylprednisolone alone	6 (24.0%)	4 (18.2%)

Disclosures. **All authors:** No reported disclosures.

1738. Incidence and Outcomes of Hospitalization with Invasive Fungal Infection Among Solid-Organ Transplant Recipients: A Population-Based Cohort Study

Kyla L. Naylor, PhD[1]; Alexandra Ouédraogo, MSc[1]; Sarah E. Bota, MSc[1]; Shahid Husain, MD[2]; J. Michael Paterson, PhD[1]; Seyed M Hosseini-Moghaddam, MD, MPH, MSc[3]; [1]The Institute for Clinical Evaluative Sciences (ICES), London, ON, Canada; [2]University Health Network, University of Toronto, Toronto, ON, Canada; [3]Western University, London, ON, Canada

Session: 166. Transplant ID: Fungal
Friday, October 4, 2019: 12:15 PM

Background. Invasive fungal infection (IFI) in solid-organ transplant (SOT) recipients is associated with significant morbidity and mortality. The long-term probability of post-transplant IFI is poorly understood.

Methods. We conducted a population-based cohort study using linked administrative healthcare databases from Ontario, Canada to determine the incidence rate, 1-, 5- and 10-year cumulative probability of IFI-related hospitalization, and 1-year post-IFI all-cause mortality in SOT recipients from 2002 to 2016. We also examined post-IFI death-censored graft failure in renal transplant patients.

Results. We included 9326 SOT recipients (median follow-up 5.35 years). Overall, the incidence of IFI was 8.3 per 1000 person-years (95% confidence interval [CI]: 7.5–9.1). The 1-year cumulative probability of IFI was 7.4% (95% CI: 5.8–9.3%), 5.4% (95% CI: 3.6–8.1%), 1.8% (95% CI: 1.3–2.5%), 1.2% (95% CI: 0.5–3.2%), and 1.1% (95% CI: 0.9–1.4%) for lung, heart, liver, kidney-pancreas, and kidney-only transplant recipients, respectively. Lung transplant recipients had both the highest incidence rate and the highest 10-year probability of IFI: 43.0 per 1,000 person-years (95% CI: 36.8–50.0) and 26.4% (95% CI: 22.4–30.9%), respectively. Lung transplantation was also associated with the highest 1-year cumulative probability of post-IFI all-cause mortality (40.2%,95% CI: 33.1–48.3%). Among kidney transplant recipients, the 1-year probability of death-censored graft failure after IFI was 9.8% (95% CI: 6.0–15.8%).

Conclusion. The 1-year cumulative probability of IFI varies widely among SOT recipients. Lung transplantation was associated with the highest incidence of IFI with considerable 1-year all-cause mortality. The findings of this study considerably improved our understanding of the long-term probability of post-transplant IFI.

Disclosures. **All authors:** No reported disclosures.

1739. Epidemiology of Invasive Fungal Infections in Allogenic Hematopoietic Stem Cell Transplant Recipients in Utah

Jessica Zurko, MD[1]; Brandon J. Webb, MD[2]; [1]University of Utah, Salt Lake City, Utah; [2]Intermountain Healthcare, Murray, Utah

Session: 166. Transplant ID: Fungal
Friday, October 4, 2019: 12:15 PM

Background. Invasive fungal infections are a leading cause of death in allo-HSCT (allogenic hematopoietic stem cell transplant) recipients. We describe the epidemiology of IFIs (invasive fungal infections) in allo-HSCT recipients at a single institution in Salt Lake City, Utah between 2006 and 2015.