2104. Susceptibility Trends in Antifungal Resistance (STAR) Study: Preliminary Data from A New Prospective Antifungal Surveillance Study

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Session: 242. Antifungals

Saturday, October 5, 2019: 12:15 PM

Background. The development of new anti-infectives has increased rapidly over the past ten years. The need to support these important, life-saving products has increased as well. The STAR program was developed in 2018 to provide a repository of recent clinical fungal isolates with known susceptibility profiles and to monitor resistance trends over time. STAR reports the susceptibility patterns of the earliest STAR data concerning echinocandins, second-generation triazoles, and fluconazole against clinical *Candida albicans* and non-albicans strains including *C. auris* from worldwide sources.

Methods. Clinical isolates of *Candida* spp. (n = 203, from 2017–2018) from culture KOL investigator sites in the United States, Asia and the EU, were tested. Of these, 203 were isolated from blood or body tissues, and the remaining 11 from miscellaneous sources. Species distribution included mainly *C. albicans*, *C. glabrata, C. krusei, C. lusitaniae, C. parapsilosis, C. tropicalis*, and the emerging pathogen *C. auris*. Antifungals tested were amphotericin B (AMB), anidulafungin (ANID), fluconazole (FLU), isavuconazole (ISA), posaconazole (POS), and voriconazole (VOR). All testing was performed according to CLSI M27-A4 methodology.

Results. Overall, MIC_{50}, MIC_{90}, MIC range and percent susceptibility for each drug are listed in Table 1. Our data showed that for ANID, ISA and POS ≥ 93% of isolates were susceptible. While 84 and 88% were susceptible to FLU and VOR, respectively. Moreover, only 78% of isolates were susceptible to AMB. Interestingly, our data show that *C. auris* isolates were resistant to at least 1 antifungal with 15% of the *C. auris* strains (n = 40) showing multidrug resistance.

Conclusion. Ongoing antifungal resistance surveillance like STAR is of utmost importance in order to monitor the efficacy of traditional empirical therapy and for the development of novel antifungal agents. This repository and ongoing STAR study will provide a resource to better support the biopharmaceutical industry's goals to develop new and more potent antifungal agents. STAR will continue to monitor yeasts and will also include more unusual fungi including *Mucor*, *Rhizopus* amongst others.

Table 1 .

	MIC_{50}	MIC_{90}	Range	% Susceptible
Amphotericin B	1	4	0.125 - 8	78
Anidulafungin	0.03	1	0.03 - 16	73
Fluconazole	1	>64	0.5 - >64	84
Isavuconazole	0.016	0.12	0.016 - 8	99.5
Posaconazole	0.03	0.25	0.03 - >16	99
Voriconazole	0.03	2	0.016 - 16	88

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

2105. Liposomal Amphotericin B Use Before and After Implementation of Voriconazole Prophylaxis in Cancer Patients

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Session: 242. Antifungals

Saturday, October 5, 2019: 12:15 PM

Background. Invasive fungal infections (IFI) are life-threatening complications of prolonged neutropenia in hematologic cancer or after hematopoietic stem cell transplantation (HSCT). Guidelines recommend mold prophylaxis (ppx) for patients at high risk of IFI. Patients receiving ppx with new signs of infection are often escalated to Liposomal Amphotericin B (L-AmB) for concerns of breakthrough mold infections. We describe the impact of implementing voriconazole (VZL) ppx in cancer patients.

Methods. We performed a quasi-experimental study of all adult patients prescribed L-AmB for ≥1 dose in Cancer Center at the University of Maryland Medical Center. VZL ppx was implemented for patients with hematologic cancer with anticipated prolonged neutropenia (≥ 7 days) in 4/2017. HSCT patients routinely received posaconazole ppx for ≥ 1 year during study period. Comparisons were made pre (November 2015–June 2017) and post (July 2017–December 2018) implementation of VZL ppx allowing for 3-month wash-in period. Cancer center-specific L-AmB days of therapy (DOT) per 1,000 patient-days (PD) were compared using segmented regression and Student t-test. Comparison of patient characteristics, mortality, nephrotoxicity and hospital length of stay (LOS) among patients receiving L-AmB in pre vs. post periods was done using X^2 and Student t-test.

Results. There were 87 (24 pre, 63 post) unique patients included in the analysis, translating to a total of 17.6 L-AmB DOT per 1,000 PD for the study period. Mean L-AmB utilization in cancer center was 9.9 and 24.4 DOT per 1,000 PD (P = 0.0037) for pre and post-implementation, respectively. There was an average 16% increase of L-Amb quarterly (P = 0.93). Among patients receiving L-AmB, most had acute myelogenous leukemia (63% vs. 60%) with lung source (71% vs. 73%, P = 0.8). More patients had proven IFI pre-implementation (42% vs. 29%, P = 0.3). Nephrotoxicity (46% vs. 48%, P = 0.9), median LOS (17 vs. 28, P = 0.4) and inpatient mortality (30 % vs. 38%, p = 0.5) all increased without statistical significance.

Conclusion. After implementation of VZL ppx there was a significant increase in L-AmB use, and associated non-significant increases in LOS, mortality and nephrotoxicity for those receiving L-AmB. Larger, robust longitudinal studies are needed to better understand the implications of VZL ppx on this population.

Figure. Liposomal Amphotericin B Days of therapy (DOT) per 1000 patient-days per quarter

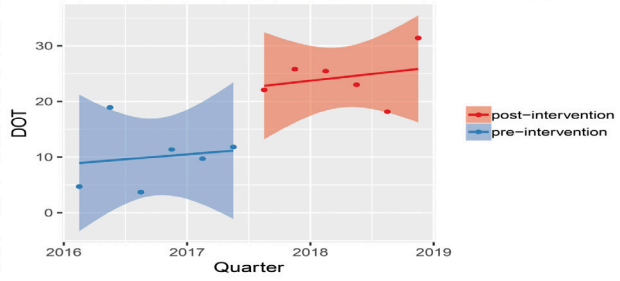

Table. Characteristics and Outcomes of Patients Receiving Liposomal Amphotericin B (L-AmB) in Cancer Center (n = 87)

	Before Mold Prophylaxis n = 24 (%)	After Mold Prophylaxis n = 63 (%)	p-value
Age (years, median, IQR)	57 (16)	59 (18)	0.34
Gender			
Male	17 (71)	38 (60)	0.36
Race			
African American	7 (29)	14 (23)	0.56
Underlying Disease condition			0.65
Acute Myeloid Leukemia	15 (63)	38 (60)	
Acute Lymphoblastic Leukemia	3 (13)	8 (13)	
Myelodysplastic Syndrome	1 (4)	5 (8)	
Multiple Myeloma	0 (0)	2 (3)	
Chronic Myeloid Leukemia	1 (4)	1 (2)	
Chronic Lymphocytic Leukemia	0 (0)	2 (3)	
Other Hematologic disorder	3 (13)	7 (11)	
Relapse or Refractory disease	9 (38)	24 (38)	0.96
Hematopoietic Stem Cell Transplant			0.44
Allogeneic	5 (21)	14 (22)	
Autologous	2 (8)	1 (2)	
Cord-blood	0	1 (1)	
None	17 (71)	47 (75)	
Graft vs Host Disease	3 (43)	6 (38)	0.81
Duration of neutropenia			
≥7 days	13 (54)	42 (67)	0.28
Site of Invasive Fungal Infection			
Lung	17 (71)	46 (73)	0.84
Sinus	4 (17)	6 (9)	0.35
Central Nervous System	2 (8)	5 (8)	0.95
Skin/Soft tissue	3 (13)	7 (11)	0.86
Blood/Disseminated	3 (13)	12 (19)	0.47
Proven Invasive Fungal Infection	10 (42)	18 (29)	0.25
Primary Antifungal prophylaxis	4 (17)	20 (32)	0.16
Prior Antifungal received			
None	2 (8)	4 (6)	0.74
Voriconazole	11 (46)	26 (42)	0.70
Posaconazole	11 (46)	20 (32)	0.22
Isavuconazole	4 (17)	18 (29)	0.25
Micafungin	4 (17)	20 (32)	0.16
Fluconazole	0 (0)	2 (3)	0.38
Nephrotoxicity from L-AmB	11 (46)	30 (48)	0.88
ICU stay during hospitalization			
Before starting L-AmB	6 (25)	22 (35)	0.38
After starting L-AmB	5 (21)	9 (14)	0.46
Length of Stay (days, median, IQR)	17 (34)	28 (30)	0.35
Mortality			
In-Hospital	7 (29)	18 (29)	0.96
30-day	7 (30)	24 (38)	0.51

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

2106. Evaluation of Isavuconazole for the Prophylaxis and Treatment of Invasive Fungal Infections at a Large Academic Medical Center

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Session: 242. Antifungals

Saturday, October 5, 2019: 12:15 PM

Background. Isavuconazole is an azole antifungal with *in vitro* activity against various fungi, including *Candida* spp, *Aspergillus*, and Mucormycetes. Currently, isavuconazole is FDA approved for the treatment of invasive aspergillosis and mucormycosis; however, there remains limited data to support prophylaxis use. Compared with other first-line azoles, isavuconazole's broad spectrum of activity, favorable safety

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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Session: 242. Antifungals
Saturday, October 5, 2019: 12:15 PM

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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Session: 242. Antifungals
Saturday, October 5, 2019: 12:15 PM

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)		