Conclusion. No meaningful differences in rezafungin C_{min} values were observed in patients grouped by sex, race, or geographic region, or across a wide range of patient factors, including age and body weight and size. These findings indicate that a single rezafungin dose regimen can be expected to provide consistent PK across diverse patient populations.

Disclosures. Shawn Flanagan, PhD, Cidara Therapeutics, Inc. (Employee, Shareholder) Christopher M. Rubino, PharMD, Institute for Clinical Pharmacodynamics, Inc. (Employee)Spero Therapeutics (Grant/Research Support) Taylor Sandison, MD, MPH, Cidara Therapeutics, Inc. (Employee, Shareholder)

1175. Pulmonary Aspergillosis in Critically Ill Patients with COVID-19: A Case Series

Hayato Mitaka, MD[1]; David C. Perlman, MD[2]; Waleed Javaid, MD, FACP, FIDSA, FSHEA[3]; Nadim Salomon, MD[4]; [1]Mount Sinai Beth Israel, New York, New York; [2]Icahn School of Medicine at Mount Sinai, New York, New York; [3]Mount Sinai Health System, Brooklyn, NY; [4]Icahn School of Medicine, Haverstraw, New York

Session: P-52. Medical Mycology

Background. Invasive pulmonary aspergillosis (IPA) has been reported in critically ill patients without pre-existing immunocompromising conditions. However, there are scant data on pulmonary aspergillosis in patients with COVID-19.

Methods. We performed a retrospective review of pharmacy records of antifungal use during 3/21-4/22, 2020, and collect longitudinal clinical data. Cases were then classified by the clinical algorithm for IPA in the ICU (AspICU).

Results. 7 out of 18 (39%) patients who received antifungal therapy had Aspergillus *fumigatus* in tracheal aspirate specimens while mechanically ventilated in the ICU. None of the patients had EORTC/MSG host factors. Median time from admission to the date of positive respiratory culture was 9 days (range: 2-15). High-dose glucocorticoids were started a mean of 5.6 days (range 3-8) before the positive respiratory culture in 5 and on the day of the culture in 2. Six received 583-1000 mg equivalent of prednisone. Two received Tocilizumab. By AspICU criteria, 4 had putative IPA. Radiographic abnormalities included cavitary pneumonia, opacities with dense consolidation, worsening infiltrates, and diffuse interstitial and patchy hazy opacities. Compatible signs included worsening respiratory failure in 3 and fever after 3 days of antibacterial agents in 1. Associated findings were leukocytosis in 4, > 1 positive cultures in 3, high procalcitonin in 2, and positive serum galactomannan in 1. The remaining three were classified as colonization as they lacked compatible signs. One had concomitant *Klebsiella aerogenes* pneumonia with bacteremia, and two later developed Candidemia and *Stenotrophomonas maltophilia* pneumonia, respectively. All 3 had fever with leukocytosis. One had elevated procalcitonin. Six received antifungal therapy; one did not due to goals of care. All 7 patients expired despite ICU care.

Conclusion. The critically ill patients with severe COVID-19 in whom respiratory culture grew *Aspergillus fumigatus* showed very high mortality despite antifungal treatment. By AspICU algorithm, 4 patients had putative IPA. Further data on risk factors and clinical predictors of IPA in COVID-19 are needed.

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

1176. Quality of Life of Previously Healthy Subjects following Cryptococcal Meningoencephalitis.

Owen Dean, n/a[1]; Seher Anjum, MD[2]; Terri Scott, MSN, CNP[3]; Lillian Ham, BA[4]; John H. Powers, MD[5]; Joseph Snow, PhD[4]; Peter Williamson, MD, PhD[6]; [1]University of Rochester School of Medicine and Dentistry, Marcellus, New York [2]National Institutes of Health, Bethesda, MD; [3]National Institute of Allergy and Infectious Diseases, Bethesda, Maryland; [4]National Institute of Mental Health, Bethesda, Maryland; [5]Support to National Institute of Allergy and Infectious Disease, Bethesda, MD; [6]National Institutes of Health, Bethesda, Bethesda, Maryland

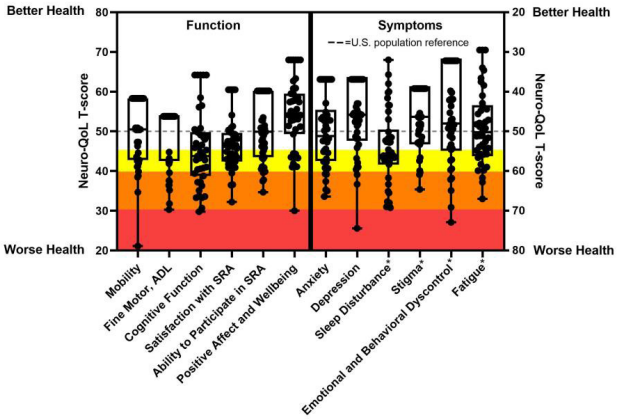
Session: P-52. Medical Mycology

Background. Cryptococcal meningoencephalitis (CM) causes significant morbidity and mortality in HIV-negative, previously healthy populations. This group has significant disease sequalae including a fronto-subcortical syndrome, hearing loss, vision loss, and spinal arachnoiditis. However, the health-related quality of life (HRQOL) of this group of patients following microbial recovery from infection has not been reported.

Methods. We cross-sectionally defined the HRQOL of previously healthy individuals with CM seen at the NIH Clinical Center since 2013 and at least one year past diagnosis using the Quality of Life in Neurological Disorders (Neuro-QoL) project short forms. These forms assess domains such as anxiety, fatigue, depression, dexterity and mobility in patients with chronic neurological disease. Form scores were calculated for each domain and centered to a general or clinical United States population reference. Impairment was considered a subject score of least one half a standard deviation (SD) lower than the population reference average.

Results. Of 43 subjects with CM (mean age 48 years, 56% male, mean time from diagnosis 5.7 years), 91% had evidence of impairment in at least one HRQOL domain. Notable findings included self-reported impaired cognitive function in 53% and sleep disturbance in 56%. Impaired satisfaction with social roles and activities was present in 44%. Mobility and dexterity were impaired in 30% respectively. The number of impaired HRQOL domains was not significantly different in subjects with a history of neurosurgical intervention during hospitalization (mean no. impaired domains 4.4 vs. 3.3, P=0.43) or methylprednisolone treatment for post-infectious inflammatory response syndrome (4.3 vs. 3.4, P=0.63). Cerebrospinal fluid glucose levels on admission were negatively correlated with the number of impaired functional domains (r_s=-0.33, P=0.05, n=38).

Patient reported quality of life domains following microbial recovery from cryptococcal meningoencephalitis. Box plots show median, 25th, and 75th percentiles.The gray dotted line represents the mean T-score (50) of the U.S. population reference for each Neuro-QoL domain. The yellow region designates mild symptoms or impairment (0.5-1.0 std below the population mean), orange, moderate (1.0-2.0), and red, severe (2.0-3.0). The asterisk* indicates measures that were centered to U.S. clinical reference population. All other domains were centered to a U.S. general population reference. Abbreviations: CNS, central nervous system, U.S., United States, ADL, activities of daily living, SRA, social roles and activities



Conclusion. This is the first report of HRQOL deficits in previously healthy individuals following microbial recovery from CM. These data reinforce and quantify the long-term morbidity of this disease and identify patient-centered outcomes for future interventional trials.

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

1177. Rapid, Non-invasive Detection of Invasive Mucormycosis Caused by Syncephalastrum monosporum Using Next-Generation Sequencing of Circulating Microbial Cell-free DNA in Plasma

Melissa Sanacore, PharmD[1]; Melhem M. Solh, MD[1]; H. Kent Holland, MD[1]; Asad Bashey, MD, PhD[1]; Samuel Webster, MD[1]; Lawrence Morris, MD[1]; Scott Solomon, MD[1]; Christiaan R. de Vries, MD, PhD[2]; [1]The Bone Marrow Transplant Program at Northside Hospital, Atlanta, Georgia; [2]Karius, Inc., Redwood City, California

Session: P-52. Medical Mycology

Background. Improving diagnostics have led to newly identified causes of invasive fungal infection (IFI) in immunocompromised hosts. *Syncephalastrum* spp. are Zygomycetes more commonly associated with skin infections and have only rarely been implicated as a cause of IFI(1). Next generation sequencing (NGS) for circulating microbial cell-free DNA (mcfDNA) in plasma offers a unique tool to diagnose rare causes of IFI (2,3).

Methods. Karius results were reviewed for *Syncephalastrum* detections with 2 identified at the same institution. McfDNA was extracted from plasma and NGS was performed by Karius, Inc. (Redwood City, California). Human sequences were removed and remaining sequences were aligned to a database of over 1,400 pathogens. Organisms present above a predefined statistical significance threshold were quantified in DNA molecules per microliter (MPM). Chart review was performed for clinical correlation.

Results. A 66 y/o male one month out of induction therapy for acute myeloblastic leukemia (AML) developed pneumonia. Although BAL was negative for mold and despite empiric antifungals, plasma NGS for mcfDNA showed *S. monosporum* at 562 MPM; the reference range is 0 MPM. Amphotericin was added to empiric posaconazole. The patient was discharged 10 days later and serial CT scans showed improvement. Repeat NGS mcfDNA 11 days later was negative. He underwent stem cell transplant (SCT) 4 months later.

In a second case, a 66 y/o female with acute prolymphocytic leukemia was admitted for fever with neutropenia. A CT chest showed new multifocal, bilateral, nodular opacities. Despite negative BAL fungal culture and pretreatment with fluconazole, plasma NGS mcfDNA revealed *S. monosporum* at 575 MPM. She was treated with micafungin, amphotericin, and posaconazole with clinical improvement. Repeat NGS mcfDNA 8 weeks later was negative. Serial CT scans showed improvement over 5 months. She proceeded to SCT.

Conclusion. Plasma-based NGS for mcfDNA enabled rapid, non-invasive detection of pulmonary mucormycosis caused by *S. monosporum* despite antifungal pretreatment and unrevealing invasive procedures in 2 patients with leukemia. The rapid identification of the specific etiology of IFI enabled targeted anti-fungal therapy and resumption of definitive oncological care including SCT.

Table 1: Clinical Parameters

	Patient 1	Patient 2
Age	66	66
Sex	Male	Female
Underlying illness	AML	B cell prolymphocytic leukemia
Chemotherapy (within prior 30 days)	FLAG-IDA induction chemotherapy	Rituximab, Ibrutinib, Bendamustine, Venetoclax, dexamethasone
Clinical manifestations	Productive cough, hypoxemia	Fever, dyspnea
Initial CT chest	Bilateral pulmonary ground-glass opacities	Multifocal, bilateral, irregular nodular opacities
Follow up CT chest	Nodular/mass-like opacities	Worsening pneumonia with multiple areas of cavitation
BAL results	Culture: *Rothia mucilaginosa* Fungal culture: Negative Path: No fungal elements	PCR: Aspergillus fumigatus, HHV-6 Culture: *Prevotella, Streptomyces* Fungal culture: Negative Path: No fungal elements
Karius Test	*Syncephalastrum monosporum* 562 MPM (RR < 10 MPM)*	*Syncephalastrum monosporum* 575 MPM (RR < 10 MPM)**
Treatment	Posaconazole, Amphotericin liposomal	Posaconazole, Micafungin, Amphotericin liposomal
Outcome	Survival, stable CT imaging, repeat KT negative, underwent haplo-HSCT	Survival, improvement in CT imaging, repeat KT negative, underwent allogeneic PBSCT

RR = reference range based on the 97.5% of a cohort of 684 healthy individuals.
**Rothia mucilaginosa* reads were present in the raw data but did not reach the required statistical significance for the commercial threshold
***Aspergillus* and *Prevotella* reads were present in the raw data but did not reach the required statistical significance for the commercial threshold; HHV6 reads were not present

References

1. Gomes, M. et al. 2011. "Mucormycosis Caused by Unusual Mucormycetes, Non-Rhizopus, -Mucor, and -Lichtheimia Species." Clinical Microbiology Reviews 24 (2): 411–45.
2. Hong, DK., et al. 2018. "Liquid Biopsy for Infectious Diseases: Sequencing of Cell-Free Plasma to Detect Pathogen DNA in Patients with Invasive Fungal Disease." Diagnostic Microbiology and Infectious Disease 92 (3): 210–13.3.
3. Rossoff J, Chaudhury S, Soneji M, Patel SJ, Kwon S, Armstrong A, et al. Noninvasive Diagnosis of Infection Using Plasma Next-Generation Sequencing: A Single-Center Experience. Open Forum Infect Dis. 2019;6.

Disclosures. Christiaan R. de Vries, MD, PhD, Karius (Consultant, Independent Contractor)Stanford University (Employee)

1178. Risk factors for death among patients with Candida endocarditis: An observational study in US academic medical centers

Jonathan Huggins, MD[1]; Michael Z. David, MD PhD[1]; Samuel F. Hohmann, PhD[2]; [1]Hospital of the University of Pennsylvania, Durham, North Carolina [2]Vizient, Chicago, Illinois

Session: P-52. Medical Mycology

Background. Candida endocarditis is a rare, sometimes fatal complication candidemia. Our understanding of this condition is limited to findings from case series and small observational studies. Using the Vizient clinical database, a repository for clinical and administrative data from 117 academic medical centers and more than 300 affiliated hospitals, we assembled the largest cohort of Candida endocarditis patients to date, reporting patient characteristics and risk factors for death.

Methods. Using ICD-10 code B37.6 (Candidal Endocarditis) we identified 703 inpatients at 179 United States hospitals from October 2015 through April 2019. We examined demographic, diagnostic, and procedural data from each patient's initial encounter. With univariate and multivariate logistic regression analyses we identified predictors of in-hospital mortality.

Results. Of 703 patients, 402 (57.2%) were male, 421 (59.9%) used tobacco, 213 (30.3%) had documented opiate abuse, 128 (18.2%) had other illicit drug abuse documented, and 190 (27.0%) had documented hepatitis C infection. Among the 703 patients, 114 (16.2%) died during the index encounter. On multivariate analysis, liver failure was the strongest predictor of death (OR 8.4, 95% CI 4.4 – 15.9), and female sex (OR 1.8, 95% CI 1.1 – 2.9), transfer from an outside facility (OR 1.7, 95% CI 1.1 – 2.7), underlying aortic valve pathology (OR 2.8, 95% CI 1.5 – 4.9), hemodialysis (OR 2.0, 95% CI 1.0 – 3.8), cerebrovascular disease (OR 2.2, 95% CI 1.2 – 3.8), neutropenia (OR 2.5, 95% CI 1.3 – 4.7) and alcohol abuse (OR 2.9, 95% CI 1.3 – 6.7) were also associated with higher odds of in-hospital death. In the same analysis, opiate abuse was associated with a lower odds of in-hospital death (OR 0.4, 95% CI 0.2 – 0.8).

Table 1. Characteristics of 703 patients with Candida endocarditis

Factor	Alive at Discharge	Dead at Discharge	p-value
N	589	114	
Age			<0.001
≤30 years	134 (22.8%)	20 (17.5%)	
31-50 years	211 (35.8%)	25 (21.9%)	
51-64 years	130 (22.1%)	31 (27.2%)	
65+ years	114 (19.4%)	38 (33.3%)	
Sex			0.28
Male	342 (58.1%)	60 (52.6%)	
Female	247 (41.9%)	54 (47.4%)	
Race			0.27
Unknown/Unavailable/Declined	18 (3.1%)	8 (7.0%)	
White	415 (70.5%)	74 (64.9%)	
Black	98 (16.6%)	19 (16.7%)	
Asian	14 (2.4%)	2 (1.8%)	
Other	44 (7.5%)	11 (9.6%)	
Insurance Payer			0.98
Private	109 (18.5%)	21 (18.4%)	
Medicare/Medicaid	439 (74.7%)	86 (75.4%)	
Uninsured	20 (3.4%)	4 (3.5%)	
Other	20 (3.4%)	3 (2.6%)	
Length of Stay, median (IQR)	19.0 (10.0, 34.0)	19.5 (10.0, 38.0)	0.52
Patient Origin			<0.001
Non-Facility	277 (47.0%)	33 (28.9%)	
Clinic	33 (5.6%)	7 (6.1%)	
Inpatient Medical Facility	269 (45.7%)	74 (64.9%)	
Other	10 (1.7%)	0 (0.0%)	
Diabetes Mellitus (DM)	165 (28.0%)	36 (31.6%)	0.44
Chronic Kidney Disease (CKD)	170 (28.9%)	49 (43.0%)	0.003
Hemodialysis (HD)	52 (8.8%)	21 (18.4%)	0.002
Cerebrovascular Disease (CVD)	75 (12.7%)	29 (25.4%)	<0.001
Chronic Obstructive Pulmonary Disease (COPD)	58 (9.8%)	16 (14.0%)	0.18
Coronary Artery Disease (CAD)	7 (1.2%)	3 (2.6%)	0.23
Other Underlying Heart Condition	41 (7.0%)	11 (9.6%)	0.32
Vascular Disease	77 (13.1%)	19 (16.7%)	0.31
Chronic Heart Failure	140 (23.8%)	40 (35.1%)	0.011
Peptic Ulcer Disease (PUD)	8 (1.4%)	0 (0.0%)	0.21
Liver Failure	27 (4.6%)	30 (26.3%)	<0.001
Cirrhosis	22 (3.7%)	3 (2.6%)	0.56
Hepatitis B Infection	19 (3.2%)	1 (0.9%)	0.17
Hepatitis C Infection	166 (28.2%)	24 (21.1%)	0.12
Human Immunodeficiency Virus (HIV) Infection	13 (2.2%)	1 (0.9%)	0.35
Connective Tissue or Autoimmune Disease	32 (5.4%)	9 (7.9%)	0.30
Long-term Steroid Use	23 (3.9%)	2 (1.8%)	0.26
Hematologic Malignancy (HM) or related	23 (3.9%)	8 (7.0%)	0.14
Neutropenia/Pancytopenia	57 (9.7%)	20 (17.5%)	0.014
Hematopoietic Stem Cell Transplant (HSCT)	3 (0.5%)	0 (0.0%)	0.45
Solid Tumor	58 (9.8%)	14 (12.3%)	0.43
Malignancy, NOS	22 (3.7%)	6 (5.3%)	0.45
Solid Organ Transplant (SOT)	19 (3.2%)	3 (2.6%)	0.74
Homeless	21 (3.6%)	3 (2.6%)	0.62
Tobacco Abuse	371 (63.0%)	50 (43.9%)	<0.001
Alcohol Abuse	33 (5.6%)	12 (10.5%)	0.049
Other Illicit Drug Use	113 (19.2%)	15 (13.2%)	0.13
Opioid Abuse/Dependence	195 (33.1%)	18 (15.8%)	<0.001

Table 2. Factors associated with in-hospital death in multivariate regression analysis

Factor	Odds Ratio	95% C.I.	p-value
Age			
≤30 years	Reference		
31-50 years	0.8	(0.4 - 1.6)	0.483
51-64 years	1.1	(0.5 - 2.2)	0.871
65+ years	1.6	(0.7 - 3.3)	0.238
Sex			
Male	Reference		
Female	1.8	(1.1 - 2.9)	0.014
Race			
Unknown/Unavailable/Declined	Reference		
White	0.4	(0.2 - 1.2)	0.112
Black	0.4	(0.1 - 1.3)	0.124
Asian	0.3	(0.0 - 2.0)	0.202
Other	0.6	(0.2 - 1.9)	0.366
Patient Origin			
Inpatient Medical Facility	1.7	(1.1 - 2.7)	0.027
Hemodialysis (HD)	2.0	(1.0 - 3.8)	0.049
Cerebrovascular Disease (CVD)	2.2	(1.2 - 3.8)	0.006
Chronic Heart Failure	1.6	(1.0 - 2.6)	0.065
Liver Failure	8.4	(4.4 - 15.9)	<0.001
Neutropenia/Pancytopenia	2.5	(1.3 - 4.7)	0.006
Alcohol Abuse	2.9	(1.3 - 6.7)	0.012
Opioid Abuse/Dependence	0.4	(0.2 - 0.8)	0.014
Aortic Valve Pathology	2.8	(1.5 - 4.9)	0.001

Conclusion. We found that for patients Candida endocarditis inpatient mortality was 16.2% and liver failure was associated with a high risk of death while opiate abuse was protective. Further investigation is necessary to better understand these associations.

Disclosures. Michael Z. David, MD PhD, GSK (Consultant)

1179. Septic shock in Coccidioides immitis Infection

Piotr Wisniewski, MD[1]; Evan C. Ewers, MD, MPH[2]; Ryan C. Maves, MD FCCP FIDSA[1]; [1]Naval Medical Center San Diego, San Diego, California; [2]Naval Medical Center, San Diego, Bethesda, Maryland