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.

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

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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.

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

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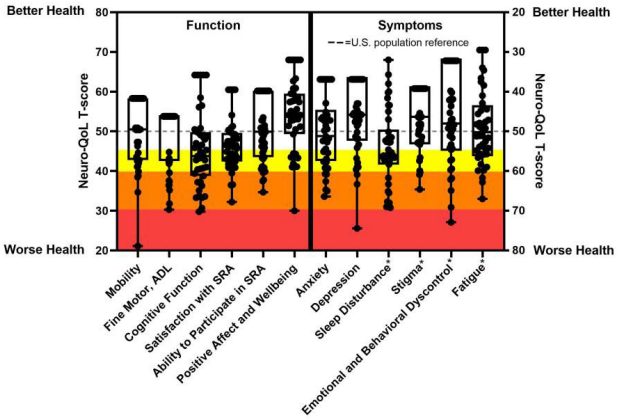
Background. Cryptococcal meningoencephalitis (CM) causes significant morbidity and mortality in HIV-negative, previously healthy populations. This group has significant disease sequalae including a fronto-subcortical syndrome, hearing loss, vision loss, and spinal arachnoiditis. However, the health-related 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.

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

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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.