S4.5 A randomized, double blind phase 3 proof-of-concept superiority trial of voriconazole 200mg or 300mg weekly dose versus itraconazole 400mg daily, all time arms in combination with surgery, in patients with eumycetoma in Sudan—top line results

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Objectives: To determine whether, in addition to surgery, voriconazole (Fov) monotherapy of either 200 mg or 300 mg weekly dose (equivalent to a maximum of 80 mg or 120 mg daily dose in patients with clinical symptoms of eumycetoma caused by Madurella mycetomatis or using a non-comparative PK analysis

Methods: Participants received either 200 mg or 300 mg voriconazole once weekly or 400 mg itraconazole daily for a total duration of 12 months. Plasma concentrations of voriconazole and itraconazole were measured on day 1 of week 1, and on week 2, 3, 4, and months 2, 3, 4, and 12 (at end of treatment) for analysis of PK. The exact time of doing the days of sample collection, and the exact time of sample collection within the collection time window, were recorded. Plasma concentrations were quantified using UltraPerformance Liquid Chromatography with fluorescence detection (UPLC-UV). Voriconazole and itraconazole plasma concentrations from these were performed using a standard two stage approach with non-compartmental analysis. Derived exposure parameters of voriconazole and itraconazole, including, but not limited to, Cmax, AUC and t1/2 were calculated. The primary outcome was how these results were compared against the results for voriconazole and itraconazole, respectively, using the new standard approach.

Conclusions: This is the first randomized controlled trial in eumycetoma, comparing two azoles, voriconazole (two dosage regimens) and itraconazole, in combination with surgery. Detailed efficacy and safety results will be communicated and discussed in the oral presentation.

S4.5d Comparing the diagnostic performance of the commonly used eumycetoma diagnostic tests using sequencing of the internally transcribed spacer region as the gold standard

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Objectives: Mycetoma is a neglected tropical disease caused by 70 different infectious agents. Identifying the causative organism to the species level is essential for appropriate patient management. Ultrasonography, histopathology, culture, and automated species-specific PCR are the most commonly used tests today. The objective of this study was to compare the diagnostic performances of these commonly used assays using sequencing of the ITS as the gold standard.

Methods: This is a cross-sectional study conducted at the Mycetoma Research Centre, University of Khartoum, Sudan. It included 222 patients suspected of fungal mycetoma caused by Madurella mycetomatis. Blood samples were taken at day 14 (±3) mg/L were correctly identified by ultrasound, histology, culture, and both species-specific PCRs. In 60 patients, a least one of the diagnostic tests failed to identify M. mycetomatis. A total of five patients had no evidence of eumycetoma, and for three, only the ultrasound was indicative of mycetoma. The two species-specific PCRs were the most specific and sensitive methods followed by culture and histology. Ultrasound was the least specific or at least allowed differentiation amongst Madurella and eumycetoma. The time to result was 9.38 minutes for ultrasound, 3.74 for PCR, 8.5 days for histopathology and 21 days for gram staining.

Conclusions: Currently, PCR directly on DNA isolated from grains in the most rapid and reliable diagnostic tool to identify M. mycetomatis eumycetoma.

P4 COVID-19-associated fungal infections

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Objectives: To analyze clinical presentations of COVID-19 pneumonitis that are possibly related to fungal infections.

Methods: This is a retrospective, observational study using clinical records of patients admitted due to COVID-19 or pneumonia at the University Hospital of Graz, Austria. Data were collected from March to November 2020. Patients were included if they had positive diagnosis of COVID-19 or pneumonia, received treatment with antifungal agents and had positive culture results for fungi, mycobacteria or viruses at least once.

Results: A total of 15 patients met inclusion criteria. The most common fungal species were Candida and Pneumocystis. The most frequent clinical signs were dyspnea, tachypnea, fever, cough, and hypoxemia. The most common fungal species were Candida and Pneumocystis. The most frequent clinical signs were dyspnea, tachypnea, fever, cough, and hypoxemia. Patients were treated with antifungal agents and achieved clinical improvement. However, 4 patients died due to severe COVID-19-related complications.

Conclusions: COVID-19 patients are at risk of developing fungal infections, which can be severe and lead to increased mortality. Identifying fungal infections can be challenging due to overlapping clinical manifestations with COVID-19. Therefore, a high index of suspicion is necessary to diagnose fungal infections early and start appropriate therapy.