Sudan—pharmacokinetic weekly, by Hadi Ahmed Siddig1,3, Bertrand Nyukonge1, Noura Mhmoud1, Omnia Abdallah1, Mustafa Bahar1, Eiman Siddig2, Etaziya2, Amna Velton1, Sabir Bahar1, Ahmed Fatah1, Wendy van de Sande1

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Objective: To determine whether, in addition to surgery, four-razonucleotide (F4) monotherapy of either 200 mg or 300 mg weekly doses versus intravenous (i.v.) twice a day (i.e., defined as a complete cure at the End of Treatment [EOT], 12-week [w]) was the standard-of-care 12-month regimen of iraconazole (ITZ) monotherapy, in patients with small to medium-sized cutaneous wounds caused by Madurella mycetomatis.

Methods: This was a single-center (Mycetoma Research Center, Khartoum, Sudan), comparative, randomised, double-blind, parallel-group, active-controlled, clinical superiority trial in patients with mycetoma requiring surgery. Participants were randomised in a 1:1:1 ratio. Arm 1 participants took a loading dose of F4 (200 mg or 300 mg) on day 1, Day 2, and Day 2, followed by a weekly dose of F4 for a total duration of 12 months. For Arm 3, participants took ITZ for 12 months. In Arm 3, patients took intravenous on 400 mg daily for 12 months. All patients underwent surgery after 6 months of treatment in which the remaining lesion was removed. Mycetoma lesions were between 2 and ≤15 cm in diameter. The age cut-off was ≤51 years. The diagnosis of M. mycetomatis was confirmed by PCR. Safety monitoring included, among other, sooner, and serious treatment-related events.

Results: A total of 122 participants were screened and 104 participants were enrolled. Results: F4 (300 mg F4) was safe, and it was in use at 360 mg and 361 mg (i.e., in 0.4 mg). Complete cure after 12 months (EOT) of treatment was demonstrated in terms of an absence of mycetoma mass, sinus, and discharge, normal ultrastructure of the lesion size or normal MMR, and a negative fungal culture from a surgical biopsy if a mycetoma mass was present. The complete cure rate was assessed in the ITZ population. Secondary efficacy analyses were performed in the Per Protocol population. In addition, the influence of age, changes in clinical symptoms and signs, and duration of the lesion on outcome were examined. Safety was leant to the comparator and other treatments.

Conclusion: This is the first randomised controlled trial in mycetoma, comparing two azoles, four-razonucleotide (two dosage regimes) and iraconazole, in combination with surgery. Detailed efficacy and safety results will be communicated and discussed in the oral presentation.

S.4.5 A randomised, double-blind phase 3 proof-of-concept superiority trial of farraconazole 200 mg or 300 mg weekly doses versus iraconazole 400 mg daily, all time in combination with surgery, in patients with mycetoma in Sudan—pharmacokinetic results

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S.4.6 Mycetoma Clinical Trial on farraconazole treatment in eumycetoma- Top Line Results, September 22, 2022, 10:30 AM - 12:00 PM

Objective: The pharmacokinetics (PK) of farraconazole (measured as farraconazole) and iraconazole in patients with small to medium-sized cutaneous wounds caused by Madurella mycetomatis using a non-compartmental PK analysis.

Methods: Participants received either 200 mg or 300 mg farraconazole once weekly or 400 mg iraconazole daily for a total duration of 12 months. Plasma concentrations of farraconazole and iraconazole were measured on day 1, week 1, and on weeks 2, 3, 5, and months 2, 3, 6, and 12 (at the end of treatment) for analysis of PK parameters. The exact time of doing on 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). Ravaconazole and iraconazole plasma concentrations thus were calculated using a standard two-stage approach with non-compartmental analysis. Derived exposure parameters of farraconazole and iraconazole, including, but not limited to, Cmax and AUC, were calculated. The PK parameters such as baseline characteristics were applied on PK was employed. AUC was determined when at least three subsequent samples within one dosing interval were available. Results: A total of 75% of samples of farraconazole in 48 participants and 226 samples of iraconazole in 56 participants were analysed. The average time of farraconazole (range) was 3.1 mg/l (0.01-123.53 mg/l) and 11.9 mg/l (0.01-53.5 mg/l).

Derived Pharmacokinetic results will be communicated and discussed in the oral presentation.

S.5.4c Using serum beta-glucan measurements and sequencing of the Madurella mycetomatis azole target gene to predict therapeutic outcome during azole treatment in human mycetoma

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S.5.4 Mycetoma Clinical Trial on farraconazole treatment in eumycetoma- Top Line Results, September 22, 2022, 10:30 AM - 12:00 PM

现出症症を挙げると、遺伝子的検査は、症例の検査の必要性を示す重要な手段であり、また、治療選択に影響を及ぼす重要な情報源である。遺伝子検査の有効性は、症例の検査との関連性を実現するための基礎的な情報であり、症例の検査の結果を基にした治療選択の指針を提供する。遺伝子検査の有効性は、症例の検査との関連性を実現するための基礎的な情報であり、症例の検査の結果を基にした治療選択の指針を提供する。遺伝子検査の有効性は、症例の検査との関連性を実現するための基礎的な情報であり、症例の検査の結果を基にした治療選択の指針を提供する。遺伝子検査の有効性は、症例の検査との関連性を実現するための基礎的な情報であり、症例の検査の結果を基にした治療選択の指針を提供する。