
Oral

[O25-7] O25-7: Infectious diseases

Chairs: Mariadelfina Molinaro, Italy / Mitsuru Sugawara, Japan

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[O25-7-3] Is the recommended dose of Micafungin suitable for every critically ill patient?

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Background

Micafungin (MCF) is an antifungal of the echinocandin class, with indications for the treatment and/or the prophylaxis of *Candida* and *Aspergillus* infections. MI-K was a multicenter study (EudraCT : 2014-000115-14) that aimed (i) to explore the pharmacokinetics (PKs) of MCF in patients hospitalized in Intensive-Care Units (ICU) and (ii) to identify covariates which could explain variations of exposure to MCF in these patients.

Methods

60 patients with suspected or proven invasive fungal infections and given 100 mg daily dose administered as a 1 h infusion for 14 days, were included. Full-PK profiles of MCF were measured on day 0, day 4 (steady-state; SS) and day 14 (end of treatment). A two-compartment open model, developed using a non-parametric approach (Pmetrics), was applied to fit the data. The relationships between the individual covariates (burns, dialysis, age, body mass index (BMI), SOFA Score, albuminemia, creatinemia, bilirubinemia) and the individual AUC values were investigated using generalized estimating equation (GEE) and principal component analyses (PCA). The calculation of individual AUC/MIC ratio values was performed using AUC at D4 and D14 and confronted with the previously published efficacy thresholds.

Results

124 PK profiles were obtained. The population was very heterogeneous: 19 patients were overweight, 15 were obese, 7 had burns, 14 were dialyzed. Parameter estimates (mean \pm SD) were 0.97 ± 0.79 L/h for clearance and 13.5 ± 8.0 L for central volume. AUC values estimated at D0, D4 and D14 were 107 ± 66 , 161 ± 99 and 168 ± 109 mg.h/L, respectively. At SS, mean observed C₀ values were 2.8 ± 2.1 mg/L [0.2; 11.0] and highly correlated with AUC ($r^2 > 0.97$). The exposure significantly increased with albumin and SOFA score (β albumine = $+2.8 \pm 0.9$ mg.h/L, $p = 0.0012$ and β SOFA = $+6.5 \pm 1.5$ mg.h/L, $p < 0.0001$). BMI did not influence the AUC, even in overweight or obese patients. For *Candida albicans* and *glabrata* strains, AUC/MIC ratios were > 3000 (except for one patient). For *Candida parapsilosis*, one third of the strains had an AUC/MIC ratio over the threshold of 285.

Conclusions

Patients with the lowest albuminemia and SOFA score values had the lowest AUC values. However, a daily dose of 100mg led to satisfactory AUC/MIC in this population.