Aim and objectives

- To develop a population pharmacokinetic model (PopPK) that describes the behavior of isavuconazole in prophylaxis and treatment of invasive fungal infections (IFI) and to evaluate possible factors affecting dosage.

Materials and Methods

- Prospective and multidisciplinary study (June 2020 to January 2022).
- Immunosuppressed patients treated with oral and intravenous isavuconazole as prophylaxis or treatment for IFI.

VARIABLES

- Demographic
- Clinical
- Biochemical
- Genetic:
  - Polymorphisms
  - Inducers and inhibitors
  - Degree of saturation of drug-metabolizing enzymes (SuperCYPsPred).

PopPK analysis

- Nonlinear mixed-effects model NONMEM v7.4 - FOCEI
- Software R v3.4

Results

PHARMACOKINETIC MODEL

- Single-compartment model with first order absorption and elimination.
- Absorption rate: 22.6 h⁻¹ (Cojutti et al. 2021)
- Volume of distribution: 147 L
- Apparent clearance (CL/F): $\text{CL/F} (\text{L/h}) = 3.54 \times (\text{ALB}/2.9)^{-0.7} \times (\text{BS}/1.9)^{1.9} \times (1+0.8)^{3\text{A4Ind}}$

ALB: serum albumin (g/dL), BS: body surface (m²), 3A4Ind: presence of inductor drugs for CYP3A4 ALB: albúmin (g/dL)

- Interindividual variability for CL/F: 40%
- Residual variability for CL/F: 30% (additive) and 0.05 µg/mL (proportional)

Conclusion and relevance

The developed PopPK model adequately characterizes the kinetic behavior of isavuconazole and includes the ALB, BD and the presence of inducers of CYP3A4 parameters that affect its clearance.