

Development and Validation of a Population Pharmacokinetic Model of Teicoplanin in Adult Patients with Hematologic Malignancies – NP-009

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Background and Importance

Teicoplanin is a widely used antibiotic in patients with hematologic malignancies (HM); however, a population pharmacokinetic (popPK) model for these patients is not available."

Aim and Objectives

To develop a popPK model for teicoplanin in adult patients with HM and validate its predictive capacity for individualizing dosages.

Materials and Methods

- Prospective and multidisciplinary study conducted from February/2021 to December/2023.
- All patients received an initial intravenous dose of 600 mg/12 h, and the dose was subsequently optimized through teicoplanin plasma concentrations (TPC) monitoring.

popPK

- Pharmacostatistical approach based on nonlinear mixed-effects models with NONMEM v7.3
- FOCEI method

Validación

- Accuracy: mean prediction error (MPE)
- Precision: mean absolute prediction error (MAPE)
- A visual predictive check (VPC) was performed to assess model performance

Results

Demographic data

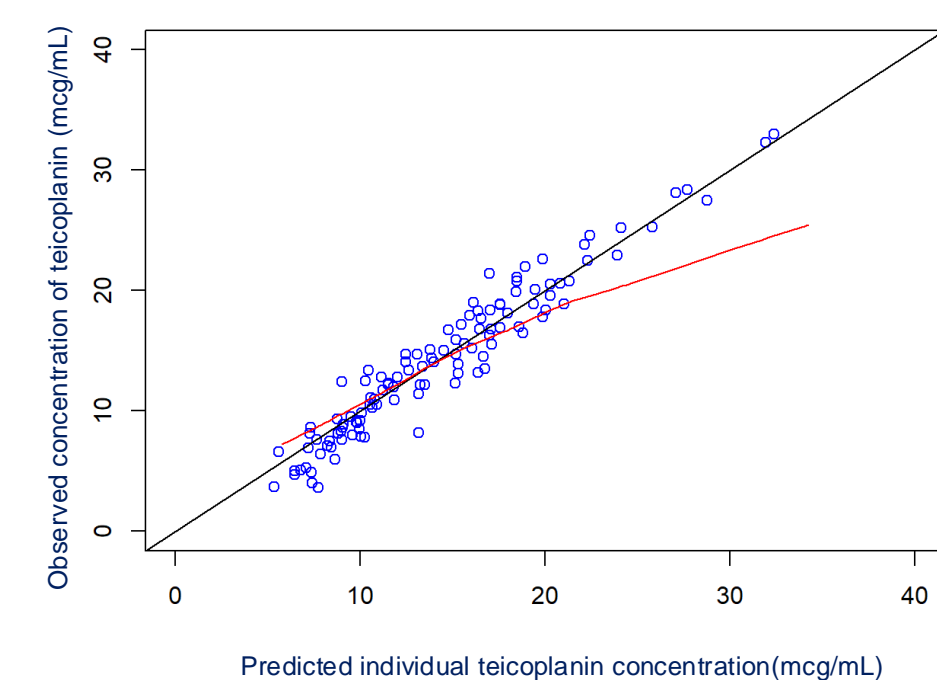
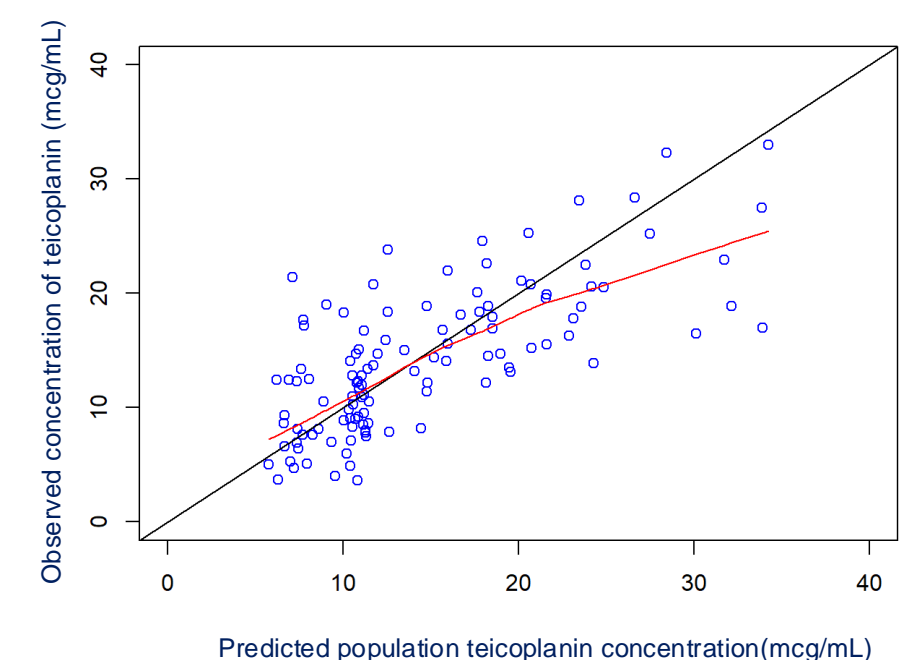
- 151 patients (65 females): 100 development group and 51 to the validation group
- Median (range) age was 62 (17-87) years, and total body weight was 68 (41.5-130) kg.

popPK

- 263 samples were analyzed, with a mean (SD) TPC of 14.27 (6.81) µg/mL.
- one-compartment model with first-order elimination.
- The volume of distribution (Vd) was estimated at 92L, and clearance (CL) was modeled by the following equation:

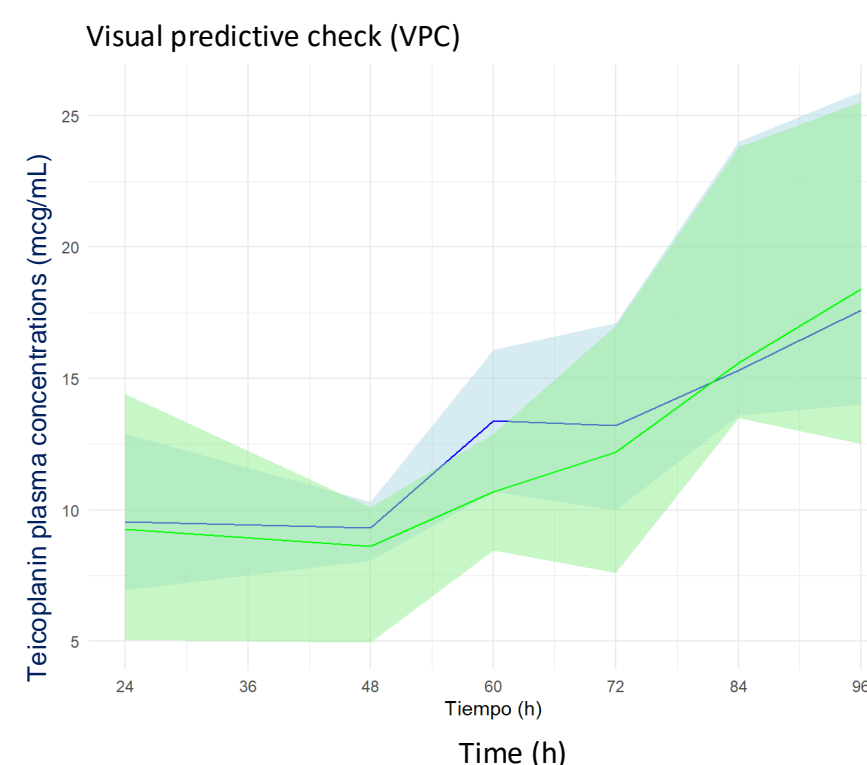
$$CL(L/h) = 1.28 * [1 - 0.01 * (AGE - 62)] * [(eGFR/92)^{0.4}] * [(Adjusted\ ideal\ weight / 61)^{3.2}]$$

Adjusted ideal weight (Kg) = ideal weight + (total weight - ideal weight) * 0.25; AGE in years; eGFR = estimated glomerular filtration rate using CKD-EPI.



Validation

Accuracy: MPE 5,2% (IC95%:-15,2-39,3%)
Precision: MAPE 13.0% (95%CI: 0.8-39.3%)
VPC graph confirmed the model's predictive ability.



Conclusion and Relevance

- A PopPK model was developed that characterizes the kinetic behavior of teicoplanin in HM patients, which included adjusted ideal weight, age and eGFR as factors influencing its clearance.
- The model predicts TPC with adequate precision and accuracy, making it a useful tool for optimizing teicoplanin dosage.

