POPULATION PHARMACOKINETIC MODEL TO OPTIMIZE VEDOLIZUMAB DOSING IN HEMATOLOGICAL PATIENTS WITH REFRACTORY GASTROINTESTINAL GRAFT-VERSUS-HOST DISEASE

M. López Álvarez[1], N. Martín Gutiérrez [1], JG. Sánchez Hernández [1], L. López Corral [2], C. Sánchez Arroyo [1], C. Aparicio Carreño [1], MJ. Otero López [1],

1. Pharmacy Department. Hospital Universitario de Salamanca 2. Hematology Department. Hospital Universitario de Salamanca

Background and importance

Vedolizumab has emerged as a therapeutic alternative for gastrointestinal graft-versus-host disease (GI-GVHD) refractory to corticosteroids and ruxolitinib. However, optimal dosing strategies in this population remain unclear.

Aim and objectives

To develop a population pharmacokinetic (popPK) model for vedolizumab in adult patients with malignant haematological neoplasms (MHN) and refractory GI-GVHD, and to propose a dosing regimen to achieve therapeutic plasma concentrations from the start of treatment.

Materials and methods

📋 Prospective and multidisciplinary study conducted between January 2021 and February 2025.

🧍 Patients with MHN receiving vedolizumab for the treatment of refractory GI-GvHD.

💊 Initial dose = vedolizumab 300 mg IV.

→ First therapeutic drug monitoring at 72 hours. Subsequent administrations and monitoring according to pharmacist recommendations.

🧪 Target vedolizumab plasma concentration (PVC) > 25 µg/mL, based on the target PVC during the induction phase of ulcerative colitis.

Analysis

- **popPK model development:**
  - ☑ Pharmacometric methodology → nonlinear mixed-effects modeling (NONMEM v7.3)
  - ☑ First-order conditional estimation method with interaction (FOCEI)
- **Statistical analysis and graphs (R v4.3.2)**
- **Deterministic simulations to evaluate drug exposure and dosing**

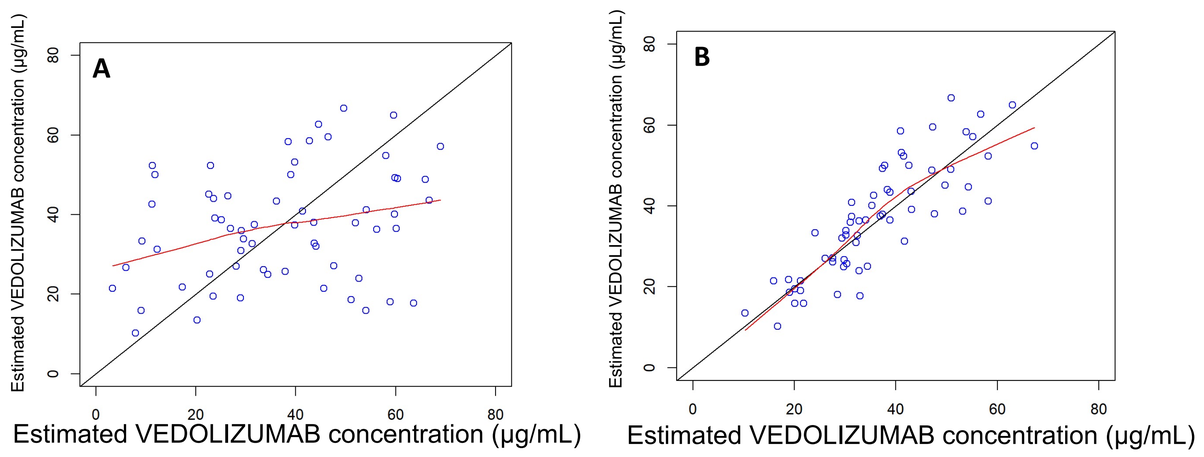
Results

- **15 patients → 60% female**
- A total of 70 samples were collected
- **Median (range) age: 54 (18–66) years**
- **Weight (range): 71 (40–100) kg**
- **Mean PVC (SD): 36.56 (14.97) µg/mL**

popPK model

Monocompartmental model → first-order elimination
Estimated volume of distribution **(Vd):** 5.53
CLEARANCE (CL) according to the following equation:

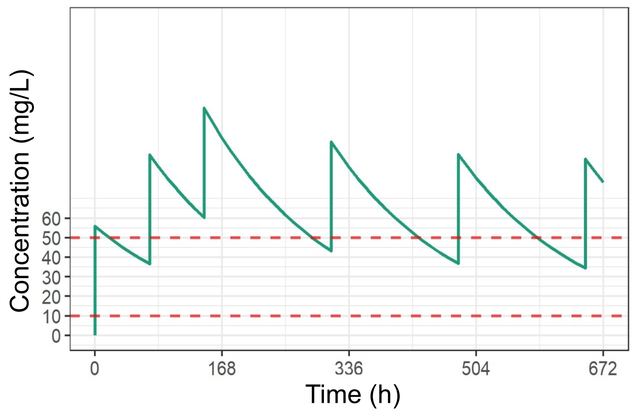
CL (L/h) = 0.053 * ((BSA / 1.9)*2.23) * (1 + 0.022 *(AGE − 54))
BSA = body surface area in m² (Dubois and Dubois formula)



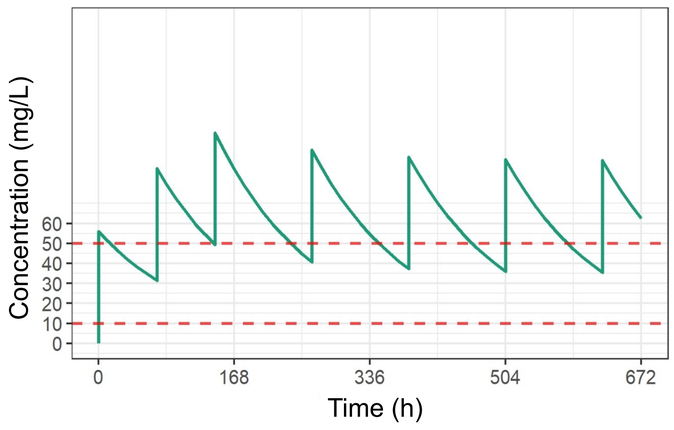
Goodness-of-fit plots comparing observed vedolizumab concentrations versus population predictions (A) and individual predictions (B)

To achieve plasma levels **> 25 µg/mL→ Loading dose** of vedolizumab **300 mg IV** on days **0, 3**, and **6 followed by 300 mg IV**:

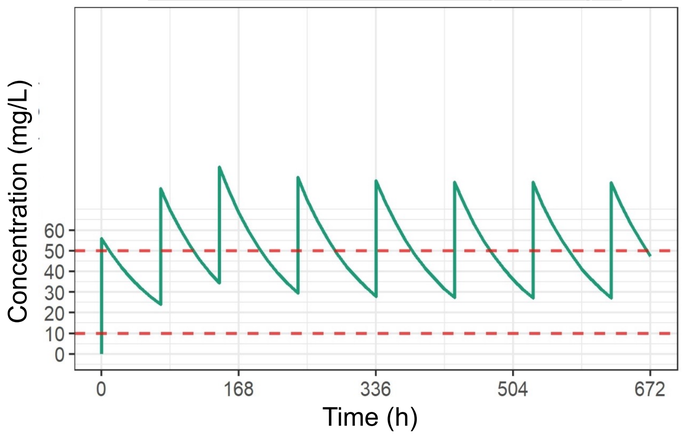
If BSA < 1.5 m² → every 7 days



If BSA > 1.5 and < 2 m² → every 5 days



If BSA > 2 m² → every 4 days



Conclusion and relevance

- ✓ A popPK model has been developed that characterizes the pharmacokinetic behavior of vedolizumab in hematological patients with GI-GvHD, including body surface area and age as factors affecting clearance.
- ✓ The application of this model allows optimization of vedolizumab dosing from the start of treatment, which could improve early drug exposure and promote a faster clinical response in these patients.