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Editorial

Optimizing Infliximab Use in Real-World Inflammatory Bowel Disease: Insights from a Population Pharmacokinetic Model Integrating Intravenous and Subcutaneous Formulations

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See "Population Pharmacokinetic Model for the Use of Intravenous or Subcutaneous Infliximab in Patients with Inflammatory Bowel Disease: Real-World Data from a Prospective Cohort Study" by Joo Hye Song, et al. on page 376, Vol. 19, No. 3, 2025

Inflammatory bowel disease (IBD) management has evolved rapidly with the advent of biologic therapies, yet tailoring treatment to individual patients remains a challenge.[1,2] Among anti-tumor necrosis factor agents, infliximab has maintained a central role for both Crohn's disease and ulcerative colitis.[3,4] However, variability in patient responses and the clinical relevance of therapeutic drug monitoring (TDM) continue to drive efforts toward more personalized treatment strategies.[5-7] In this issue of *Gut and Liver*, Song *et al.*[8] present a timely and practical contribution to this field with the development of a population pharmacokinetic (PK) model of infliximab, using real-world data that encompasses both intravenous (IV) and subcutaneous (SC) administration. This study is notable for its prospective design and robust sample size, incorporating 2,132 infliximab level measurements from 181 IBD patients. By integrating both IV and SC data in the same model—a rare approach in current PK research—the authors provide a comprehensive framework that reflects actual clinical practice, where patients often switch between formulations based on efficacy, tolerability, or convenience.

One of the major strengths of the study lies in its thoughtful covariate selection. The final model includes body mass index (BMI), albumin, C-reactive protein, and anti-drug antibody (ADA) levels as predictors of clearance, with BMI and ADA also influencing bioavailability (F) in the SC formulation. These variables are clinically relevant and easily obtainable in routine care, enhancing the model's applicability. Interestingly, BMI emerged as a stronger predictor than body weight, especially for SC infliximab, likely reflecting the role of SC tissue in drug absorption. Moreover, the study challenges the assumption that ADA status is best treated as a binary variable. Instead, Song *et al.*[8] incorporated ADA concentrations as a continuous covariate, allowing for a more nuanced reflection of immunogenicity's impact on drug exposure. This approach underscores the authors' commitment to maximizing the clinical utility of their model.

While previous studies have demonstrated higher trough levels (TL) with SC infliximab compared to IV,[9] the relationship between TL and therapeutic efficacy remains complex. Song *et al.*[8] observed significantly higher TLs with SC infliximab (median, 18.65 μg/mL) than IV (median, 4.15 μg/mL), yet the area under the curve—a more comprehensive measure of drug exposure—was similar when accounting for IV dose intensification. This finding reiterates the need for caution when interpreting TLs in isolation, particularly as clinical outcomes may not differ significantly despite PK disparities.

The authors also provide intriguing insights into ADA dynamics. Among patients who switched from IV to SC infliximab, approximately two-thirds demonstrated ADA negativity over time, including some with dramatic reductions. Although causality cannot be established, this observation supports previous hypotheses that SC dosing, with its more stable drug concentrations, may reduce immunogenicity by avoiding peak-trough fluctuations associated with IV administration.[6,10]

The practical implications of this model are compelling. By enabling the prediction of steady-state TLs under various dosing scenarios and patient characteristics, clinicians can better anticipate subtherapeutic exposure and adjust treatment proactively. Importantly, this tool bridges a critical gap in the real-world application of SC infliximab, where fixed dosing complicates individualized TDM strategies. Of course, certain limitations must be acknowledged. The model does not incorporate immunomodulator use due to its complexity and variability, though the authors note its potential impact on ADA formation and infliximab clearance. Additionally, the model was developed using data exclusively from Korean patients, which may limit its generalizability across diverse populations. Nonetheless, this study represents an important step toward precision medicine in IBD. It reflects the growing need for data-driven, patient-centered approaches in therapeutic decision-making. As SC formulations become more widely adopted and biologic options continue to expand, integrating PK modeling into clinical practice will be essential. The model proposed by Song *et al.* provides both a methodological template and a practical tool for advancing this effort.

CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

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