

Estimation of infliximab clearance in patients with acute severe ulcerative colitis prior to and after achieving clinical remission using a population pharmacokinetic modelling approach

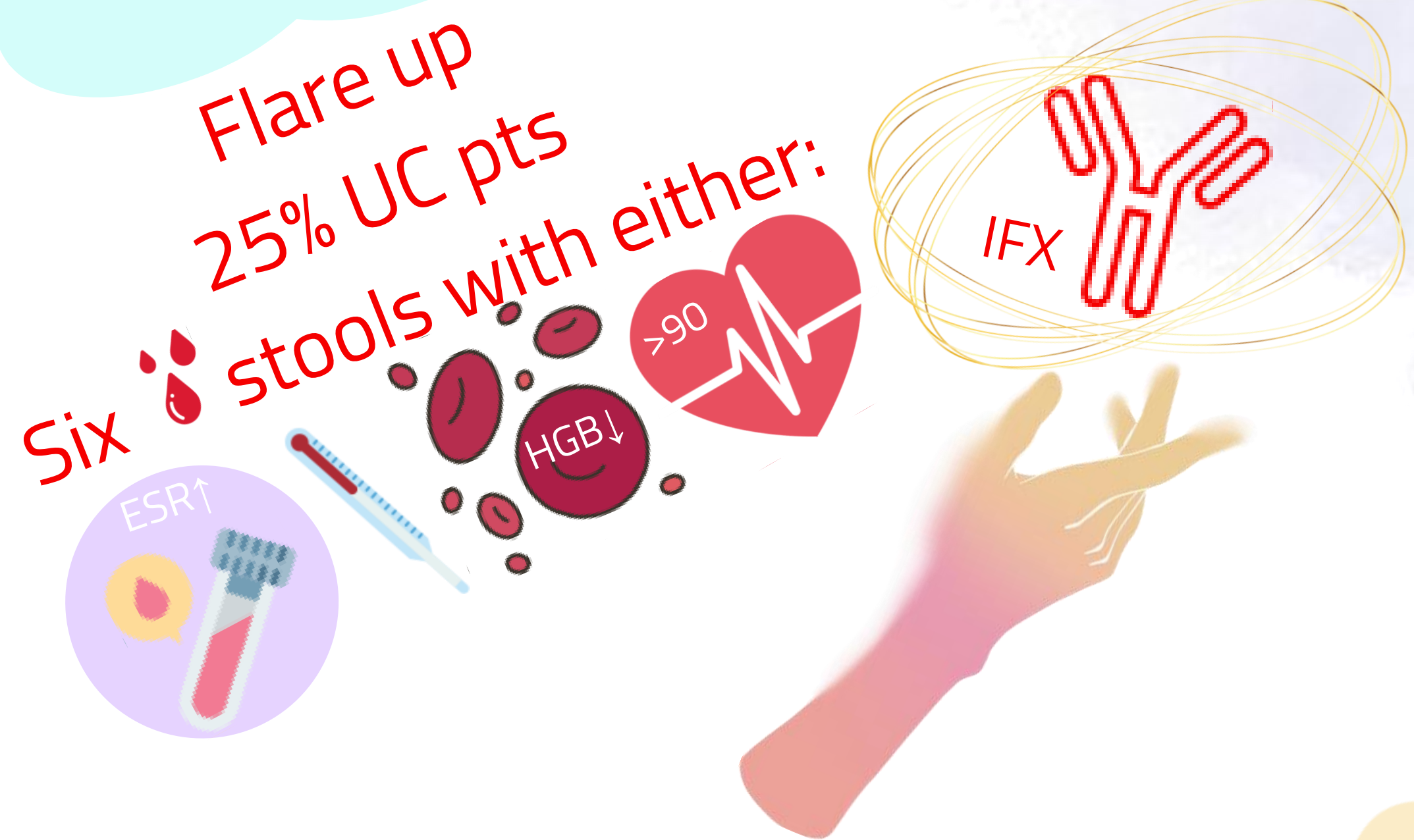
A. Homšek (1), S. Marković (2), P. Svorcan (2), M. Jovanović (1), K. Vučićević (1)

(1) Faculty of Pharmacy – University of Belgrade, Department of Pharmacokinetics and Clinical Pharmacy, Belgrade, Serbia

(2) University Hospital Medical Center "Zvezdara", Gastroenterology and Hepatology Department, Belgrade, Serbia

ana.homsek@pharmacy.bg.ac.rs

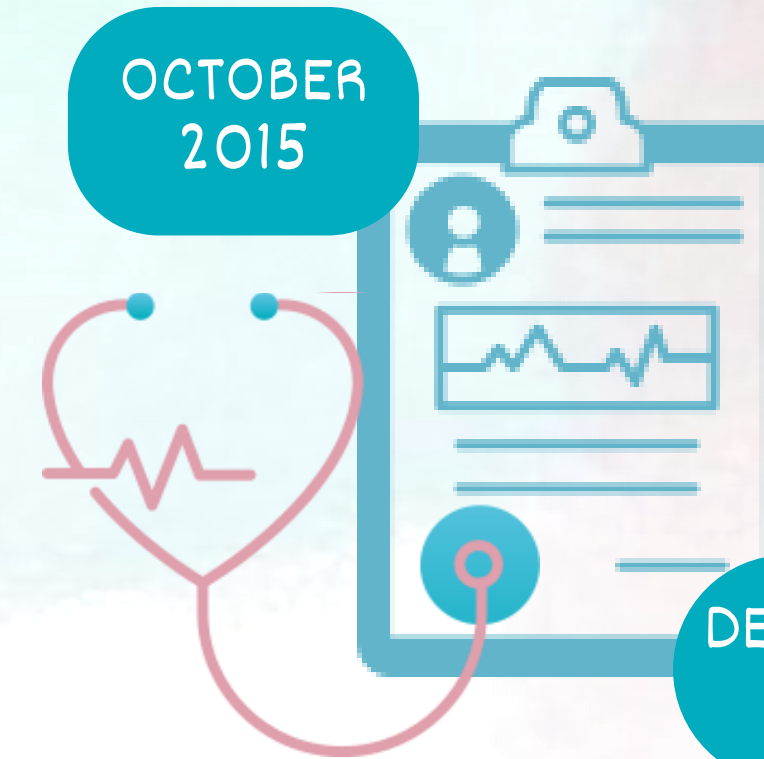
Introduction



Aim

- ◆ To obtain a PK model on ASUC patients
- ◆ To compare with available UC models

Methods



300-700 mg
Induction*: **0, 2, 6 W**

Maintenance: **Q4W, Q6W, Q8W**

*Accelerated: **every, every other W**



```
$PROBLEM PK model IFX
$INPUT C ID IDOL TIME AMT TAU SS II ADDL EVID
$DATA INPUTASUCnodat.csv IGNORE=C
$SUBROUTINE ADVAN3 TRANS3
$PK
... CLREMIS-DEFINITION START
IF(REMIS.EQ.1) CLREMIS = 1 ; Most common
IF(REMIS.EQ.0) CLREMIS = ( 1 + THETA(7))
... CLREMIS-DEFINITION END
... CL-RELATION START
CLCOV=CLREMIS
... CL-RELATION END
TVCL = THETA(1)
TVCL = CLCOV*TVCL
CL = TVCL * EXP(ETA(1))
TVVSS = THETA(2)
```

Results

46 pts: M 63%, AGE 39.5 (19-67) yo, WGT 75.5 (47-110) kg
C over the ULOQ → excluded (4.1 %)+ C below the LLOQ → the M3 method

Final dataset contained 210 C_{trough}
Clinical remission status maintained in
156 (74.28%) time points

2-COMP model

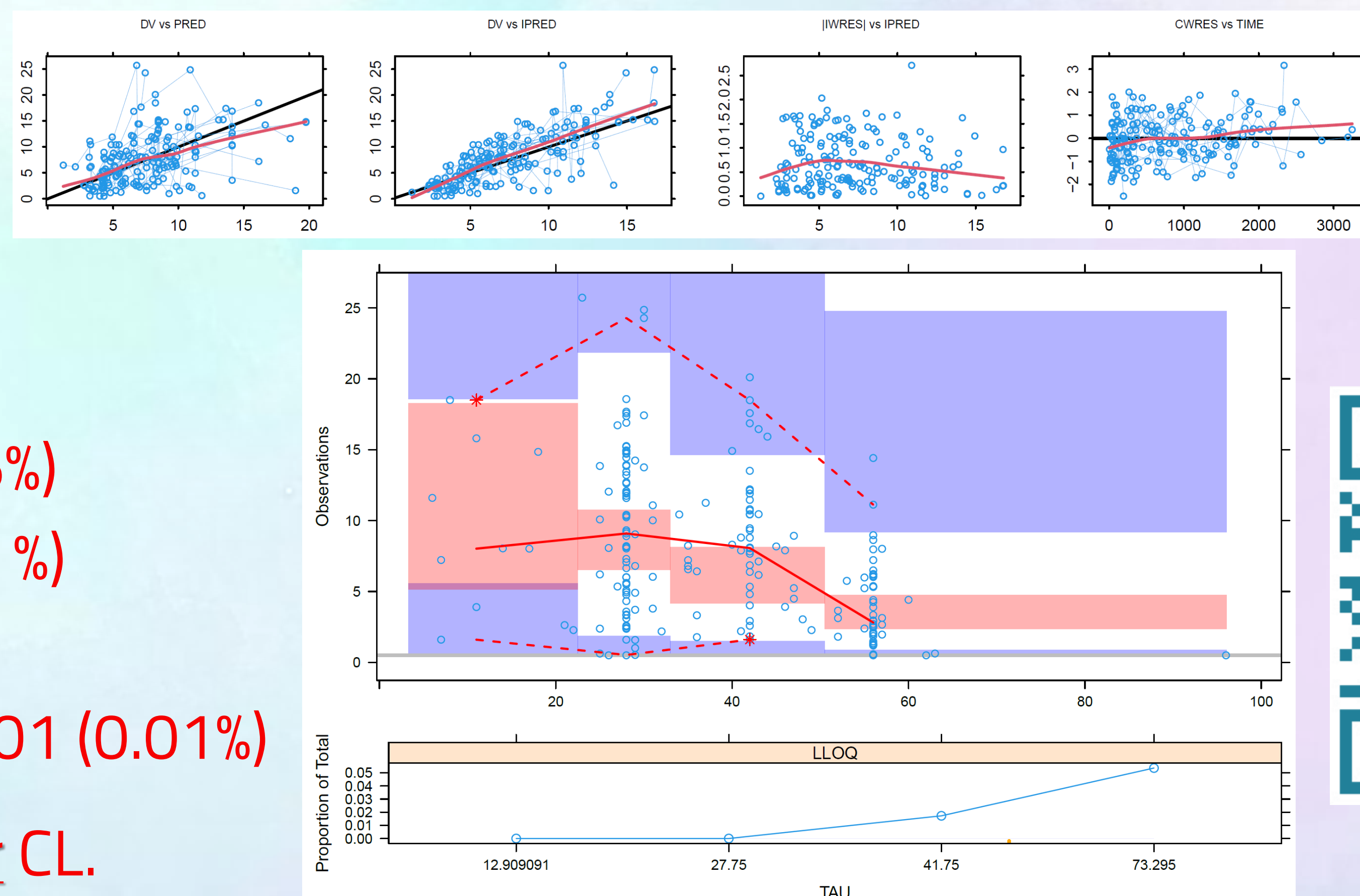
First order elimination and a proportional error model best described the data.
Clinical remission was included as a covariate ($\Delta\text{OFV} = -15.25$) in the final model.
The estimated values of parameters (with relative standard error) were:

- $\text{CL} = 0.329 \text{ L/day}$ (6.1 %)
- $V^{\text{SS}} = 6.83 \text{ L}$ (0.04 %)
- $Q = 0.148 \text{ L/day}$ (fixed)
- $V_c = 1.02 \text{ L}$ (fixed)
- $\text{CL-Relapse} = 0.245$ (3.6%)
- $\text{IIV on CL} = 0.0651$ (12.3 %)
- $\text{IIV on } V^{\text{SS}} = 0.2$ (0.03 %)
- Proportional error = 0.501 (0.01%)

Available models had higher CL.

Slightly lower CL in remission (mean CL = 0.336 L/day).

Increase in CL in relapse (mean CL= 0.446 L/day).



Conclusion

Patients with ASUC have higher IFX clearance during disease relapse. Each patient would benefit from calculating an individual dose to maintain the steady state concentrations.



Acknowledgement

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