

The Combination of Predictive Factors of Pharmacokinetic Origin Associates with Enhanced Disease Control During Treatment of Pediatric Crohn's Disease with Infliximab

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Table S1. Predictive Factors of PK origin and time to CRP based clinical remission in pediatric CD.

	Time (days)	HR	p value
Infusion 2			
Clearance above 0.294 L/day	110±27	ref.	
Clearance below 0.294 L/day	71±14	1.3 (0.9 to 2.0)	0.188
IFX below 20µg/mL	95±18	ref.	
IFX above 20µg/mL	69±13	1.4 (0.9-2.1)	0.140
Infusion 3			
Clearance above 0.294 L/day	138±28	ref.	
Clearance below 0.294 L/day	76±13	1.5 (1.0 to 2.3)	0.047
IFX below 15µg/mL	139±20	ref.	
IFX above 15µg/mL	46±12	2.3 (1.5-3.6)	<0.001
Infusion 4			
Clearance above 0.294 L/day	188±35	ref.	
Clearance below 0.294 L/day	68±11	2.1 (1.3 to 3.2)	0.001
IFX below 10µg/mL	142±21		
IFX above 10µg/mL	53±12	2.2 (1.4-3.3)	<0.001

Table S2. PF of PK origin either alone or combined at the end of induction and during maintenance and disease control over maintenance period.

	parameter*	estimates
Time and IFX >5µg/mL	θ_{pop}	-0.38±0.53 (p=0.473)
	θ_{time}	0.004±0.002 (p=0.046)
	$\theta_{concentration}$	1.53±0.43 (p<0.001)
	-2LL	361.6
Time and Clearance <0.294 L/day	θ_{pop}	1.53±0.58 (p=0.008)
	θ_{time}	0.004±0.002 (p=0.046)
	θ_{Cl}	2.57±0.50 (p<0.001)
	-2LL	353.7 (Δ =-7.9; p=0.005)
Time and PF of PK origin (IFX >5µg/mL with Clear- ance <0.294 L/day)	θ_{pop}	1.06 ±0.48 (p<0.001)
	θ_{pop}	0.004±0.001 (p<0.001)
	$\theta_{both\ PF\ of\ PK}$	2.97±0.81 (p<0.001)
	-2LL	396 (Δ =-12.6; ; p<0.001)
Time and both PF of PK origin at infusion 4 (IFX >10µg/mL with Clearance <0.294 L/day) and during maintenance	θ_{pop}	0.35±0.50 (p=0.012)
	$\theta_{both\ PF\ of\ PK\ 4th\ inf}$	2.44±0.64 (p<0.001)
	θ_{time}	0.002±0.001 (p=0.046)
	$\theta_{both\ PF\ of\ PK}$	2.51±0.73 (p<0.001)
	-2LL	377.8 (Δ =-23.2; p<0.001)

*Model: $\text{logit}(\text{Probability of CRP based remission}) = \theta_{pop} + \theta_{cov1} * \text{cov1} + \dots$

Panel A: infusion 2; panel B: infusion 3; panel C: infusion 4; panel D: maintenance.

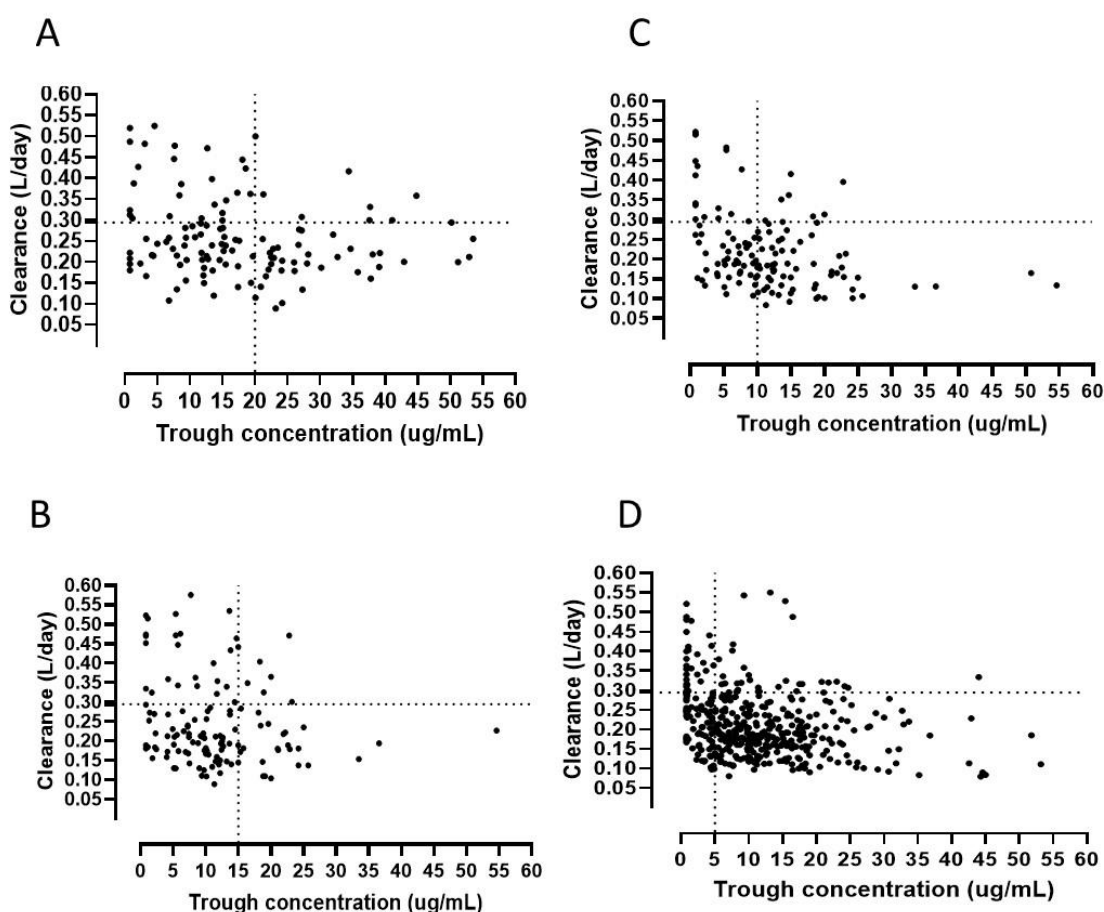


Figure S1. IFX concentration and Clearance at each of the Induction time point and maintenance.

Panel A: Clearance below or above 0.294 L/day, infusion 2; Panel B: Clearance below or above 0.294 L/day, infusion 3; Panel C: Clearance below or above 0.294 L/day, infusion 4; Panel D: IFX concentrations above or below 20 µg/mL, infusion 2; Panel E: IFX concentrations above or below 15 µg/mL, infusion 3; Panel F: IFX concentrations above or below 10 µg/mL, infusion 4; Estimates are provided in **Table S1**.

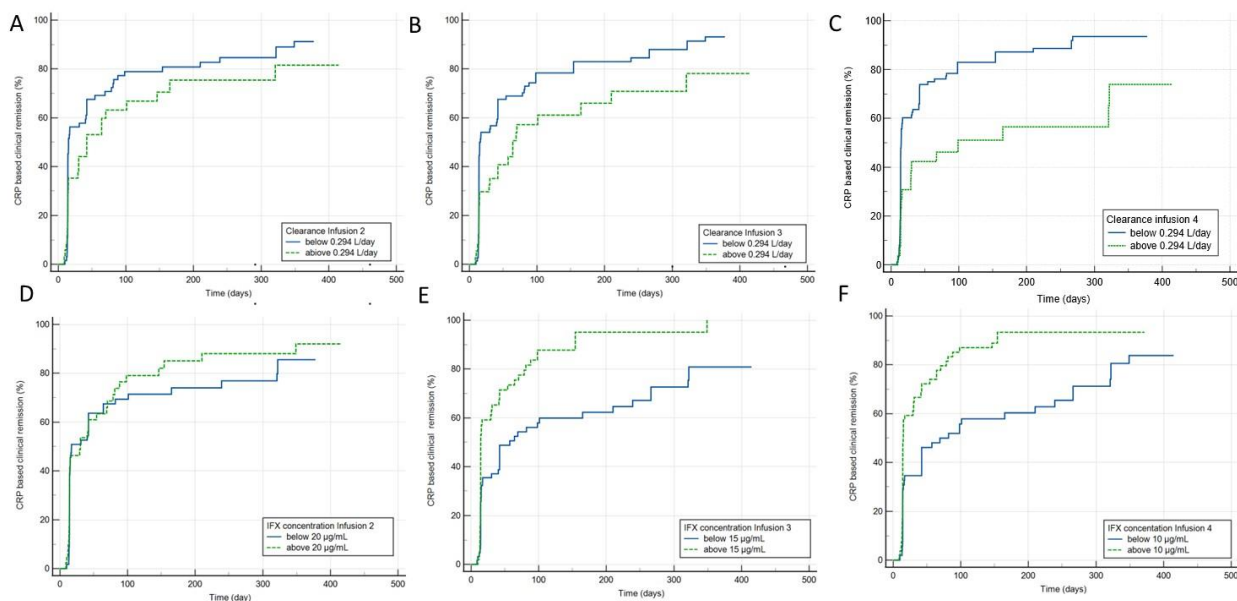


Figure 2. Predictive factors of Pharmacokinetic origin in association with CRP-based clinical remission status.