Supplematary information

Table S1. Selected Population pharmacokinetic models for infliximab in ulcerative colitis/inflammatory bowel diseases patients.

Model	**Structural PK model**				**Covariate model**	**IIV/IOV model**	**Residual error model**	**Specified implementation**			
	Parameter estimates (RSE)				*Parameter estimate (RSE)*	*CV (RSE)*	*Type: parameter estimate (RSE)*	*Full model code*	*ODEs/ model schematic*	*Covariate relationships*	*Random effects*
Ternant-model (2008)	**2-CMT model, first order elimination**							NO	NO	YES	YES
Article	*CL (L/h)*	*V1 (L)*	*V2 (L)*	*Q (L/h)*							
Ternant (2008)[1]	ADA-: 0.012 (7.9%) ADA+: 0.032 (10.9%)	Smen: 2.3 (18.1%) women: 1.1 (31.4%) WT: 1.7 (19.6%)	1.0 (22.6%)	0.0054 (34.5)	NA, see structural model	*CL ADA-*: 22.5% *CL ADA+*: 22.7% $V1_{men}$: 14.1% $V1_{women}$: 11.3% *V1 WT:* 1.719.3% *V2*: 15% *Q*: 10%	Additiative: 1.04 mg/L (12.0%)				
Fasanmade-model (2009)	**2-CMT model, first order elimination**							NO	NO	YES	YES
Article	*CL (L/day)*	*V1 (L)*	*V2 (L)*	*Q (L/day)*							
Fasanmade (2009)[2]	0.407 L/day (2.5%)	3.29 L (2.1%)	4.13 L (3.9%)	7.14 L/day (6.8%)	ALB~CL: -1.54 (2.5%)	CV (RSE) *CL*: 37.68% (8.5%)	Proportional error: 40.30% (2.6%) Additive error: 0.0413 µg/L (3.5%)				

					ADA~CL: 0.471 (22.5%) SEX_{Female}~CL: -0.236 (11.9%) WT~V1: 0.538 (13.5%) SEX_{Female}~V1: -0.137 (23.2%)	*V1*: 22.11 (16.6%)				
Vande Casteele (2019)[3]	*Fasanmade (2009)*				*Fasanmade (2009)*	*Fasanmade (2009)*	*Fasanmade (2009)*	*NO*	*NO*	
Kimura (2019)[4]	*Fasanmade (2009, 2011)*				*Fasanmade (2009, 2011)*	*Fasanmade (2009, 2011)*	*Fasanmade (2009, 2011)*	*NO*	*YES*	
Kimura (2020)[5]	CD: 0.353 (0.212–0.442) UC: 0.450 (0.223–0.811)	CD: 2.97 (1.96–5.00) UC: 2.25 (1.60–3.22)	CD: 0.137 (0.0944–0.273) UC: 3.71 (3.29–4.06)	CD: 1.22 (1.10–1.51) UC 7.10 (6.96–7.32)	*NA*	*NA*	*NA*	*NO*	*NO*	
Fasanmade-model (2011, CD)	**2-CMT model, first order elimination**							NO	NO	YES	YES
Article	*CL (mL/kg/day)*	*V1 (mL/kg)*	*V2 (mL/kg)*	*Q (mL/kg/day)*						
Fasanmade (2011)[6]	5.42 (2.0)	52.4 (0.9)	19.6 (4.2)	2.26 (9.9)	ALB~CL: –0.855 (13.5%) ADA~CL: 0.291 (15.2%) IMM~CL: –0.137 (20.5%) WT~CL: –0.313 (14.6%) WT~V1: –0.233 (12.3%)	CL: 30.7% (8.1%) V1: 12.6% (19.2%) V2: 55.3% (18.5%)	Proportional error: 29.2% (2.7) Additive error: 0.371 µg/mL (18.3%)			

					WT~V2: –0.588 (16.1%)					
Santacana (2018)[7]	*Fasanmade (2011)*				*Fasanmade (2011)*	*Fasanmade (2011)*	*Fasanmade (2011)*	*NO*	*NO*	
Kimura (2019)	*see above under Fasanmade (2009)*									
Kimura (2020)	*see above under Fasanmade (2009)*									
Candel (2020)[8]	*kel (1/h)*	*V1 (L)*	*V2 (L)*	*Q (L/h)*				NO	NO	
	0.0038 (SD: 0.0011)	3.57 L (SD: 0.041)	1.43 L (SD: 0.39)	0.014 L/h (SD: 0.004)	*Fasanmade (2011)*	*Fasanmade (2011)*	*Fasanmade (2011)*			
Santacana (2020)[9]	*Fasanmade (2011)*				*Fasanmade (2011)*	*Fasanmade (2011)*	*Fasanmade (2011)*	*NO*	*NO*	
Bauman (2020)[10]	*Fasanmade (2011)*				$CL_{ind} = CL_{pop} \times (WT/65)^{0.7} \times (ALB/3.5)^{-1.1} \times (ESR/9)^{0.11} \times 1.18^{ADAlevel}$	NS	NA	NO	NO	
Xu-model (2012)	**2-CMT model, first order elimination**							NO	NO	YES	YES
Article	*CL (L/h)*	*V1 (L)*	*V2 (L)*	*Q (mL/kg/day)*						
Xu (2012)[11]	0.296 (1.5%)	3.3 (1.1%)	1.16 (4.9%)	0.0781 (11.4%)	WT~CL : 0.612 (4.7%) ALB~CL: -2.3 (9.3%) ADA~CL: 0.231 (24.7%) WT~V1: 0.696 (2.9%) WT~V2: 0.604 (19.5%) WT~Q: 1.15 (21.2%)	CL: 31.3% (6.9%) V1: 9.85% (33.9%) V2: 76.1% (12.3%) Q: 111% (14.4%)	Proportional: 41.9% (1.0%)			

Dubinsky (2017)[11]	Xu (2012)				Xu (2012)	Xu (2012)	Xu (2012)	NO	NO
Wojciechowski (2017) [12]	Xu (2012)				Xu (2012)	Xu (2012)	Xu (2012)	NO	
Eser (2018)[13]								NO	NO
Model 1	0.246 (10.1%)	4 (20.1%)	2.34 (28.8%)	0.07 (20.5%)	WT~CL: 1.59 (20.1%) ALB~CL: -1.45 (27.7%) ADA~CL: 0.44 (23%) WT~V1: 2.16 (28.6%) WT~V2: NE WT~Q: NE	CL: 33.02% (33.1%) V1: 40.12% (58.7%) V2: 122.07% (40.3%) Q: NE	Proportional: 53.10% (5.1%)		
Model 2	0.28 (NE)	3.16 (NE)	0.477 (NE)	0.04 (NE)	WT~CL: 1.56 (NE) ALB~CL: -0.763 (NE) ADA~CL: 0.76 (NE) WT~V1: 2.25 (NE) WT~V2: NE WT~Q: NE	CL: 24.04% (NE) V1: 56.66% (NE) V2: 81.30% (NE) Q: NE	Proportional: 54.40% (NE)		
Model 3	0.243 (7.7%)	4.04 (13.2%)	3.02 (52.3%)	0.03 (24.4%)	WT~CL: 0.921 (29%) ALB~CL: -1.24 (28.1%) ADA~CL: 1.11 (13.5%) WT~V1: 1.12(41.3%) WT~V2: NE WT~Q: NE	CL:25.10% (47.5%) V1: 49.80% (32.6%) V2: 92.47% (68.1%) Q: NE	Proportional: 56.70% (4.7%)		

Dubinsky (2022)[14]	Xu (2012)				Xu (2012)	Xu (2012)	Xu (2012)	NO	NO		
Dotan-model (2014)	**2-CMT model, first order elimination**							NO	NO	YES	YES
Article	*CL (L/day)*	*V1 (L)*	*V2 (L)*	*Q (L/day)*							
Dotan (2014)[15]	0.381 (0.5%)	2.37 (0.2%)	1.37 (0.4%)	0.122 (0.4%)	WT~CL: 0.612 (2.1%) ALB~CL: -1.39 (1.5%) ADA~CL: 1.59 (13%) WT~V1: 0.696 (1.9%) WT~Q: 1.15 (3.6%) WT~V2: 0.604 (10.2%)	CL: 13.45 (4%) V1: 42.07 (1.5%) V2: 32.40 (1.7%) Q: 85.15 (1.2%)	NR				
Buurman-model (2015)	**2-CMT model, first order elimination**							NO	NO	YES	NO
Article	*CL (L/day)*	*V1 (L)*	*V2 (L)*	*Q (L/day)*							
Buurman (2015)[16]	0.199 (6%)	4.94 (10%)	3.13 (32%)	0.0618 (23%)	Period~CL: +40% (11%) ADA~CL: +72% (35%) SEX_{male}~CL: +35% (34%) HBI~V1: -3.6% (28%)	CL: 18% (18%) V1: 17.1% (31%)	Proportional: 21.7% (30%) Additional: 0.98 mg/L (18%)				
Passot-model (2016)	**1-CMT model, first order elimination**							NO	NO	YES	YES
Article	*CL (L/day)*	*V1 (L)*									
Passot (2016)[17]	0.23 (4%)	5.2 (4%)			SEX_{Male}~V: 0.209 (45%) $Age_{<=15}$~V: -0-396 (37%	V: 0.224 (12%) CL: 0.304 (7%)	Proportional: 0.223 (7%) Additional: 0.72 mg/L (19%)				

					CD~V: 0.399 (17%) WT~CL: 0.603 (18%) SEX_{Male}~CL: 0.181 (30%) CD on CL: 0.384 (15%) UC~CL: 0.472 (21%) RA~CL: 0.392 (32%) MTX~CL: -0.336 (52%)					
Brandse-model (2017)	**2-CMT model, first order elimination**							NO	N	NO	NO
Article	*CL (L/day)*	*V1 (L)*	*V2 (L)*	*Q (L/day)*							
Brandse (2017)[18]	0.358	4.72	2.4	0.0697	WT~CL: 0.523 ALB~CL: -1.38 Previous exposure ~CL: 0.0521 ADA~CL: 0.601 WT~V_c: 0.473 WT~Q: 0.523 WT~V_P: 0.473	CL: 38.1% V1: 68.6% V2: 71.7% Q: 58.1%	NR			
Kevans-model (2018)	**2-CMT model, time varying CL**							NO	NO	NO	NO
Article	*CL (L/day)*	*V1 (L)*	*V2 (L)*	*Q (L/day)*							
Kevans (2018)[19]	0.368 (0.5%)	3.3 (0.2%)	3.42 (0.5%)	0.308 (0.1%)	rate constant of CL increase with ADA: 0.138 (25.5%)	CL: 50.10% (1.2%)	Proportional error: 28.5% (0.3%)				

	Time dependent CL: 0.105 (0.4%)					WT~CL: 0.709 (0%) ALB~CL: -0.445 (2.6%) ADA~CL: -0.0373 (4.9%) WT~V1: 0.64 (0%) WT~V2: 0.991 (0%) WT~Q: 1.52 (0%)	V1: 35.92% (0.8%) V2: 75.70% (0.8%) Q: 55.14% (0.4%)				
Petitcollin-model (2019)	**1-CMT model, time varying CL**			**logit-risk model of immunization**					NO	NO	YES	YES
Article	*CL_base (L/day)*	Slope (L/day/year)	*V1 (L)*	CLvar 1 FIX		UC~CL: 0.377 (29%)	V: 25.4% (15%)	Proportional: 20.6% (6%)				
Petitcollin (2019)[20]	0.273 (7%)	0.0348 (9%)	11.5 (5%)	intercept: 10.9 (5%) Beta: 0.0526 (21%)		Dose~CL: −0.267 (22%) CRP~CL: 0.0654 (15%) Mayo score~CL: 0.0934 (30%) AZA~CL: 0.849 (2%) WT~Slope: 31.1 (31%)	CL_{base}: 44.3% (10%) β_{dose}: 33.3% (19%) slope: 32% (26%) beta: 102% (17%) CL_{var}: 44.4% (11%)	Additional: 0.446 ug/mL (22%)				
Berends-model (2019)	**2-CMT model, first order elimination**				**TMDD model**				YES	YES	YES	YES
Article	*CL (L/day)*	*V1 (L)*	*V2 (L)*	*Q (L/day)*								
Berends (2019)[21]	0.404 (9.9%)	3.18 (9.1%)	1.64 (6.3%)	0.344 (20%)	Bmax : 0.38 pM (20%) Bmax : 19.8 pg/mL (-) Kss : 14 nM (24%)	ADA~CL: 2.15 (12%) ALB~CL: -1.13 (36%)	CL: 29.2% (19%) V1: 22.7% (16%) V2: 74.2% (19%)	Proportional IFX: 0.210 (13%) Proportional TNF: 0.406 (9%)				

				Ke : 0.984 1/d (19%) Kdeg : 5.12 1/d (-)		CL-V1: 12.3% (106%) Bmax: 39.4% (16%)					
Dreesen-model (2019)	**1-CMT model, first order elimination**							YES	YES	YES	YES
Article	*ke (1/day)*	*V (L)*									
Dreesen (2019)[22]	MAYO 1: 0.0521 (11%) MAYO 2: 0.0543 (3.6%) MAYO 3: 0.0667 (8.1%)	6.34 (3.2%)			CRP~Ke: 0.0859 (25%) ALB~Ke: -0.808 (39%) FFM~V: 0.544 (29%) Corticosteroid ~V: 1.33 (6.9%) Pancolitis ~V: 1.23 (0.019%)	Ke: 29.8% (7.8%) V: 26.5% (20%) IOV Ke: 18.7% (17%)	Proportional: 19.2 % (9.4%) Additional: 0.300 ug/mL (FIX)				
Faelens (2021)[23]	MAYO 1: 0.0422 (14%) MAYO 2: 0.0463 (3.8%) MAYO 3: 0.0570 (5.0%)	6.97 (5.0%)			CRP~Ke: Not included ALB~Ke: Not included FFM~V: 0.517 (39%) Corticosteroid ~V: 1.30 (7.7%) Pancolitis ~V: 1.25 (6.9%)	Ke: 33.4% (5.78%) V: 23.6% (41%) IOV Ke: 6.7% (100%)	Proportional: 32.9 % (5.8%) Additional: 0.300 ug/mL (FIX)	YES	NO		
Hanzel-model (2021)	**2-CMT model, first order elimination, subcutaneous admin.**							NO	YES	YES	YES
Article	*CL (L/day)*	*V1 (L)*	*V2 (L)*	*Q (L/day)*	*ka (1/day)*	*F (%)*					

Hanzel (2021)[24]	0.355 (2%)	3.10 (3%)	1.93 (2%)	0.598 (4%)	0.273 (8%)	79.1 (3%)	ALB~CL: -0.826 (11%) BW~CL: 0.666 (15%) ADA~CL: 1,39 (3%) BW~V1: 0.385 (34%) BW~V2: 1.08 (9%) BW~Q: 1.26 (15%)	CL: 27.7% (14%) V1: 21.4% (21%) ka 48.5% (45%) F1: 16.4% (15%) CL-V1:0.028% (31.4%) CL-ka: -0.046% (53.2%) CL-F1: -0.013% (42.2%) V1-ka: -0.069% (47%) V1-F1: 0.00008% (744%) ka-F1: 0.003% (413%) IOV CL: 17.5% (6%)	Proportional: 0.102 (2%) Additional: 1.66 (3%) ug/mL				
Grisic-model (2021)	**2-CMT model, first order elimination**									NO	YES	YES	YES
	CL (L/h)	*V1 (L)*	*V2 (L)*	*Q (L/h)*									
Grisic (2021)[25]	0.0109 (3%)	3.67 (-)	0.956 (11%)	0.0067 (-)			ALB~CL: -1.17 (21%) ADA~CL: 0.972 (4%) IMM~CL: 0.847 (5%) WT~CL:0.356 (41%)	CL: 34.9% (8%) V1: 12.8% (-) V2: 55.3% (-)	Proportional error: 24% (14%) Additive error (SD): 0.478 (21%) µg/mL				

ADA: Anti-drug antibodies; ADA_{cat}: Categorical ADA; Add: additional residual variability; ALB: Albumin concentrations; AZA: Azathioprine; B_{maxTNF}: Baseline TNF concen-tration; BW: Body weight; CD: Crohn's disease; CL: Clearance; CL_{base}: Baseline clearance; CL_{time}: Time dependant CL; CMT: Compartment; CORT: Corticosteroids; CRP: C-Reactive protein; F: Bioavailability; FFM: Free fat mass; HBI: Harvey-Bradshaw index; IFX: Infliximab; IIV: Interindividual variability; IMM: Immunomodulators; IOV: Interoccasion variability; ka: Absorption rate constant; $K_{ss,TNF-IFX}$: Steady-state equilibrium constant; $k_{deg,TNF}$: Degradation constant TNF receptor; ke: elimination rate con-stant; ke(p),TNF-IFX: Internalisation rate complex; MTX: Methotrexate; NR: Not reported; ODE: Ordinary differential equation; Prop: Proportional residual variability; Q: Inter-compartmental clearance; V1: Central volume of distribution; V2: Peripheral volume of distribution; RA: Rheumatoid arthritis; s.c.: subcutaneous; SD: Standard deviation; TMDD: Target mediated drug disposition; TNF: Tumour necrosis factor; UC: Ulcerative colitis; WT: Weight; y.o.: Years old.

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