Investigation of Monoclonal Antibody Pharmacokinetics in Pediatric Population and Characterization Using a Platform PBPK Model

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Supplementary Information

Table S1. List of mAbs with PK data reported in the literature. The table provides the antibody name and details on the administered dose, age of pediatric patients studied and corresponding references. Sources of adult PK data used for comparison is also provided.

ID	Name	Doses	Age	Adult and pediatric data source
1.	Atezolizumab	15mg/kg	2y-16y	(1)
2.	Avelumab	10, 20mg/kg	3y, 8-15y	(2, 3)
3.	Basiliximab	10 mg	5-6y	(4, 5)
4.	Belimumab	10mg/kg	13-14y	(6, 7)
5.	Bevacizumab	5, 15 mg/kg	13y	(8, 9)
6.	Canakinumab	0.5, 1, 1.5, 3, 4.5, 9mg/kg	9.5y	(10, 11)
7.	Dupilumab	3, 6mg/kg	1.3y, 3-5y	(12, 13)
8.	Eculizumab	600mg	2-5y	(14-16)
9.	Emicizumab	3mg/kg + 1.5/3/6mg/kg	7.5y	(17, 18)
10.	Evinacumab	15mg/kg	8.8y	(19, 20)
11.	Infliximab	1, 5, 10mg/kg	14-15y, 0-6y	(21-23)
12.	Mepolizumab	40mg, 100mg	6-11y	(24, 25)
13.	Naxitamab	3 mg/kg	5y, 8y, 10y, 17y	(26)
14.	Nirsevimab	10,25, 50, 100, 300mg	0.1-0.6y	(27-30)
15.	Pagibaximab	3, 10, 30, 60, 90mg/kg	3 to 7 days	(31, 32)
16.	Palivizumab	3, 10, 15mg/kg	0.6y	(33, 34)
17.	Rituximab	375mg/m^2	8y	(35-39)
18.	SB 209763	0.25, 1.25, 5, 10mg/kg	0.02-2.75y	(40, 41)
19.	Tocilizumab	8, 10mg/kg	6-8y, 13y	(42, 43)
20.	Urtoxazumab	0.1, 0.3, 1, 3mg/kg	0.4-5y	(44)
21.	Ustekinumab	3, 9mg/kg	10-14y	(45)

Figure S1. A priori pediatric PBPK model predicted and observed plasma PK profiles of (A-C) atezolizumab (46, 47) (D-E) belimumab (48) and (F-G) infliximab (49) in A) 12 to 18y patients B) 2 to 12y patients C) 0 to 2y patients D) 5 to 11y patients E) 12 to 17y patients F-G) 4 to 18y patients.

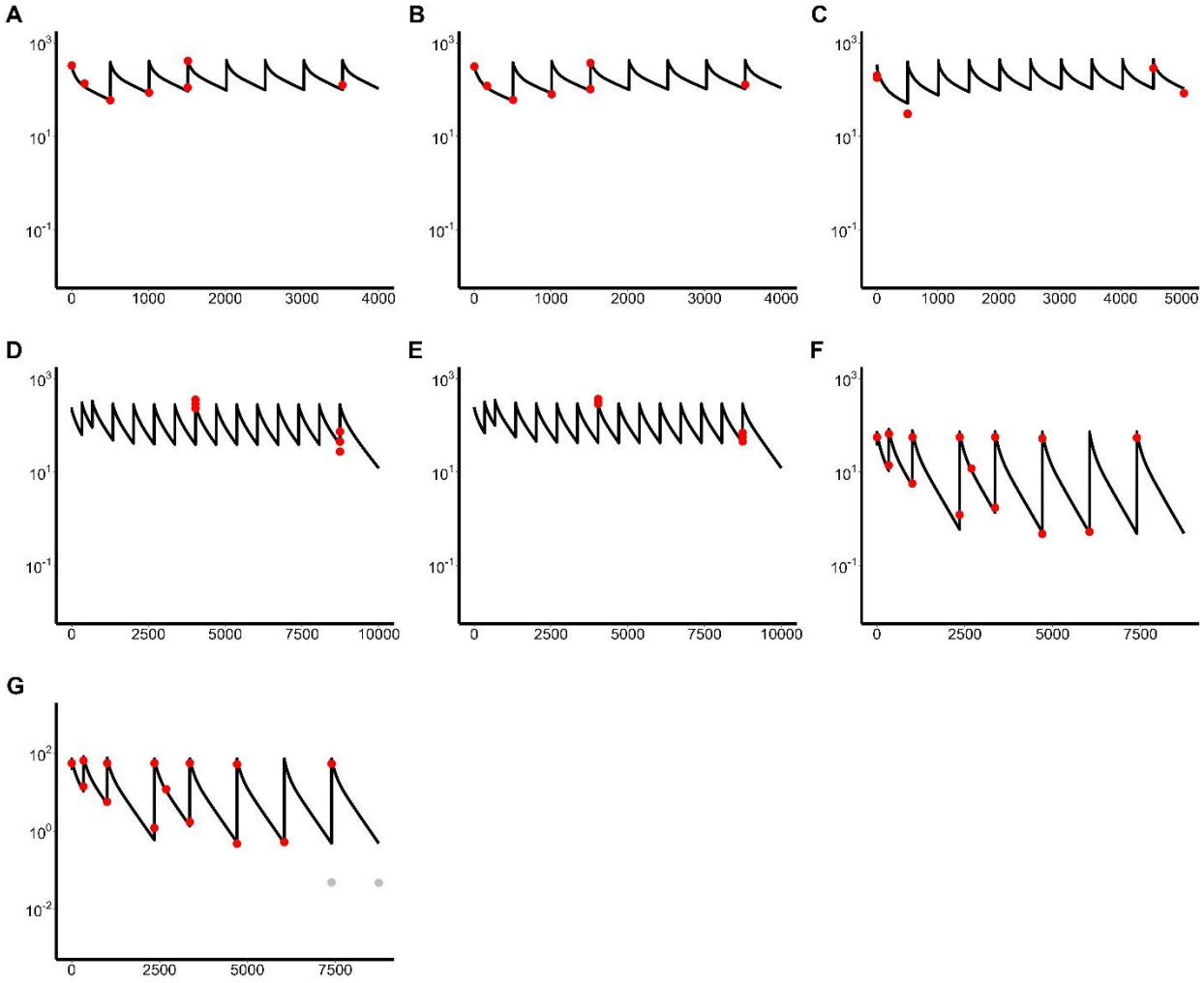
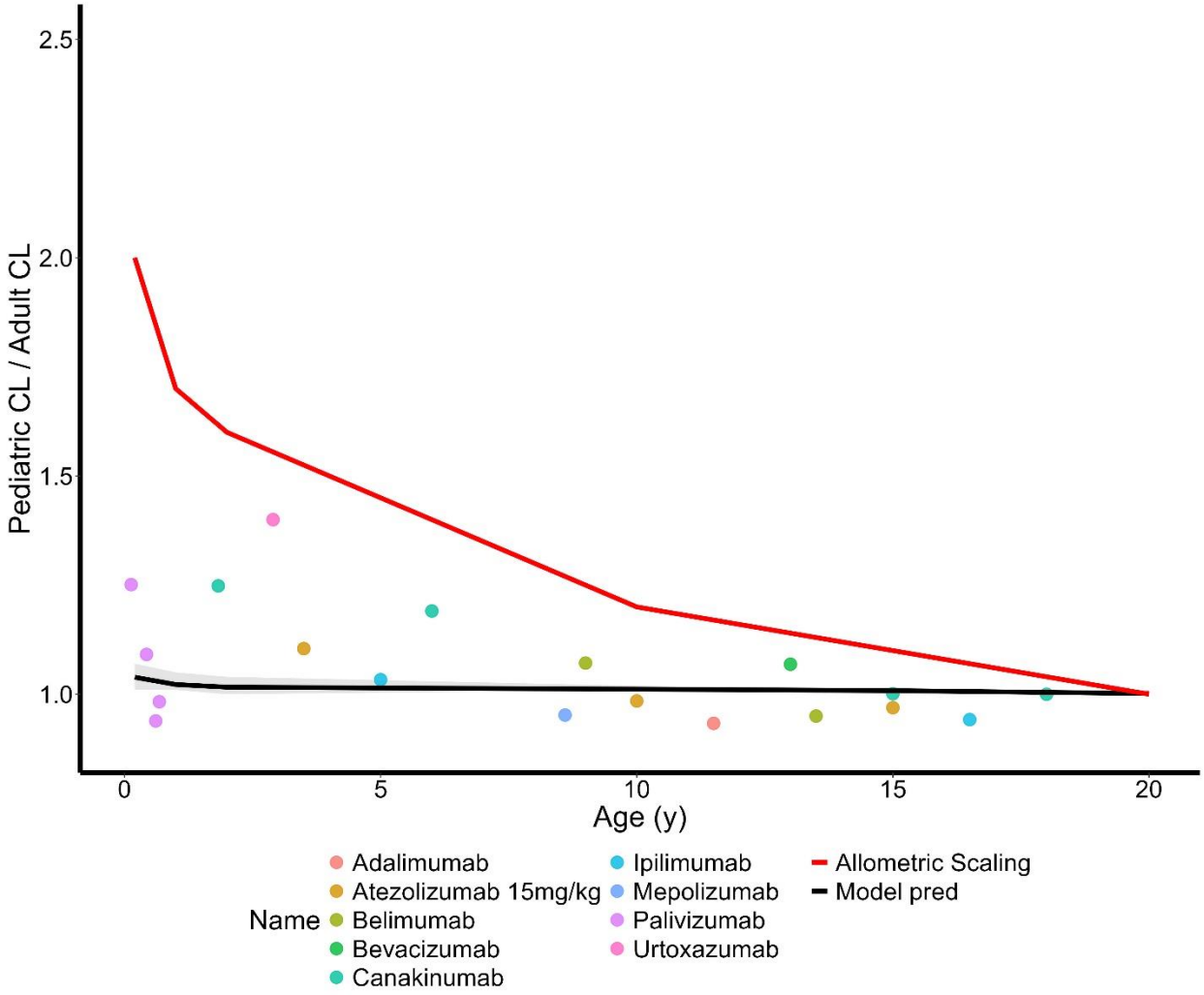


Figure S2. Impact of incorporated age-dependent physiological parameters on antibody CL. Ratio of pediatric and adult bodyweight normalized systemic CL values vs age calculated from model simulations (black line), observed values (colored points) and allometric scaling (red line). The ratio calculated by allometric scaling overpredicts increase in CL of mAbs in pediatric patients indicating limitations of empirical techniques. Ratios simulated by developed PBPK model indicate marginal increase in CL in very young patients by incorporated age-dependent physiology. Results indicate the presence of other age-dependent processes which contribute to increased CL in certain antibodies like urtoxazumab and canakinumab.


2.5
2.0
1.5
1.0
Pediatric CL / Adult CL
0
5
10
15
20
Age (y)
Name
Adalimumab
Atezolizumab 15mg/kg
Belimumab
Bevacizumab
Canakinumab
Ipilimumab
Mepolizumab
Palivizumab
Urtoxazumab
Allometric Scaling
Model pred

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