

Table S2: Model parameters

Parameter (unit)	Definition	Cyno Value	Human Value	Source
MW_{FC} (Da)	Molecular weight of FLT3L-Fc	83000	83000	In-house measurement
MW_{CDX} (Da)	Molecular weight of CDX-301	35000	35000	Ref. (1)
BW (kg)	Body weight	2.6	70	Nominal body weight value for species
V_{lymph} (L)	Volume of lymph	0.086	5.2	Cyno fit from data, human from (2)
V_{plasma} (L)	Volume of plasma	0.09	2.6	Cyno fit from data, human from (2)
CL_p (L/h)	Nonspecific clearance of FLT3L-Fc	4.2E-04	6.94E-03	Cyno fit from data, human allometrically scaled
CL_p (mL/d/kg)	Nonspecific clearance of FLT3L-Fc	3.87	2.4	Cyno fit from data, human allometrically scaled
σ_{leaky}	Leaky reflection coefficient	0.656	0.656	Fit from data
σ_{tight}	Tight reflection coefficient	0.985	0.985	Fit from data
σ_{lymph}	Lymph reflection coefficient	0.2	0.2	Ref. (2)
L (L/h)	Lymph flow rate	0.012	0.121	Cynomolgus monkey fit from data, human from (2)
K_p	Partition coefficient	0.8	0.8	Ref. (2)
ISF (mL/kg)	Interstitial fluid	0.579	15.6	Cynomolgus monkey fit from data, human from (3)
f_{leaky}	Fraction of leaky flow from blood to leaky	0.65	0.65	Ref. (2)
f_{tight}	Fraction of lymph flow from blood to tight	0.35	0.35	Ref. (2)
$C_{R,0}$ (nM)	Initial concentration of FLT3 receptors in circulation	11.3	4	Fit from data
vm_{prolif} (h^{-1})	Maximum rate of FLT3 expansion induced by double-bound FLT3 receptor-drug complex	1.90E-03	3.30E-3	Fit from data
km_{prolif}	Amount of double-bound FLT3 receptor-drug complex to achieve 50% vm_{prolif}	0.547	0.02	Fit from data
α	Hill coefficient of FLT3 expansion induced by double-bound FLT3 receptor-drug complex	3.93	1	Fit from data
k_{deg} (h^{-1})	Turnover rate of FLT3 receptors in circulation	0.016	0.016	Fit from data
$kon1$ (1/nM/h)	On-rate for monovalent binding of drug to FLT3 receptors	0.1	0.1	Assumption
$KD1$ (nM)	monovalent binding affinity of drug to FLT3 receptors	9	9	Ref. (4)
$kon2$ (1/nM/h)	On-rate for binding of single-bound drug-FLT3 complex to the second FLT3 receptor	3.6	3.6	in-house Biacore measurement
$KD2$ (nM)	Binding affinity of single-bound drug-FLT3 complex to the second FLT3 receptor	0.2	0.2	in-house Biacore measurement
$kabs_{CDX}$ (h^{-1})	Absorption rate of CDX-301 from SC to plasma	NA	0.04	Fit from CDX-301 data (5)

V_{dCDX} (mL/kg)	Volume of distribution of CDX-301	NA	213	Fit from CDX-301 data (5)
vm_{CDX} (mL/h/kg)	Maximum nonlinear elimination rate of CDX-301	NA	3.72	Fit from CDX-301 data (5)
km_{CDX} (μ g/mL)	Concentration of CDX-301 needed to achieve 50% of Vm_{CDX}	NA	0.394	Fit from CDX-301 data (5)
$init_{DC1}$ (cells/mL)	Mean initial cDC1 count	NA	1180	Human estimated from (5)
$kdeg_{DC1}$ (h^{-1})	Turnover rate of the cDC1 population	NA	1.60E-02	Fit from CDX-301 data (5, 6)
$vm1_{DC1}$ (h^{-1})	Maximum rate of cDC1 expansion induced by free drug	NA	1.61	Fit from CDX-301 data (5, 6)
$km1_{DC1}$ (nM)	Concentration of free drug to increase cDC1 counts to 50% $Vm1_{DC1}$	NA	0.072	Fit from CDX-301 data (5, 6)
del_{DC1} (h^{-1})	Transit rate between cDC1 compartments	NA	0.114	Fit from CDX-301 data (5, 6)
$n1_{DC1}$	Hill coefficient of free drug effect on cDC1 expansion	NA	5.85	Fit from CDX-301 data (5, 6)
$init_{DC2}$ (cells/mL)	Mean initial cDC2 count	NA	12700	Human estimated from (6)
$kdeg_{DC2}$ (h^{-1})	Turnover rate of the cDC2 population	NA	1.70E-03	Fit from CDX-301 data (5, 6)
$vm1_{DC2}$ (h^{-1})	Maximum rate of cDC2 expansion induced by free drug	NA	16.1	Fit from CDX-301 data (5, 6)
$km1_{DC2}$ (nM)	Concentration of free drug to increase cDC2 counts to 50% $Vm1_{DC2}$	NA	0.209	Fit from CDX-301 data (5, 6)
del_{DC2} (h^{-1})	Transit rate between cDC2 compartments	NA	0.053	Fit from CDX-301 data (5, 6)
$n1_{DC2}$	Hill coefficient of free drug effect on cDC2 expansion	NA	0.888	Fit from CDX-301 data (5, 6)
$kdeg2_{DC}$ (h^{-1})	Second-order apoptosis rate of cDC2	NA	3.64E-04	Fit from CDX-301 data (5, 6)
f_{DC1}	Fractional rate of cDC1 second-order apoptosis rate compared to that of DC2	NA	0.476	Fit from CDX-301 data (5, 6)

References

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