Table list:

Table S1: Demographic and clinical data for 22 renal transplant patients

Age (years), median (range)	57.5 (25 – 76)
Male/female, n/n	18/4
Mycophenolate mofetil yes/no, n/n	12/10
Creatinine clearance (mL/min), median (range)	45.7 (18.8 – 95.7)
CMV serology +/2, n/n	10/12

	First blood sample after drug introduction	Blood sample at PK sampling
Hemoglobin concentration (g/L), median (range)	11.55 (7.85–13.7)	12.05 (9.29–15.6)
Platelets (10^9 /L), median (range)	198 (117–532)	204 (139 –337)
Lymphocytes (10^9 /L), median (range)	1.63 (0.35–5.44)	1.51 (0.28–3.59)
Neutrophils (10^9 /L), median (range)	5.31 (1.78–8.88)	3.85 (0.6 –8.04)

Table S2: Performance analysis of ML algorithms

ML algorithms	RMSE, mg.h/L	R^2	Relative MPE, %	Relative RMSE, %
XGBoost	0.83	0.99	0.032	1.30
Random forest	1.56	0.99	3.51	2.18
glmet	4.23	0.96	-0.434	7.97
MARS	3.89	0.97	0.325	6.56
SVM	0.77	0.99	0.063	1.48

Values obtained after 10-fold cross-validation

Table S3: Impact of imperfect sampling times on the performance of XGBoost and MAP-BE models in the simulated patients of the validation set

	AUCss estimation method	Performances	Patients from Caldés et al. model (*n* = 98)	Patients from Chen et al. model (*n* = 98)
			2 samples (C4 & C10)	
900 mg/24h of VGCV	XGBoost (C4 & C12)	Relative MPE, (%)	7.79	27.1
		Relative RMSE, (%)	17.5	29.3
		Number of MPE of the ±20% interval	30 (30.6%)	74 (75.5 %)
	MAP-BE Vezina et al.	Relative MPE, (%)	-12.5	19.1
		Relative RMSE, (%)	14.3	23.5
		Number of MPE of the ±20% interval	15 (15.3 %)	41 (41.9 %)
	MAP-BE Lalagkas et al.	Relative MPE, (%)	42.7	78.4
		Relative RMSE, (%)	48.0	82.9
		Number of MPE of the ±20% interval	83 (84.7 %)	97 (99.0 %)
			2 samples (C4 & C10)	
450 mg/24h of VGCV	XGBoost (C4 & C12)	Relative MPE, (%)	9.68	25.7
		Relative RMSE, (%)	15.7	28.0
		Number of MPE of the ±20% interval	17 (17.3%)	71 (72.5 %)
	MAP-BE Vezina et al.	Relative MPE, (%)	17.2	14.1
		Relative RMSE, (%)	11.0	18.3
		Number of MPE of the ±20% interval	7 (7.14 %)	29 (29.6 %)
	MAP-BE Lalagkas et al.	Relative MPE, (%)	34.8	76.5
		Relative RMSE, (%)	43.4	80.4
		Number of MPE of the ±20% interval	71 (72.4%)	98 (100 %)
			2 samples (C0 & C10)	
450 mg/48h of VGCV	XGBoost (C0 & C12)	Relative MPE, (%)	4.46	29.7
		Relative RMSE, (%)	15.6	36.4
		Number of MPE of the ±20% interval	17 (17.3 %)	57 (58.2 %)
	MAP-BE Vezina et al.	Relative MPE, (%)	-16.0	24.3
		Relative RMSE, (%)	19.0	32.7
		Number of MPE of the ±20% interval	32 (32.6 %)	52 (53.1 %)
	MAP-BE Lalagkas et al.	Relative MPE, (%)	24.4	76.1
		Relative RMSE, (%)	29.4	79.3
		Number of MPE of the ±20% interval	57 (58.2 %)	98 (100 %)
			2 samples (C0 & C6)	
450 mg/72h of VGCV	XGBoost (C0 & C7)	Relative MPE, (%)	12.0	-
		Relative RMSE, (%)	14.7	-
		Number of MPE of the ±20% interval	14 (14.3 %)	-
	MAP-BE Lalagkas et al.	Relative MPE, (%)	31.1	-
		Relative RMSE, (%)	37.1	-
		Number of MPE of the ±20% interval	80 (81.6%)	-

Table S4: Performances of the generalized linear regression algorithms in the training and testing datasets

VGCV dosage	Data set	RMSE, mg.h/L	R^2	Relative MPE, %	Relative RMSE, %	Number of MPE of the ± 20% interval, *n (%)*
900 mg/24h	Training set (n = 3,671)	8.86[a]	0.84[a]	-	-	-
	Testing set (n =1,224)	8.86	0.84	1.43	14.5	200 (16.3 %)
450 mg/24h	Training set (n = 3,660)	5.85	0.89[a]	-	-	-
	Testing set (n = 1,223)	6.33	0.88	0.05	13.4	162 (13.2 %)
450 mg/48h	Training set (n = 3,672)	11.1[a]	0.82[a]	-	-	-
	Testing set (n = 1,225)	11.0	0.82	2.22	17.4	223 (18.2 %)
450 mg/72h	Training set (n = 1,835)	25.1[a]	0.76[a]	-	-	-
	Testing set (n = 612)	25.0	0.77	3.53	20.1	213 (34.8 %)

[a] Values obtained after 10-fold cross-validation

Table S5: Performances of the generalized linear regression algorithms in the simulated validation datasets

VGCV dosage	Performances	Patients from	
		Caldés et al. model (n = 98)	Chen et al. model (n = 98)
900 mg/24h	Relative MPE, (%)	- 16.9	-13.8
	Relative RMSE, (%)	19.3	24.0
	Number of MPE of the ±20% interval	31 (31.6 %)	31 (31.6 %)
450 mg/24h	Relative MPE, (%)	-14.1	-16.8
	Relative RMSE, (%)	17.4	32.7
	Number of MPE of the ±20% interval	23 (23.5 %)	37 (37.8 %)
450 mg/48h	Relative MPE, (%)	-25.7	0.05
	Relative RMSE, (%)	27.7	37.5
	Number of MPE of the ±20% interval	69 (70.4 %)	71 (72.4 %)
450 mg/72h	Relative MPE, (%)	-28.4	-
	Relative RMSE, (%)	31.1	-
	Number of MPE of the ±20% interval	73 (74.5 %)	-

Table S6: Training of XGBoost models separately on simulations from each popPK model (Vezina et al. and Lalagkas et al.) and comparison of their performance in predicting AUCss in the validation simulated patient's dataset. This comparison was conducted exclusively on simulated patients receiving 900 mg/24h of ganciclovir.

	AUCss estimation method	**Performances**	**Patients from**					
			Caldés et al. model (*n* = 98)	**Chen et al. model (*n* = 98)**	**Caldés et al. model (*n* = 98)**	**Chen et al. model (*n* = 98)**	**Caldés et al. model (*n* = 98)**	**Chen et al. model (*n* = 98)**
			2 samples (C4 and C12)		**3 samples (C3, C4 and C12)**		**3 samples (C3, C4 and C6)**	
900 mg/24h of VGCV	XGBoost	Relative MPE, (%)	- 0.10	15.0	1.54	8.89	5.16	18.1
		Relative RMSE, (%)	13.6	17.5	10.6	10.7	15.5	23.2
		Number of MPE of the ±20% interval	12 (12.2%)	33 (33.7 %)	5 (5.10 %)	2 (2.04 %)	14 (14.3 %)	46 (46.9%)
	XGBoost (Lalagkas et al.)	Relative MPE, (%)	0.08	16.4	1.06	7.72	8.09	19.9
		Relative RMSE, (%)	13.3	18.8	9.78	9.61	16.0	25.0
		Number of MPE of the ±20% interval	12 (12.2 %)	36 (36.7 %)	4 (4.08 %)	1 (1.02 %)	19 (19.4 %)	54 (55.1 %)
	XGBoost (Vezina et al.)	Relative MPE, (%)	- 2.93	13.5	2.23	12.5	- 2.93	19.7
		Relative RMSE, (%)	15.8	16.6	14.6	14.8	17.7	25.8
		Number of MPE of the ±20% interval	15 (15.3 %)	26 (26.5 %)	11 (11.2 %)	14 (14.3 %)	25 (25.5 %)	49 (50 %)

Figure list:

Figure F1: Scatterplots of bias as a function of reference AUCss in the validation set