

Table 1S – Association of Top SNPs with TAC Longitudinal Troughs and No Additional Covariates in Discovery cohort. Adjusted for enrolling center.

CHR	SNP	BP	Locus	BETA	SE	P-value
7	rs17161880	99348361	<i>CYP3AP2</i>	-0.3894	0.04852	9.26 x 10 ⁻¹⁴
7	rs34880695	99348055	<i>CYP3AP2</i>	-0.3885	0.05093	1.03 x 10 ⁻¹²
7	rs6465750	99235522	<i>ZSCAN25</i>	0.3614	0.05654	1.34 x 10 ⁻⁰⁹
7	rs17161780	99238141	<i>ZSCAN25</i>	-0.5266	0.08329	1.70 x 10 ⁻⁰⁹
7	rs776746	99270539	<i>CYP3A5</i>	0.3458	0.05517	2.28 x 10 ⁻⁰⁹
7	rs17161774	99210648	<i>ZSCAN25</i>	-0.5551	0.09517	2.24 x 10 ⁻⁰⁸
7	rs3735451	99355975	<i>CYP3A4</i>	0.2949	0.05478	2.07 x 10 ⁻⁰⁷
7	rs1419745	99260092	<i>CYP3A5</i>	-0.2858	0.05497	5.04 x 10 ⁻⁰⁷
X	rs144708905	8359071	---	0.7596	0.1478	6.70 x 10 ⁻⁰⁷
18	rs554238	5986825	<i>L3mbtl4</i>	0.2752	0.05425	9.07 x 10 ⁻⁰⁷
X	rs115026930	113500375	---	0.4119	0.08336	1.67 x 10 ⁻⁰⁶
4	rs78317738	124709544	<i>LINC01091</i>	1.196	0.2469	2.58 x 10 ⁻⁰⁶
7	rs2394741	97495441	<i>ASNS</i>	0.5893	0.122	2.74 x 10 ⁻⁰⁶
18	rs1941267	30429313	<i>LOC105372058</i>	0.2736	0.05706	3.24 x 10 ⁻⁰⁶
2	rs74613074	106183094	---	1.005	0.2101	3.39 x 10 ⁻⁰⁶
7	rs1043466	99054289	<i>CPSF4</i>	0.335	0.07122	4.84 x 10 ⁻⁰⁶
6	rs73774057	134742751	---	0.6507	0.1388	5.16 x 10 ⁻⁰⁶
6	rs6454237	82343415	---	0.3062	0.06534	5.21 x 10 ⁻⁰⁶
7	rs10242455	99240179	<i>ZSCAN25</i>	0.2707	0.05777	5.26 x 10 ⁻⁰⁶
5	rs76900544	12431911	<i>LOC105374655</i>	0.4841	0.1037	5.64 x 10 ⁻⁰⁶
10	rs76413989	88296949	<i>LOC105378408</i>	0.6007	0.1291	6.01 x 10 ⁻⁰⁶
7	rs28988607	99354299	<i>CYP3A4</i>	-0.2682	0.05771	6.13 x 10 ⁻⁰⁶
7	rs55897278	43368490	<i>HECW1</i>	0.5437	0.1172	6.35 x 10 ⁻⁰⁶
1	rs57170892	236671737	<i>LGALS8</i>	-0.4597	0.09939	6.85 x 10 ⁻⁰⁶
X	rs4827173	39694548	<i>LOC105373179</i>	0.1975	0.04334	9.14 x 10 ⁻⁰⁶
5	rs114077855	177741760	<i>COL23A1</i>	-0.8805	0.1932	9.20 x 10 ⁻⁰⁶
2	rs7605051	76641171	---	0.2512	0.05512	9.24 x 10 ⁻⁰⁶
10	rs116239652	72699435	<i>LOC105378349</i>	-0.5633	0.1241	9.83 x 10 ⁻⁰⁶

Base pairs (BP) location based on assembly GRCh37.p13

Table 2S. Association of Top SNPs with Longitudinal TAC Troughs Adjusted for CYP3A5*3 (rs776746) in the Discovery Cohort

CHR	SNP	BP	Locus	BETA	Lower	Upper	P-value
7	rs6956305	99643687	ZSCAN25	0.5128	0.3861	0.6394	2.90 x 10 ⁻¹⁵
7	rs17161880	99750738	CYP3AP2	-0.2771	-0.3633	-0.1908	3.50 x 10 ⁻¹⁰
3	rs528004021	192127260		1.3039	0.887	1.7209	9.90 x 10 ⁻¹⁰
7	rs34880695	99750432	CYP3AP2	-0.2768	-0.3676	-0.186	2.60 x 10 ⁻⁹
11	rs73456465	44945675	TP53I11	0.628	0.4188	0.8373	4.40 x 10 ⁻⁹
14	rs74064870	75242744	---	0.4799	0.3198	0.6401	4.70 x 10 ⁻⁹
X	rs115026930	113500375	---	0.342	0.2125	0.4714	2.40 x 10 ⁻⁷
8	rs114484963	16869931	---	1.1102	0.6874	1.5331	2.80 x 10 ⁻⁷
6	rs73774057	134421613	---	0.5785	0.3571	0.7999	3.20 x 10 ⁻⁷
X	rs144708905	8359071	---	0.6032	0.3702	0.8362	4.10 x 10 ⁻⁷
3	rs114972846	113363113	KIAA2018	1.0002	0.6122	1.3881	4.60 x 10 ⁻⁷
7	rs114447591	99099823	ZNF394	0.5154	0.3149	0.7158	4.90 x 10 ⁻⁷
5	rs76900544	12431911	LOC105374655	0.4135	0.2514	0.5755	6.00 x 10 ⁻⁷
7	rs55638814	99009873	BUD31	0.4763	0.2876	0.665	7.90 x 10 ⁻⁷
19	rs73546081	39848216	SAMD4B	0.3104	0.1846	0.4362	1.40 x 10 ⁻⁶
18	rs17067022	58172922	---	0.5623	0.3339	0.7907	1.50 x 10 ⁻⁶
1	rs74414717	231630430	LOC102724041	0.8739	0.5174	1.2305	1.60 x 10 ⁻⁶
2	rs74613074	106183094	---	0.8326	0.492	1.1732	1.70 x 10 ⁻⁶
12	rs2723834	12055413	ETV6	0.2726	0.1606	0.3847	1.90 x 10 ⁻⁶
9	rs12686780	95382297	IPPK	0.3222	0.1889	0.4555	2.30 x 10 ⁻⁶
2	rs2541379	217594516	LOC101928250	0.5499	0.3203	0.7796	2.80 x 10 ⁻⁶
1	rs74691910	182305870	EIF1P3	0.7299	0.4225	1.0374	3.40 x 10 ⁻⁶
13	rs190368405	30083432	SLC7A1	1.4055	0.8124	1.9985	3.50 x 10 ⁻⁶
7	rs5887568	132040954	PLXNA4	0.458	0.2647	0.6514	3.50 x 10 ⁻⁶
22	rs116324909	24583271	SUSD2	1.4039	0.811	1.9968	3.60 x 10 ⁻⁶
20	rs75727840	31581049	SUN5	0.5452	0.3144	0.776	3.80 x 10 ⁻⁶
8	rs116405247	5418659	---	0.8363	0.4794	1.1932	4.50 x 10 ⁻⁶
7	rs17161774	99210648	GSI-259H13.2	-0.3754	-0.5363	-0.2144	5.00 x 10 ⁻⁶
12	rs11051969	32537123	BICD1	0.2506	0.1429	0.3584	5.30 x 10 ⁻⁶
1	rs72959728	87695723	LOC101927844	0.517	0.2946	0.7394	5.40 x 10 ⁻⁶
1	rs4652106	175655562	TNR	0.7161	0.4047	1.0274	6.80 x 10 ⁻⁶
12	rs12829636	94639322	PLXNC1	0.6684	0.3777	0.9591	6.80 x 10 ⁻⁶
12	rs75934992	105564414	APPL2	0.8214	0.4621	1.1807	7.70 x 10 ⁻⁶
18	rs554238	5986825	L3MBTL4	0.2022	0.1136	0.2909	8.00 x 10 ⁻⁶
16	rs16972052	19487835	TMC5	0.2449	0.1371	0.3527	8.70 x 10 ⁻⁶
4	rs10002236	91608632	CCSER1	0.4618	0.2583	0.6652	8.90 x 10 ⁻⁶
1	rs74113796	109784294	SARS	0.487	0.2723	0.7016	9.00 x 10 ⁻⁶
4	rs60778684	7953472	AFAP1	-0.2731	-0.3937	-0.1525	9.30 x 10 ⁻⁶
14	rs73267896	64761816	ESR2	1.0029	0.5599	1.4458	9.40 x 10 ⁻⁶
14	rs73271817	64830793	ESR2	1.0035	0.5602	1.4467	9.40 x 10 ⁻⁶
4	rs191935015	180014111	---	0.7349	0.4094	1.0605	9.90 x 10 ⁻⁶

Base pairs (BP) location based on assembly GRCh37.p13

Table 3S. TAC Model in African Americans in the discovery cohort: ln of Dose-Normalized TAC Trough Concentrations with Clinical Factors and rs776746 and rs41303343 (CYP3A5*3 and *7) LOF Alleles.*

Variable	Group#	Reference Group	Estimate	Lower	Upper	P-value
Intercept			-1.378	-1.686	-1.071	7.30 x 10-16
Transplant Center	B	A	0.521	0.226	0.817	2.10 x 10-03
	C	A	0.123	-0.116	0.361	.
Time (days)			0.098	0.077	0.118	1.40 x 10-17
Time Post Day 9 (days)			-0.097	-0.118	-0.077	7.10 x 10-17
Age Group	18-34	65-84	-0.311	-0.592	-0.031	6.10 x 10-02
	35-64	65-84	-0.162	-0.411	0.087	.
GFR			-0.002	-0.004	-0.001	1.00 x 10-03
Anti CMV Drug Use			0.084	0.051	0.117	6.10 x 10-07
SPK			0.429	0.158	0.700	1.90 x 10-03
Antibody Induction	Combination	Polyclonal	-0.272	-0.724	0.181	6.60 x 10-02
	Monoclonal	Polyclonal	0.134	0.015	0.253	.
	None	Polyclonal	0.106	-0.300	0.513	.
rs776746 (*3)			0.3622	0.276	0.449	3.80 x 10-16
rs41303343 (*7)			0.5754	0.438	0.713	3.00 x 10-16

*Longitudinal model with random intercept and time slopes.

#Three centers included in the discovery cohort.

Table 4S. TAC Levels Model in African Americans in Validation Cohort. ln of Dose-Normalized TAC Trough Concentration with Clinical Factors.*

Variable	Group#	Reference Group	Estimate	Lower	Upper	P-value
Intercept			-0.9	-1.292	-0.507	1.20 x 10 ⁻⁰⁵
Transplant Center	B	A	0.723	0.406	1.039	3.40 x 10 ⁻⁰⁴
	D	A	0.01	-0.287	0.307	.
	C	A	0.189	-0.109	0.487	.
	E	A	-0.019	-0.264	0.227	.
Time (days)			0.059	0.035	0.083	3.00 x 10 ⁻⁰⁶
Time Post Day 9 (days)			-0.058	-0.082	-0.034	5.60 x 10 ⁻⁰⁶
Age Group	18-34	65-84	-0.307	-0.66	0.046	3.80 x 10 ⁻⁰²
	35-64	65-84	-0.084	-0.405	0.238	.
GFR			-0.001	-0.003	0.001	3.00 x 10 ⁻⁰¹
Anti CMV Drug Use			0.082	0.04	0.125	1.40 x 10 ⁻⁰⁴
SPK			0.491	0.134	0.848	7.00 x 10 ⁻⁰³
Antibody Induction	Combination	Polyclonal	-0.068	-0.599	0.464	4.50 x 10 ⁻⁰²
	Monoclonal	Polyclonal	0.188	0.031	0.345	.
	None	Polyclonal	-0.3523	-0.9808	0.2761	.

*Longitudinal model with random intercept and time slopes.

#All 5 centers included in the validation cohort.

Table 5S. TAC Model in African Americans in the validation cohort. ln of Dose-Normalized TAC Trough Concentration with Clinical Factors and *CYP3A53, *6, and *7 (rs776746, rs10264272, and rs41303343) LoF Alleles.***

Variable	Group	Reference Group	Estimate	Lower	Upper	P-value
Intercept			-1.248	-1.606	-0.89	1.60 x 10 ⁻¹⁰
Transplant Center	B	A	0.646	0.372	0.919	2.40 x 10 ⁻⁰⁴
	D	A	0.062	-0.193	0.318	.
	C	A	0.12	-0.133	0.373	.
	E	A	0.004	-0.205	0.212	.
Time (days)			0.057	0.034	0.081	4.10 x 10 ⁻⁰⁶
Time Post Day 9 (days)			-0.057	-0.081	-0.033	7.40 x 10 ⁻⁰⁶
Age Group	18-34	65-84	-0.253	-0.552	0.047	4.30 x 10 ⁻⁰²
	35-64	65-84	-0.065	-0.336	0.207	.
GFR			-0.001	-0.002	0.001	4.60 x 10 ⁻⁰¹
Anti CMV Drug Use			0.085	0.043	0.127	7.70 x 10 ⁻⁰⁵
SPK			0.481	0.176	0.785	2.00 x 10 ⁻⁰³
Antibody Induction	Combination	Polyclonal	-0.193	-0.646	0.26	7.30 x 10 ⁻⁰²
	Monoclonal	Polyclonal	0.151	0.017	0.285	.
	None	Polyclonal	-0.1316	-0.665	0.402	.
rs776746 (*3)			0.4084	0.306	0.511	9.40 x 10 ⁻¹⁵
rs10264272 (*6)			0.2436	0.11	0.377	3.50 x 10 ⁻⁰⁴
rs41303343 (*7)			0.3699	0.216	0.524	2.50 x 10 ⁻⁰⁶

*Longitudinal model with random intercept and time slopes

Table 6S. TAC Model in African Americans in the Validation Cohort. ln of Dose-Normalized TAC Trough Concentration with Clinical Factors and Number of *CYP3A53, *6, and *7 (rs776746, rs10264272, and rs41303343) LoF Alleles.**

Variable	Group	Reference Group	Estimate	Lower	Upper	P-value
Intercept			-1.269	-1.632	-0.907	1.30 x 10 ⁻¹⁰
Transplant Center	UMN	UAB	0.662	0.388	0.936	1.40 x 10 ⁻⁰⁴
	HCMC	UAB	0.034	-0.222	0.289	.
	Mayo	UAB	0.141	-0.115	0.396	.
	UI	UAB	0.002	-0.209	0.214	.
Time (days)			0.058	0.035	0.082	3.00 x 10 ⁻⁰⁶
Time Post Day 9 (days)			-0.058	-0.082	-0.034	5.50 x 10 ⁻⁰⁶
Age Group	18-34	65-84	-0.246	-0.55	0.058	5.60 x 10 ⁻⁰²
	35-64	65-84	-0.064	-0.34	0.212	.
GFR			-0.001	-0.002	0.001	4.70 x 10 ⁻⁰¹
Anti CMV Drug Use			0.085	0.043	0.127	7.40 x 10 ⁻⁰⁵
SPK			0.478	0.171	0.785	2.30 x 10 ⁻⁰³
Antibody Induction	Combination	Polyclonal	-0.219	-0.677	0.238	2.70 x 10 ⁻⁰²
	Monoclonal	Polyclonal	0.171	0.036	0.307	.
	None	Polyclonal	-0.1842	-0.722	0.354	.
LoF*			0.3582	0.267	0.45	2.20 x 10 ⁻¹⁴

*LoF: Loss of function allele