Table 1. S1. Clinical factors associated with statin exposure.

Factor	Statin	Effect	References
Clinical			
Advanced age	ATV, LVT, PIT, PVT, SVT,	-↑AUC: **ATV** (30%), **PIT** (30%), **PVT** (~37%) -↑mean plasma level of HMG-CoA reductase inhibitory activity: **LVT** (45%), **SVT** (45%)	[1-5]
	FVT, RVT	No significant difference	[6,7]
Gender	ATV	Women: 20% ↑**ATV** C_{max}, 10% ↓AUC	[1]
	FVT, PIT	Women: ↑ **FVT** or **PIT** AUC	[6,8]
	PVT	Women: ↑ **PVT** AUC (in subjects homozygous wild type at *SLCO1B1* rs4149056)	[9]
	RVT	No significant difference	[7,10]
	SVT	- **SVT acid**: ↑ exposure in women - SVT: no significant difference	[11]
Dose	ATV, FVT, LVT, PIT, PVT,RVT, SVT,	↑ statin plasma exposure	[1-7]
Evening compared to morning dosing	ATV, PVT	- **ATV** AUC ↓ by 29% - **PVT** bioavailability ↓ by 60%	[1,4,12]
	PIT, RVT	No significant difference in AUC	[3,7,13]
Ethnicity (compared to Caucasian)			
African American	PVT	1.4 fold ↑ **PVT** AUC	[14]
Asian	ATV	No significant difference in ATV AUC	[15]
Asian-Indian	RVT	26% non-significant ↑ in RVT AUC	[16]
East Asian	RVT	64-84% ↑ **RVT** AUC	[16]
Japanese	RVT, SVT, PIT	- 55% ↑ exposure to **RVT** - 34-68% ↑ exposure to **SVT acid** - no significant difference for PIT	[3,17,18]
Mexican	PVT	No significant difference in AUC	[19]
Alcohol	FVT	- 30% ↑ **FVT** AUC in chronic alcohol consumption - no significant difference in FVT AUC in acute alcohol consumption:	[20]
Co-administration with food	LVT	~50% ↑ **LVT** AUC	[2]
	PVT	↓ **PVT** C_{max} (by 49%) and AUC (by 31%)	[21]
	ATV, FVT, PIT	- Significant ↓ in C_{max} (**ATV** by 47.9%, **FVT** by 40-60%, PIT by 43%) - Non-significant ↓ in AUC (ATV 9-13%, FVT by 11%)	[3,6,22,23]

	RVT, SVT	No significant difference in AUC	[5,7]
Diabetes mellitus	ATV	↑ plasma concentrations of ATV and metabolites when sampled >5-24 hours post dose	[24]
Hepatic impairment	ATV, FVT, PIT, PVT	↑ AUC: **ATV** (4-11 fold), **FVT** (2.5 fold), **PIT** (1.6-3.8 fold) **PVT** (34%)	[1,3,6,25]
	RVT	No significant difference	[26]
Renal impairment	LVT, PIT, PVT, RVT	↑ AUC: **LVT** (2 fold), **PIT** (2 fold), **PVT** (69%), **RVT** (3 fold)	[2-4,7]
	ATV, FVT	No significant difference	[1,27]
	SVT	Potentially no difference	[28]
Following bariatric surgery	ATV	- 2 fold ↑ **ATV** AUC 3-8 weeks after surgery -↓ **ATV** AUC ~2 years after surgery	[29]
		Selected co-medications	
		Strong CYP3A4 inhibitors	
Itraconazole	ATV, LVT, PVT, RVT, SVT	↑ AUC: **ATV** (3.3 fold), **LVT** (>15-20 fold), **LVT acid** (15-20 fold), **PVT** (11-72%), **RVT** (28-39%), **SVT** (10 fold), **SVT acid** (19 fold)	[1,4,30-34]
	PIT	**PIT** AUC ↓ by 23%	[35]
	FVT	No significant difference	[34]
Ketoconazole	RVT	No significant difference	[36]
Clarithromycin	ATV, PVT, SVT	↑ AUC: **ATV** (4.4. fold), **PVT** (2.1 fold), **SVT** (10 fold), **SVT acid** (12 fold)	[1,4,37]
		Moderate CYP3A4 inhibitors	
Erythromycin	ATV, PIT, SVT	↑ AUC: **ATV** (33%), **PIT** (2.8 fold), **SVT** (6.2 fold), **SVT acid** (3.9 fold)	[1,3,38,39]
	RVT	**RVT** AUC ↓ by 20%	[40]
	FVT	No significant difference	[20]
Grapefruit juice (low dose)	ATV, LVT, PIT, SVT	↑ AUC: **ATV** (40-83%), **LVT** (1.94 fold), **PIT** (14%), **SVT** (1.9-3.6 fold), **SVT acid** (1.3-3.3 fold)	[5,41-45]
	PVT	No significant difference	[42]
Diltiazem	ATV, LVT, SVT	↑ AUC: **ATV** (51%), **LVT** (3.57 fold), **SVT** (3.10-4.6 fold), **SVT acid** (2.69 fold)	[1,2,5]
	PIT	10% ↑ PIT AUC, but statistical significance unknown	[3]
	PVT	No significant difference	[4]
		Weak CYP3A4 inhibitors	
Amlodipine	ATV, SVT	↑ AUC: **ATV** (18%), **SVT** (1.77 fold), **SVT acid** (1.58 fold)	[5,46]
	FVT	No significant different	[47]
		Other drugs	
Ciclosporin (inhibits CYP3A4, OATP1B1/1B3/2B1, ABCG2, P-gp)	ATV, FVT, LVT, PIT, PVT, RVT, SVT	↑ AUC: **ATV** (8.7 fold), **FVT** (90%), **LVT** (5-8 fold), **PIT** (4.6 fold), **PVT** (3.8 fold), **RVT** (7 fold), **SVT** (8 fold)	[1-7,48]

Fluconazole (inhibits CYP2C9, 2C19 & 3A)	FVT	84% ↑ **FVT** AUC	[49]
	PVT, RVT	No significant difference	[49,50]
Gemfibrozil (inhibits CYP2C8, OATP1B1 & OAT3)	ATV, LVT acid, PIT, PVT, RVT, SVT	↑ AUC: **ATV** (35%), **LVT acid** (2.8 fold), LVT (no significant difference), **PIT** (45%), **PVT** (2 fold), **RVT** (1.9 fold), **SVT** (1.35 fold), **SVT acid** (2.85 fold)	[51-56]
	FVT	No significant difference	[56,57]
Letermovir (inhibits OATP1B1/1B3 & CYP3A)	ATV	- 3 fold ↑ **ATV** AUC	[58]
Rifampicin (induces CYP3A; inhibits OATP1B1)	ATV	- 7 fold ↑ **ATV** AUC if single rifampicin dose co-administered with a single ATV dose - 30% ↑ **ATV** AUC if ATV/rifampicin co-administered after a 5 day course of rifampicin - **ATV** AUC ↓ by 80% if ATV given separately after a 5 day course of rifampicin	[1,59,60]
	PIT	6.7 fold ↑ **PIT** AUC if single rifampicin dose co-administered with a single PIT dose	[61]
	PVT	- 2.3 fold ↑ **PVT** AUC if single rifampicin dose co-administered with a single PVT dose - **PVT** AUC ↓ by 31% if PVT given separately after a 5 day course of rifampicin	[62,63]
	FVT, SVT	↓ AUC if statin given separately following rifampicin pre-treatment: **FVT** (by 53%), **SVT** (by 87%), **SVT acid** (by 93%). (Probable ↓ in LVT AUC)	[6,64,65]
	RVT	No significant difference when RVT given separately after a 6 day course of rifampicin	[66]
Tocilizumab (inhibits IL-6R)	SVT	**SVT** AUC ↓ by 57%	[67]

Unless otherwise stated, reported changes were statistically significant (statin highlighted in bold font).
AUC = area under the concentration-time curve.

Table S2. Genetic variants associated with statin exposure

Gene	Variant	Comparison	Statin	Effect	References
SLCO1B1	rs4149056 (521T>C, p.V174A)	CC vs TT	ATV	- ↑ AUC: **ATV** (2.44 fold, 144%), **2-OH ATV** (2.0 fold) - Non-significant ↑ in AUC: ATV L (2.0 fold), 2-OH ATV L (1.6 fold)	[68]
			FVT	1.19 (19%) fold non-significant ↑ in FVT AUC	[9]
			LVT	- 3.86 fold (286%) ↑ **LVT acid** AUC - LVT AUC ↓ non-significantly by 16%	[69]
			PIT	- 3.08 fold (208%) ↑ **PIT** AUC - No significant difference in PIT L AUC	[70]
			PVT	- 1.91 (91%) fold ↑ **PVT** AUC	[9]
			RVT	- 1.65 (65%) fold ↑ **RVT** AUC	[68]
			SVT	- 3.21 (221%) fold ↑ **SVT acid** AUC - 1.43 fold non-significant ↑ in SVT AUC	[71]
	rs2306283 (388A>G, p.N130D)	Haplotype **14* (rs2306283 but not rs4149056) vs **1a*	ATV	↓ **ATV** AUC	[72]
		GG (**1b/*1b*) vs AA (**1a/*1a*)	LVT	- **LVT acid** AUC ↓ by 32% - LVT AUC ↓ non-significantly by 28%	[69]
SLCO2B1	rs12422149 (935G>A, p.R312Q)	AA vs GG	SVT	79% ↑ apparent clearance of **SVT acid**	[17]
SLC10A1	rs2296651 (p.S267F, **2*)	**2* carriers vs **1/*1*	RVT	- 57% ↑ **RVT** AUC - No significant differences in RVT or N-desmethyl RVT plasma concentrations	[73,74]
SLC22A8	rs2276299 (723T>A)	A carriers vs TT	PVT	No significant difference in renal clearance	[75]
	rs749911923 (1166C>T, p.A389V)	CT vs CC	PVT	No significant difference in renal clearance	[75]
ABCC2	rs113646094 (1446C>G)	GC vs CC	PVT	- ↓ PVT AUC by 68%	[76]
ABCB1	rs1128503-rs2032582-rs1045642 (1236C-T-2677G-T-3435C-T)	TTT/TTT vs CGC/CGC	ATV	- 55% ↑ **ATV** AUC - No significant differences for ATV L	[77]
			SVT	- 60% ↑ **SVT acid** AUC - No significant differences for SVT	[77]
			FVT	No significant differences	[78]
			LVT	No significant differences	[78]
			PVT	No significant differences	[78]
			RVT	No significant differences	[78]
	rs2032582-rs1045642 (2677G-T-3435C-T)	TT/TT vs GG/CC and GT/CT	ATV	- ↑ elimination $t_{1/2}$: **ATV**, **ATV L**, **2-OH ATV**, **2-OH ATV L** - No significant differences in AUC	[79]

ABCB11	rs2287622 (1331T>C, p.V444A)	CC vs CT vs TT	PVT	No significant differences	[14]
	rs11568364 (2029A>G, p.M677V)	GG vs GA vs GG	PVT	No significant differences	[14]
ABCC2	rs717620 (-24C>T)	TT vs CT vs CC	PIT	- ↓ **PIT** AUC - **PIT** AUC ↓ by 62% in TT compared to CC subjects	[80]
	rs113646094 (1446C>G, p.T482=)	CG vs CC	PVT	**PVT** AUC ↓ by 67%	[76]
ABCG2	rs2231142 (421C>A, p.Q141K)	AA vs CC	ATV	- ↑ AUC: **ATV** (1.7 fold), **ATV L** (1.9 fold) - Non-significant ↑ in AUC: 2-OH ATV (1.4 fold), 2-OH ATV L (1.5 fold), 4-OH ATV L (1.4 fold)	[81]
			FVT	1.7 fold ↑ **FVT** AUC	[82]
			PIT	No significant differences	[80,83]
			PVT	No significant differences	[82]
			RVT	- 2.4 fold ↑ **RVT** AUC -2 fold ↑ in **N-desmethyl RVT** plasma concentration	[73,81]
			SVT	- 2.1 fold ↑ **SVT** AUC - 1.2 non-significant ↑ in SVT acid AUC	[82]
PPARA	rs4253728 (209-1003G>A)	GA vs GG	ATV	↓ **2-OH ATV** to ATV AUC ratio	[84]
		GA/AA vs GG	SVT	24% ↓ apparent clearance of **SVT acid**	[17]
CYP2C9	rs1799853 (p.R144C, **2*)	**2/*2* vs **1/*1*	FVT	No significant differences	[85]
	rs1057910 (p.I359L, **3*)	**3/*3* vs **1/*1*	FVT	3.1-5.0 fold ↑ in **FVT** AUC	[85]
		**3* carriers vs *1/*1*	PIT	- 2.9 fold ↑ in **PIT** AUC - 1.7 fold ↑ in **PIT L** AUC	[83]
			RVT	No significant differences in RVT or N-desmethyl RVT plasma concentrations	[10,73]
			SVT	No significant differences	[86]
CYP2C19	- rs4244285 (p.P227=, **2*) - rs4986893 (p.W212Stop gained, **3)*	**2/*2*, **2/*3* or **3/*3* (PMs) vs **1/*2*, **1/*3* or **1/*1* (EMs)	RVT	- No significant differences in RVT, N-desmethyl RVT or RVT L pharmacokinetics	[73,87]
CYP2D6	whole gene deletion (**5*)	**5/*5* vs *wt/wt* (**1* or **2*)	LVT	- 5.1 fold ↑ **LVT** AUC - no significant difference in LVT acid AUC	[88]
		**5/wt* vs *wt/wt*	SVT	- **SVT** AUC ↓ by 23% - no significant difference in SVT acid AUC	[89]
	rs1065852 (p.S34P, **10*)	**10/*10* vs *wt/wt* (**1* or **2*)	LVT	- 2.2 fold ↑ **LVT** AUC - no significant difference in LVT acid AUC	[88]
	rs5030865 (p.G169Stop gained, **14*)	**14/*14* vs *wt/wt*	SVT	- 1.5 fold ↑ **SVT** AUC - no significant difference in SVT acid AUC	[89]

	rs28371725 (**41*)	**41/*41* vs *wt/wt*	SVT	↑ C_{max} of both **SVT** and **SVT acid**	[89]
CYP3A4	rs35599367 (**22*)	**22* carriers vs **1/*1*	ATV	↓ **2-OH ATV** to ATV AUC ratio	[84]
			SVT	White patients: - 14% ↑ **SVT acid** concentration - 20% non-significantly ↑ SVT concentration African American patients: - 170% ↑ **SVT** concentration - no significant difference in SVT acid concentration	[90]
CYP3A5	rs776746 (**3*)	**3/*3* vs **1* carriers	ATV	- 36% ↑ **ATV L** AUC - No significant difference in ATV AUC	[91]
		**3/*3* vs **1/*3*	PIT	No significant differences for PIT or PIT L	[83]
		**3/*3* vs **1/*3*	RVT	No significant differences	[10]
		**3/*3* vs **1/*1*	SVT	- 3.3 fold ↑ **SVT** AUC - No significant difference in SVT acid plasma levels	[90,92]
UGT1A1	**28*	**28* vs **1/*1*	ATV	- 41% ↓ **ATV L** AUC	[93]
UGT1A3	**2*	**2/*2* vs **1/*1*	ATV	- 72% ↑ **ATV L** AUC - 160% ↑ **2OH ATV L** AUC	[94,95]
		**1/*2* vs **1/*1*		↑ **ATV L** to ATV AUC ratio	[94]

Unless otherwise stated, reported changes were statistically significant (statin highlighted in bold font).
AUC = area under the concentration-time curve; wt = wild type.

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