Major HIV-1 Drug Resistance Mutations

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Updated summary from the HIV Drug Resistance Database. This document can be downloaded from the hivdb.stanford.edu home page.

Stanford HIVDB

Major Nucleoside RT Inhibitor (NRTI) Resistance Mutations

	Non-TAMs					TAMs						MDR	
	184	65	70	74	115	41	67	70	210	215	219	69	151
Cons	M	K	K	L	Y	M	D	K	L	T	K	T	Q
3TC	**VI**	**R**										**Ins**	**M**
FTC	**VI**	**R**										**Ins**	**M**
ABC	VI	**R**	E	**VI**	**F**	L			W	FY		**INS**	**M**
TDF	***	**R**	E		F	L		**R**	W	FY		**INS**	**M**
ZDV	***	***	*	*		**L**	**N**	**R**	**W**	**FY**	QE	**INS**	**M**

Bold underline: High-level reduced susceptibility or virological response.

Bold: Reduced suceptibility or virological response.

Plain text: Reduced susceptibility in combination with other NRTI-resistance mutations.

Asterisk: Increased susceptibility.

TAMs: Thymidine analog mutations. Selected by AZT and d4T and facilitate primer unblocking. Non-TAMs prevent NRTI incorporation.

MDR: Multidrug resistance mutations. T69 insertions occur with TAMs. Q151M occurs with non-TAMs and the accessory mutations A62V, V75I, F77L, and F116Y.

M184VI: The most common NRTI-resistance mutations. Although they cause high-level in vitro resistance to 3TC/FTC, they are not contraindications to 3TC/FTC because they increase TDF and AZT susceptibility and decrease viral replication fitness.

Additional mutations: K65N similar but weaker than K65R. K70GQNT similar to K70E. T69D and V75MT reduce susceptibility to d4T and ddI, which are not shown because they are no longer recommended for HIV treatment. T215SCDEIV (T215 revertants) emerge from T215YF in the absence of NRTIs. E40F, E44DA, D67GE, V118I, and K219NR are accessory TAMs. T69 deletions occur in combination with K65R and/or Q151M.

References: hivdb.stanford.edu/dr-summary/resistance-notes/NRTI/

Major Non-Nucleoside RT Inhibitor (NNRTI) Resistance Mutations

	100	101	103	106	181	188	190	230
Cons	L	K	K	V	Y	Y	G	M
NVP	**I**	**EP**	**NS**	**AM**	**CIV**	**LCH**	**ASEQ**	**L**
EFV	**I**	E**P**	**NS**	**AM**	CIV	**LC**H	**ASEQ**	**L**
ETR	**I**	E**P**			**CIV**	L	AS**EQ**	**L**
RPV	**I**	**EP**			**CIV**	**L**	AS**EQ**	**L**

Bold underline: High-level reduced susceptibility or virological response.

Bold: Reduced suceptibility or virological response.

Plain text: Reduced susceptibility in combination with other NNRTI-resistance mutations.

Abbreviations: nevirapine (NVP), efavirenz (EFV, etravirine (ETR), rilpivirine (RPV).

Synergistic combinations: V179D+K103R reduce NVP and EFV susceptibility >10-fold. Y181C+V179F cause high-level ETR and RPV resistance.

ETR genotypic susceptibility score (DRV package insert): Y181IV (3.0); L100I, K101P, Y181C, M230L (2.5); V90I, E138A, V179F, G190S (1.5); A98G, K101EH, V106I, V179DT, G190A (1.0); <2.5 susceptible; 2.5 to 3.0 intermediate; >3.0 high-level. V90I, A98G, V106I, E138A, V179DT, G190A/S have little effect on ETR susceptibility unless they occur with a bolded mutations.

E138 mutations: E138GQK are nonpolymorphic mutations associated with intermediate/high-level RPV resistance. E138A is a polymorphic mutation associated with low-level RPV resistance.

Additional accessory mutations: V90I (ETR), A98G (NVP, EFV, ETR, RPV), V108I, V179T (ETR), V179L (RPV), P225H (EFV), K238T (NVP, EFV), L318F.

References: hivdb.stanford.edu/dr-summary/resistance-notes/NNRTI/

Major Integrase Inhibitor (INI) Resistance Mutations

	66	92	138	140	143	147	148	155	263
Cons	**T**	**E**	**E**	**G**	**Y**	**S**	**Q**	**N**	**R**
RAL	AI**K**	**Q**	**KAT**	**SAC**	**RCH**		**HRK**	**H**	K
EVG	**AIK**	**Q**	**KAT**	**SAC**		**G**	**HRK**	**H**	K
DTG	K	Q	KAT	SAC			**HRK**	H	K

Bold underline: High-level reduced susceptibility or virological response.

Bold: Low-level reduced susceptibility or reduced suceptibility or virological response.

Plain text: Rreduced susceptibility in combination with other INI-resistance mutations.

Abbreviations: Dolutegravir (DTG), elvitegravir (EVG), raltegravir (RAL).

Additional mutations: H51Y, L74M, T97A, S153YF, QISC, G163RK, and S230R are relatively nonpolymorphic RAL and/or EVG-selected accessory resistance mutations. E92GV, G118R, F121Y, Y143KSGA, P145S, Q146P, and N155ST are rare nonpolymorphic IN mutations that reduce RAL and/or EVG susceptibility.

References: hivdb.stanford.edu/dr-summary/resistance-notes/INSTI/

Major Protease Inhibitor (PI) Resistance Mutations

	24	32	46	47	48	50	54	76	82	84	88	90
Cons	**D**	**V**	**M**	**I**	**G**	**I**	**I**	**L**	**V**	**I**	**N**	**L**
ATV/r		I	IL	V	**VM**	**L**	VTALM		ATFS	**V**	**S**	**M**
DRV/r		**I**		**VA**		**V**	**LM**	**V**	F	V		
LPV/r	I	**I**	IL	V**A**	VM	**V**	**VTALM**	**V**	**AFTS**	**V**		M

Bold underline: High-level reduced susceptibility or virological response.

Bold: Reduced suceptibility or virological response.

Plain text: Reduced susceptibility in combination with other PI-resistance mutations.

Abbreviations: atazanavir (ATV), darunavir (DRV), lopinavir (LPV), '/r' (ritonavir).

Additional mutations: L10F, V11I, K20TV, L23I, K43T, F53L, Q58E, A71IL, G73STCA, T74P, N83D, and L89V are common nonpolymorphic accessory mutations. L10RY, V11L, L24F, M46V, G48ASTLQ, F53Y, I54S, V82CM, I84AC, N88TG are rare nonpolymorphic variants.

Hypersusceptibility: I50L (each PI except ATV); L76V (ATV).

References: hivdb.stanford.edu/dr-summary/resistance-notes/PI/

HIV-1 RT and Protease Mutations for Drug-Resistance Surveillance*

NRTIs		NNRTIs		PIs	
M41	L	**L100**	I	**L23**	I
K65	R	**K101**	E,P	**L24**	I
D67	N,G,E	**K103**	N,S	**D30**	N
T69	D,Ins	**V106**	M,A	**V32**	I
K70	R,E	**V179**	F	**M46**	I,L
L74	V,I	**Y181**	C,I,V	**I47**	V,A
V75	M,T,A,S	**Y188**	L,H,C	**G48**	V,M
F77	L	**G190**	A,S,E	**I50**	V,L
Y115	F	**P225**	H	**F53**	F,Y
F116	Y	**M230**	L	**I54**	V,L,M,A,T,S
Q151	M			**G73**	S,T,C,A
M184	V,I			**L76**	V
L210	W			**V82**	A,T,F,S,C,M,L
T215	Y,F,I,S,C,D,V,E			**N83**	D
K219	Q,E,N,R			**I84**	V,A,C
				I85	V
				N88	D,S
				L90	M

*Bennett DE, Camacho RJ, Otelea D,et al. Drug Resistance Mutations for Surveillance of Transmitted HIV-1 Drug-Resistance: 2009 Update, PLoS One 2009;4:e4724.

Reference: hivdb.stanford.edu/page/who-resistance-list/