

PI Major Mutations:

G48V • I54V • V82A • I84V

PI Accessory Mutations:

None

PR Other Mutations:

L10I • G17E • N37D • L63P • C67S • A71V • I72IV • V77I • I93L

Protease Inhibitors	
atazanavir/r (ATV/r)	High-Level Resistance
darunavir/r (DRV/r)	Low-Level Resistance
fosamprenavir/r (FPV/r)	High-Level Resistance
indinavir/r (IDV/r)	High-Level Resistance
lopinavir/r (LPV/r)	High-Level Resistance
nelfinavir (NFV)	High-Level Resistance
saquinavir/r (SQV/r)	High-Level Resistance
tipranavir/r (TPV/r)	Intermediate Resistance

PR comments

Major

- G48V is a nonpolymorphic mutation selected by SQV and less often by IDV and LPV. It confers intermediate resistance to ATV but has little if any effect on LPV susceptibility.
- I54V is a non-polymorphic PI-selected mutation that contributes reduced susceptibility to each of the PIs except DRV.
- V82A is a non-polymorphic mutation selected primarily by IDV and LPV. It is associated with reduced susceptibility to LPV and to a lesser extent ATV. It increases DRV susceptibility.
- I84V is a nonpolymorphic substrate-cleft mutation selected by each of the PIs. I84V reduces susceptibility to LPV, ATV, and DRV.

Other

- L10I/V are polymorphic, PI-selected accessory mutations that increase the replication of viruses with other PI-resistance mutations.
- A71V/T are polymorphic, PI-selected accessory mutations that increase the replication of viruses with other PI-resistance mutations.

- There is evidence for low-level DRV resistance. If DRV is administered it should be used twice daily.

Drug resistance mutation scores of PI:

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Rule	ATV/r ÷	DRV/r ÷	FPV/r ÷	IDV/r ÷	LPV/r ÷	NFV ÷	SQV/r ÷	TPV/r ÷
G48V	30	0	0	10	10	30	60	0
I54V	15	0	10	15	15	20	15	20
I54V + V82A	10	0	10	10	10	10	10	0
V82A	15	0	15	30	30	30	15	0
I84V	60	15	60	60	30	60	60	30
Total	130	15	95	125	95	150	160	50

NRTI Mutations:

M41L • L74LV • T215Y

NNRTI Mutations:

V106VA • Y181YC

RT Other Mutations:

P4PS • D123E • I135T • I142T • D177E • V179I • G196E • K273Q • T286A • A288G • I293V • P294T • E297R • E298K • A299Q • E300S

Nucleoside Reverse Transcriptase Inhibitors		Non-nucleoside Reverse Transcriptase Inhibitors	
abacavir (ABC)	Intermediate Resistance	doravirine (DOR)	High-Level Resistance
zidovudine (AZT)	High-Level Resistance	efavirenz (EFV)	High-Level Resistance
stavudine (D4T)	High-Level Resistance	etravirine (ETR)	Intermediate Resistance
didanosine (DDI)	High-Level Resistance	nevirapine (NVP)	High-Level Resistance
emtricitabine (FTC)	Susceptible	rilpivirine (RPV)	Intermediate Resistance
lamivudine (3TC)	Susceptible		
tenofovir (TDF)	Low-Level Resistance		

RT comments

NRTI

- **M41L** is a TAM that usually occurs with T215Y. In combination, **M41L** plus T215Y confer intermediate / high-level resistance to AZT and d4T and contribute to reduced ddI, ABC and TDF susceptibility.
- **L74V** causes intermediate ABC resistance. L74I causes low-level ABC resistance.
- **T215Y/F** are TAMs that causes intermediate/high-level resistance to AZT and potentially low-level resistance to ABC and TDF.

NNRTI

- **V106A** is a non-polymorphic mutation that confers high-level resistance to NVP and DOR, and intermediate resistance to EFV. It is commonly selected in vitro and in vivo by DOR.
- **Y181C** is a non-polymorphic mutation selected in persons receiving NVP, ETR and RPV. It confers high-level resistance to NVP, intermediate resistance to ETR and RPV, and low-level resistance to EFV. It does not significantly reduce DOR susceptibility.

Other

- **V179I** is a polymorphic mutation that is frequently selected in persons receiving ETR and RPV. However, it has little, if any, direct effect on NNRTI susceptibility.
- This virus is predicted to have intermediate-level reduced susceptibility to **RPV**. The use of the combination of CAB/**RPV** should be considered to be contraindicated.

Mutation scoring: RT

HIVDB 9.5.1 (2023-11-05)

Drug resistance mutation scores of NRTI:

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Rule	ABC ⚡	AZT ⚡	D4T ⚡	DDI ⚡	FTC ⚡	3TC ⚡	TDF ⚡
<u>M41L</u>	5	15	15	10	0	0	5
<u>M41L + T215Y</u>	10	10	10	10	5	5	10
<u>L74LV</u>	30	0	0	60	0	0	0
<u>T215Y</u>	10	60	40	15	0	0	10
Total	55	85	65	95	5	5	25

Drug resistance mutation scores of NNRTI:

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Rule	DOR ⚡	EFV ⚡	ETR ⚡	NVP ⚡	RPV ⚡
<u>V106VA</u>	60	45	0	60	0
<u>Y181YC</u>	10	30	30	60	45
Total	70	75	30	120	45