

PI Major Mutations:None

PI Accessory Mutations:None

PR Other Mutations:

V11X

 • T12A • I13S • K14S • G16E • E35D • M36I • R41K • H69K • L89M

Protease Inhibitors	
atazanavir/r (ATV/r)	Susceptible
darunavir/r (DRV/r)	Susceptible
fosamprenavir/r (FPV/r)	Susceptible
indinavir/r (IDV/r)	Susceptible
lopinavir/r (LPV/r)	Susceptible
nelfinavir (NFV)	Susceptible
saquinavir/r (SQV/r)	Susceptible
tipranavir/r (TPV/r)	Susceptible

No drug resistance mutations were found for PI.

NRTI Mutations:

K65R

 •

S68G

 •

Δ69

NNRTI Mutations:

Y181C

 •

G190S

RT Other Mutations:E6D • V35T • V60I • K101Q • K122E • D123N • I135T • P170L • K173S • Q174K • D177E • V179I • T200A • Q207A • R211S •

K219X

 • L228S • W229L •

M230D

 • E233D •

Δ234

 •

H235S

 • P236S •

D237*

 • K238Q • V245E • P247Q •

N255M

 •

D256I

 •

I257Y

 • Q258R •

K259I

Nucleoside Reverse Transcriptase Inhibitors	
abacavir (ABC)	High-Level Resistance
zidovudine (AZT)	Susceptible
stavudine (D4T)	High-Level Resistance
didanosine (DDI)	High-Level Resistance
emtricitabine (FTC)	Intermediate Resistance
lamivudine (3TC)	Intermediate Resistance
tenofovir (TDF)	High-Level Resistance

Non-nucleoside Reverse Transcriptase Inhibitors	
doravirine (DOR)	Intermediate Resistance
efavirenz (EFV)	High-Level Resistance
etravirine (ETR)	Intermediate Resistance
nevirapine (NVP)	High-Level Resistance
rilpivirine (RPV)	High-Level Resistance

RT comments

NRTI

- K65R** confers intermediate reductions in susceptibility to TDF, ABC, and 3TC/FTC. It increases AZT susceptibility. In NRTI-experienced, INSTI-naïve patients with **K65R**, TDF+3TC+DTG is usually highly effective and more effective than AZT/3TC/DTG. However, in patients receiving TDF+3TC+DTG, there is a risk of emergent DTG resistance that does not arise in NRTI-naïve patients receiving TDF+3TC+DTG.
- S68G** is a polymorphic mutation that is often selected in combination with K65R. It partially restores the replication defect associated with K65R.
- Amino acid deletions between codons 67 and 70 are rare and usually occur in combination with multiple TAMs, K65R, or the Q151M mutation complex. Deletions at position 67 are more often associated with multiple TAMs. Deletions at positions 69 and 70 are more often associated with K65R or the Q151M mutation complex. Deletions at codon 68 are extremely rare and less well characterized.

NNRTI

- 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.
- G190S** is a non-polymorphic mutation that confers high-level resistance to NVP and EFV. It may also be associated low-levels reductions in DOR susceptibility. It does not appear to be selected by ETR or RPV or to reduce their in vitro susceptibility.

Other

- K101Q** is a relatively non-polymorphic mutation that is weakly selected in persons receiving NVP and EFV. It is of uncertain phenotypic and clinical significance.
- 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.
- M230L is an uncommon non-polymorphic mutation selected in persons receiving EFV, NVP, and RPV. It causes intermediate to high-level resistance to each of the NNRTIs. M230I is a rare mutation selected by RPV. Its effects on NNRTI susceptibility have not been well studied. It also often occurs as a result of APOBEC-mediated G-to-A hypermutation resulting in viruses that are likely to be noninfectious. **M230D** is a highly unusual mutation at this position.
- L234I is a nonpolymorphic mutation selected in persons receiving NVP and EFV. It is also selected in vitro by ETR and DOR. In combination with V106A, it is associated with high-level DOR resistance. Its effect on susceptibility when it occurs alone has not been well characterized. **L234del** is a highly unusual mutation at this position.
- P236L is a rare mutation selected commonly by DLV, which appears to have little if any effect on current NNRTIs. **P236S** is a highly unusual mutation at this position.
- K238T/N are uncommon non-polymorphic mutations selected in persons receiving NVP and EFV usually in combination with K103N. Alone, K238T/N appear to have minimal effects on NNRTI susceptibility. **K238Q** is a highly unusual mutation at this position.

Drug resistance mutation scores of NRTI:

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Rule	ABC ⚡	AZT ⚡	D4T ⚡	DDI ⚡	FTC ⚡	3TC ⚡	TDF ⚡
<u>K65R</u>	45	-10	60	60	30	30	50
<u>T69del</u>	15	0	30	30	15	15	15
<u>K65R + S68G</u>	0	0	0	0	0	0	5
Total	60	-10	90	90	45	45	70

Drug resistance mutation scores of NNRTI:

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Rule	DOR ⚡	EFV ⚡	ETR ⚡	NVP ⚡	RPV ⚡
<u>Y181C</u>	10	30	30	60	45
<u>Y181C + G190S</u>	10	0	10	0	10
<u>G190S</u>	20	60	10	60	15
Total	40	90	50	120	70