

PI Major Mutations:None

PI Accessory Mutations:L24F

PR Other Mutations:V11K • T12M • I13V • K14V • I15N • G16E • Q18G • L19G • K20C • E21G • A22K • D25R • T26C • V32G • M36I • R41K • P44S • G48W • I50K • G51I • G52A • F53* • I54F • K55N • V56D • R57P • Q58S • Y59* • Q61L • L63E • I64M • H69K • T74R • 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)	Potential Low-Level Resistance
saquinavir/r (SQV/r)	Susceptible
tipranavir/r (TPV/r)	Susceptible

PR comments

Accessory

- L24I is a non-polymorphic mutation selected by IDV and LPV. It contributes reduced susceptibility to ATV and LPV. **L24F/M** are uncommon non-polymorphic PI-selected mutations. **L24F** has a susceptibility profile similar to L24I.

Other

- V32I is a non-polymorphic mutation selected by LPV, ATV, and DRV which is associated with reduced susceptibility to each of these PIs. **V32G** is a highly unusual mutation at this position.
- 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. G48M is an uncommon 2-base-pair nonpolymorphic substrate-cleft mutation nearly always selected in viruses with multiple PI-resistance mutations. It has a resistance profile similar to G48V. G48A/S/T/Q/L are extremely rare nonpolymorphic PI-selected mutations nearly always selected in viruses with multiple PI-resistance mutations. **G48W** is a highly unusual mutation at this position.
- I50V is a nonpolymorphic mutation selected by FPV, LPV and DRV. It reduces susceptibility to LPV and DRV. I50L is a non-polymorphic mutation selected by ATV. It causes high-level resistance to ATV and increases susceptibility to LPV and DRV. **I50K** is a highly unusual mutation at this position.
- I54V is a non-polymorphic PI-selected mutation that contributes reduced susceptibility to each of the PIs except DRV. I54A/T/S are non-polymorphic PI-selected mutations that occur almost exclusively in viruses with multiple PI-resistance mutations. I54A/T/S are associated with reduced susceptibility to each of the PIs except DRV. I54M/L are non-polymorphic mutations selected primarily by FPV and DRV. I54M/L reduce susceptibility to LPV, ATV, and DRV. **I54F** is a highly unusual mutation at this position.

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 ÷
L24F	5	0	5	5	5	10	5	0

NRTI Mutations:K219N

NNRTI Mutations:V106I • Y188L • G190A • P225H • F227L

RT Other Mutations:V35T • V60I • S105F • V108G • L109P • V111G • D113G • A114G • Y115* • S117L • V118A • K122G • D123E • Y127D • T128S • A129C • T131P • I132L • S134G • I135P • N137X • T139N • I142S • Y144N • Q145H • N147M • L149X • Q151P • S156T • Q161X • S162K • K173* • Q174X • D177E • V179I • G196R • R199T • I202V • E204X • Q207A • L210X • R211S • P217S • K220S • H221I • Q222R • K223R • E224P • P226S • L228M • W229E • M230* • G231A • Y232H • E233L • L234Q • H235* • P236Q • D237S • K238A • W239M • T240S • V241T

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

RT comments

NRTI

- K219E/Q/N/R are accessory TAMs that usually occur in combination with multiple other TAMs.

NNRTI

- V106I occurs in 1% to 2% of viruses from untreated persons. It contributes to reduced NNRTI susceptibility only in combination with other NNRTI-resistance mutations. It is commonly selected in persons receiving DOR in combination with mutations at position 227.
- Y188L is a non-polymorphic mutation that confers high-level resistance to NVP, EFV, RPV, and DOR, and potentially low-level resistance to ETR.
- G190A is a non-polymorphic mutation that causes high-level resistance to NVP and intermediate resistance to EFV. It does not significantly reduce susceptibility to RPV, ETR, or DOR.
- P225H is a non-polymorphic EFV-selected mutation that usually occurs in combination with K103N. The combination of **P225H** and K103N synergistically reduces NVP, EFV and DOR susceptibility.
- F227L is a non-polymorphic mutation that usually occurs in combination with V106A. It is selected in vivo and in vitro with both NVP and DOR. In this context it is associated with high-level reductions in NVP and DOR susceptibility and intermediate reductions in EFV susceptibility. F227I/V are extremely rare mutations that have been selected in vitro by DOR.

Other

- V108I is a relatively non-polymorphic accessory mutation selected in vitro and/or in vivo with each of the NNRTIs. It appears to contribute to reduced susceptibility to most NNRTIs only in combination with other NNRTI-resistance mutations. **V108G** is a highly unusual mutation at this position.
- I132M is an extremely rare non-polymorphic mutation associated with uncertain amount of reduced NVP and EFV susceptibility. **I132L** is a more common, non-polymorphic NNRTI-selected mutation that has not been well studied.
- Q151M causes intermediate/high-level resistance to AZT and ABC, and low-level resistance to TDF, 3TC and FTC. In combination with two or more accessory mutations at positions 62, 73, 77, and 116, it confers high-level resistance to AZT and ABC and intermediate resistance to TDF, 3TC and FTC. Q151L is an extremely rare transitional mutation that may precede the emergence of the Q151M. **Q151P** is a highly unusual mutation at this position.
- 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.
- 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. **L234Q** 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. **P236Q** 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. **K238A** 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>K219N</u>	5	10	10	5	0	0	5

Drug resistance mutation scores of NNRTI:

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Rule	DOR	EFV	ETR	NVP	RPV
<u>V106I</u>	10	0	10	10	10
<u>Y188L</u>	60	60	10	60	60
<u>P225H</u>	20	45	0	45	0
<u>F227L</u>	60	15	0	30	0
<u>G190A</u>	0	45	10	60	15
Total	150	165	30	205	85