Drug resistance interpretation: PR

HIVDB 9.5.1 (2023-11-05)

PI Major Mutations: None
PI Accessory Mutations: K20T
PR Other Mutations: V11X • T12C • I13S • K14Q • I15V • E35D • M36I • N37D • R41K • R57K • D60E • H69Q • 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)	Low-Level Resistance
saquinavir/r (SQV/r)	Susceptible
tipranavir/r (TPV/r)	Susceptible

PR comments

Accessory

- **K20T** is a non-polymorphic accessory PI-selected mutation associated with reduced susceptibility to ATV and LPV.

Mutation scoring: PR

HIVDB 9.5.1 (2023-11-05)

Drug resistance mutation scores of PI: Download CSV

Rule	ATV/r	DRV/r	FPV/r	IDV/r	LPV/r	NFV	SQV/r	TPV/r
K20T	5	0	5	5	0	15	5	0

Drug resistance interpretation: RT

HIVDB 9.5.1 (2023-11-05)

NRTI Mutations: K65R • L74I • Y115F • K219Q
NNRTI Mutations: L100I • K103N • Y188H • K238T
RT Other Mutations: V35R • V60I • D121H • K122E • I135T • T139A • K173L • Q174K • D177E • V179M • M184X • G196E • R199S • T200S • K201I • Q207A • L210* • R211A • W212G • F214L • D218G • K223R • E224N • P225L • Δ226-227 • L228X • W229F • M230F • Y232W • E233I • L234* • H235A • P236H • D237L • W239V • T240D • V241S • P243T • P247Q • E248S • D250K • S251A • W252D • T253C • V254H • N255E

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-naive 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-naive patients receiving TDF+3TC+DTG.
- L74V causes intermediate ABC resistance. **L74I** causes low-level ABC resistance.
- **Y115F** causes intermediate resistance to ABC and low-level resistance to TDF.
- **K219E/Q/N/R** are accessory TAMS that usually occur in combination with multiple other TAMs.

NNRTI

- **L100I** is a non-polymorphic mutation that usually occurs in combination with K103N. In this setting it confers high-level resistance to NVP, EFV, and RPV and intermediate resistance to ETR and DOR.
- **K103N** is a non-polymorphic mutation that confers high-level reductions in NVP and EFV susceptibility. It is the most commonly transmitted DRM.
- **Y188H** is a non-polymorphic mutation selected in persons receiving NVP and EFV. It causes about 5 to 10-fold reduced susceptibility to NVP and EFV. It appears to cause little if any reduction in susceptibility to RPV, ETR, or DOR.
- **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.

Other

- V179D/E are somewhat polymorphic accessory NNRTI-selected mutation. In combination with other NNRTI DRMs, they appear to contribute low-levels of reduced susceptibility to each of the NNRTIs. In particular, the combinations of K103R/V179D and V106I/V179D act synergistically to reduce NVP and EFV susceptibility. V179F is a non-polymorphic mutation selected in combination with Y181C in persons receiving ETR. Alone it has little effect on NNRTI susceptibility, however in combination with Y181C it is associated with high-level reductions in ETR and RPV susceptibility. V179T is a rare non-polymorphic mutation occasionally selected in persons receiving NNRTIs. It is associated with minimal, if any, reduction in ETR and RPV susceptibility. V179L is a rare non-polymorphic mutation listed as a RPV-associated resistance mutation by the FDA package insert. Its effects on NNRTI susceptibility have not been well studied. **V179M** is an unusual mutation at this position.
- 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. **P225L** is a highly unusual mutation at this position.
- 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. F227C is a nonpolymorphic mutation selected in persons receiving DOR and rarely in persons receiving ETR and RPV. It usually occurs in combination with other DRMs and in this setting has consistently been associated with the highest possible levels of DOR resistance. It is also usually associated with intermediate or high-level reductions in susceptibility to NVP, EFV, ETR, and RPV. **F227del** is a highly unusual mutation at this position.
- 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. **M230F** 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. **P236H** is a highly unusual mutation at this position.

Mutation scoring: RT

HIVDB 9.5.1 (2023-11-05)

Drug resistance mutation scores of NRTI: Download CSV

Rule	ABC	AZT	D4T	DDI	FTC	3TC	TDF
K65R	45	-10	60	60	30	30	50
L74I	15	0	0	60	0	0	5
Y115F	30	0	0	0	0	0	15
K219Q	5	10	10	5	0	0	5
Total	95	0	70	125	30	30	75

Drug resistance mutation scores of NNRTI: Download CSV

Rule	DOR	EFV	ETR	NVP	RPV
L100I	15	60	30	60	60
L100I + K103N	15	0	0	0	0
Y188H	5	30	0	60	0
K103N	0	60	0	60	0
K238T	0	30	0	30	0
Total	35	180	30	210	60