

Drug resistance interpretation: PR

HIVDB 9.5.1 (2023-11-05)

PI Major Mutations:

None

PI Accessory Mutations:

None

PR Other Mutations:

T12N • I13P • K14V • I15R • G16R • Q18K • K20R • M36I • R41K • D60E • Q61N • I62V • L63E • I64V • E65D

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

PR comments

Other

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K20R is a highly polymorphic PI-selected accessory mutation that increases replication fitness in viruses with PI-resistance mutations.

Mutation scoring: PR	HIVDB 9.5.1 (2023-11-05)
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No drug resistance mutations were found for PI.

Drug resistance interpretation: RT	HIVDB 9.5.1 (2023-11-05)
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NRTI Mutations:	K65R • S68G • M184I		
NNRTI Mutations:	K103N • L234I		
RT Other Mutations:	V35T • T39M • K46Q • K49R • V60I • V90I • K104R • D121Y • K122E • I135M • D177E • I178M • Y181L • Q182S • T200A • Q207E • T216I • K219X • P225X • P226S • M230V • Y232L • E233* • P236A • P243T • V245S • P247S • D250A • S251A • W252G • T253L • V254S • N255* • D256Y • I257T • Q258E • K259L • L260V • V261G • G262N • K263Q • L264M • N265G • W266* • A267Q • S268I		
Nucleoside Reverse Transcriptase Inhibitors		Non-nucleoside Reverse Transcriptase Inhibitors	
abacavir (ABC)	High-Level Resistance	doravirine (DOR)	Intermediate Resistance
zidovudine (AZT)	Susceptible	efavirenz (EFV)	High-Level Resistance
stavudine (D4T)	Intermediate Resistance	etravirine (ETR)	Susceptible
didanosine (DDI)	High-Level Resistance	nevirapine (NVP)	High-Level Resistance
emtricitabine (FTC)	High-Level Resistance	rilpivirine (RPV)	Susceptible
lamivudine (3TC)	High-Level Resistance		
tenofovir (TDF)	Intermediate 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.
- **S68G** is a polymorphic mutation that is often selected in combination with K65R. It partially restores the replication defect associated with K65R.
- **M184V/I** cause high-level in vitro resistance to 3TC and FTC and low/intermediate resistance to ABC (3-fold reduced susceptibility). **M184V/I** are not contraindications to continued treatment with 3TC or FTC because they increase susceptibility to AZT and TDF and are associated with clinically significant reductions in HIV-1 replication.

NNRTI

- **K103N** is a non-polymorphic mutation that confers high-level reductions in NVP and EFV susceptibility. It is the most commonly transmitted DRM.
- **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.

Other

- **V90I** is a polymorphic accessory mutation weakly selected by each of the NNRTIs. It is associated with minimal, if any, detectable reduction in NNRTI susceptibility.
- 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. Y181I/V are 2-base pair non-polymorphic mutations selected by NVP and ETR. They cause high-level resistance to NVP, ETR, and RPV but not EFV. Their effects on DOR have not been well-characterized. **Y181L** 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. **M230V** 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. **P236A** is a highly unusual mutation at this position.

Mutation scoring: RT

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Drug resistance mutation scores of NRTI:

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Rule	ABC ↕	AZT ↕	D4T ↕	DDI ↕	FTC ↕	3TC ↕	TDF ↕
<a href="#">K65R</a>	45	-10	60	60	30	30	50
<a href="#">M184I</a>	15	-10	-10	10	60	60	-10
<a href="#">K65R + S68G</a>	0	0	0	0	0	0	5
Total	60	-20	50	70	90	90	45

Drug resistance mutation scores of NNRTI:

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Rule	DOR ↕	EFV ↕	ETR ↕	NVP ↕	RPV ↕
<a href="#">L234I</a>	45	0	0	0	0
<a href="#">K103N</a>	0	60	0	60	0
Total	45	60	0	60	0