Drug resistance interpretation: PR

HIVDB 9.5.1 (2023-11-05)

PI Major Mutations: None
PI Accessory Mutations: None
PR Other Mutations: R8X • P9L • L10A • V11C • T12S • I13N • K14S • I15Q • G16E • E35D • M36I • R41K • G48W • I50K • G51T • G52P • F53K • I54F • K55N • V56D • R57P • Q58S • Y59K • Q61L • L63D • I64K

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

- L10F is a common non-polymorphic, PI-selected accessory mutation associated with reduced in vitro susceptibility to LPV and DRV. L10I/V are polymorphic, PI-selected accessory mutations that increase the replication of viruses with other PI-resistance mutations. L10R/Y are rare, non-polymorphic PI-selected mutations. Their effects on PI susceptibility have not been well studied. **L10A** 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.

Mutation scoring: PR

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No drug resistance mutations were found for PI.

Drug resistance interpretation: RT

HIVDB 9.5.1 (2023-11-05)

NRTI Mutations: K65R • S68G • K70T • M184V
NNRTI Mutations: K103N • G190A
RT Other Mutations: P4S • V35T • T39K • K101R • D123E • A158S • K173S • Q174K • D177E • T200X • Q207A • R211S • P225X • E233* • L234T • L246T • P247A • N255M • D256I • I257Y • Q258R • K259S • L260S • V261G • G262K • K263S • L264N • N265G • W266Q • A267Q • S268I • Q269Y • I270P • Y271G • A272L • G273E • I274* • K275Y

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

Non-nucleoside Reverse Transcriptase Inhibitors	
doravirine (DOR)	Susceptible
efavirenz (EFV)	High-Level Resistance
etravirine (ETR)	Potential Low-Level Resistance
nevirapine (NVP)	High-Level Resistance
rilpivirine (RPV)	Low-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.
- **S68G** is a polymorphic mutation that is often selected in combination with K65R. It partially restores the replication defect associated with K65R.
- **K70/E/Q/N/T/S/G** cause low-leve resistance to ABC and TDF.
- **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.
- **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.

Other

- 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. **L234T** is a highly unusual mutation at this position.
- This virus is predicted to have low-level reduced susceptibility to **RPV**. The use of the combination of CAB/**RPV** should be considered to be relatively contraindicated.

Mutation scoring: RT

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Drug resistance mutation scores of NRTI: Download CSV

Rule	ABC	AZT	D4T	DDI	FTC	3TC	TDF
K65R	45	-10	60	60	30	30	50
K70T	15	0	15	15	10	10	15
M184V	15	-10	-10	10	60	60	-10
K70T + M184V	0	0	10	0	0	0	10
K65R + S68G	0	0	0	0	0	0	5
Total	75	-20	75	85	100	100	70

Drug resistance mutation scores of NNRTI: Download CSV

Rule	DOR	EFV	ETR	NVP	RPV
K103N	0	60	0	60	0
G190A	0	45	10	60	15
Total	0	105	10	120	15