Drug resistance interpretation: PR

HIVDB 9.5.1 (2023-11-05)

PI Major Mutations: M46I 99% (prev=1,858) • I84V 99% (prev=1,291)

PI Accessory Mutations: L10F 99% (prev=823) • L89T 100% (prev=1,158)

PR Other Mutations: I13V 94% (prev=644) • K20I 99% (prev=897) • L33I 100% (prev=1,368) • E35N 99% (prev=1,858) • M36I 100% (prev=1,858) • R41K 99% (prev=1,827) • L63P 100% (prev=1,325) • H69K 98% (prev=1,240) • T74S 99% (prev=1,269)

Protease Inhibitors	
atazanavir/r (ATV/r)	High-Level Resistance
darunavir/r (DRV/r)	Low-Level Resistance
fosamprenavir/r (FPV/r)	High-Level Resistance
indinavir/r (IDV/r)	High-Level Resistance
lopinavir/r (LPV/r)	Intermediate Resistance
nelfinavir (NFV)	High-Level Resistance
saquinavir/r (SQV/r)	High-Level Resistance
tipranavir/r (TPV/r)	Intermediate Resistance

PR comments

Major

- **M46I/L** are relatively non-polymorphic PI-selected mutations. In combination with other PI-resistance mutations, they are associated with reduced susceptibility to each of the PIs except DRV.
- **I84V** is a nonpolymorphic substrate-cleft mutation selected by each of the PIs. **I84V** reduces susceptibility to LPV, ATV, and DRV.

Accessory

- **L10F** is a common non-polymorphic, PI-selected accessory mutation associated with reduced in vitro susceptibility to LPV and DRV.
- L89V is a nonpolymorphic accessory mutation weakly selected by each of the PIs. It appears to be minimally associated with reduced PI susceptibility. **L89T** is an uncommon non-polymorphic PI-selected mutation selected primarily by ATV.

Other

- **K20I** is the consensus amino acid in subtype G and CRF02_AG. In subtypes B and C, **K20I** is a PI-selected mutation of uncertain effects on currently used PIs.
- **L33I/V** are minimally polymorphic mutations that do not appear to be selected by PIs or to reduce their susceptibility.
- **T74S** is a PI-selected accessory mutation that is polymorphic in most non-B subtypes.

- There is evidence for low-level **DRV** resistance. If **DRV** is administered it should be used twice daily.

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
M46I	10	0	10	10	10	30	10	5
I84V	60	15	60	60	30	60	60	30
L10F	0	5	15	10	5	15	0	0
Total	70	20	85	80	45	105	70	35

Drug resistance interpretation: RT

HIVDB 9.5.1 (2023-11-05)

NRTI Mutations: K70R 96% (prev=1,105) • M184V 98% (prev=2,573) • K219Q 99% (prev=2,029)

NNRTI Mutations: P225H 87.88%, H: 12% (prev=2,016)

RT Other Mutations: P4H 98% (prev=2,110) • E6A 100% (prev=1,264) • K11T 100% (prev=1,264) • V35T 100% (prev=1,233) • T39N 100% (prev=1,220) • I94L 100% (prev=1,133) • K122E 100% (prev=1,196) • D123N 99% (prev=1,196) • I135V 90%, V: 11% (prev=2,017) • S162C 100% (prev=2,958) • K173S 99% (prev=2,725) • Q174K 100% (prev=2,725) • T200A 99% (prev=2,067) • Q207A 100% (prev=1,775) • R211S 100% (prev=2,042) • F214FL L: 79%, F: 20% (prev=2,241) • L228R 99% (prev=1,982) • V245E 98% (prev=654) • D250E 93% (prev=560) • K512KR K: 52%, R: 44% (prev=52) • S519N 100% (prev=87) • Q524K 100% (prev=30) • K527E 93% (prev=93) • E529D 100% (prev=106) • A534S 99% (prev=113) • A554T 100% (prev=115) • K558R 100% (prev=103)

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

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

RT comments

NRTI

- **K70R** is a TAM that confers intermediate resistance to AZT and contributes to reduced ABC and TDF susceptibility in combination with other TAMs.
- **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.
- **K219E/Q/N/R** are accessory TAMS that usually occur in combination with multiple other TAMs.

NNRTI

- **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.

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
K70R	5	30	15	10	0	0	5
M184V	15	-10	-10	10	60	60	-10
K219Q	5	10	10	5	0	0	5
Total	25	30	15	25	60	60	0

Drug resistance mutation scores of NNRTI: Download CSV

Rule	DOR	EFV	ETR	NVP	RPV
P225PH	20	45	0	45	0

Drug resistance interpretation: IN

HIVDB 9.5.1 (2023-11-05)

INSTI Major Mutations: R263K

INSTI Accessory Mutations: A49G

IN Other Mutations: K14R • A21T • A23V • V31I • L45V • M50I • I72V • I84M • T124A • T125A • G134N • K136N • G163A • V201I • I220IV • S230SG • L234I • V249VI • S283G • D288N

Integrase Strand Transfer Inhibitors

bictegravir (BIC)	Intermediate Resistance
cabotegravir (CAB)	Intermediate Resistance
dolutegravir (DTG)	Intermediate Resistance
elvitegravir (EVG)	Intermediate Resistance
raltegravir (RAL)	Low-Level Resistance

IN comments

Major

- **R263K** is a nonpolymorphic mutation selected in vitro by EVG, DTG, BIC, and CAB. It occurs in a high proportion of persons who develop VF and emergent HIVDR while receiving DTG. Alone, it reduces DTG, BIC, and CAB susceptibility about 2-fold.

Accessory

- **A49G** is a rare nonpolymorphic accessory INSTI-selected mutation with uncertain effects on INSTI susceptibility.

Other

- **M50I** is a highly polymorphic mutation, which has a prevalence of 3% to 34% in INSTI-naïve persons depending on subtype. It has been selected in vitro by DTG and BIC in combination with R263K. It may contribute to reduced DTG and CAB susceptibility in combination with R263K.
- This virus is predicted to have intermediate-level reduced susceptibility to **CAB**. The use of the combination of **CAB**/RPV should be considered to be contraindicated.
- There is evidence for intermediate **DTG** resistance. If **DTG** is used, it should be administered twice daily.

Mutation scoring: IN

HIVDB 9.5.1 (2023-11-05)

Drug resistance mutation scores of INSTI: Download CSV

Rule	BIC	CAB	DTG	EVG	RAL
R263K	30	30	30	30	25