Drug resistance interpretation: PR

HIVDB 9.5.1 (2023-11-05)

PI Major Mutations: None
PI Accessory Mutations: None
PR Other Mutations: T12M • G16E • L19V • E35D • M36I • R41K • R57RK • L63TV • H69K • I72V • 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)	Susceptible
saquinavir/r (SQV/r)	Susceptible
tipranavir/r (TPV/r)	Susceptible

Mutation scoring: PR

HIVDB 9.5.1 (2023-11-05)

No drug resistance mutations were found for PI.

Drug resistance interpretation: RT

HIVDB 9.5.1 (2023-11-05)

NRTI Mutations: D67N • T215CL • K219Q
NNRTI Mutations: K103N • Y181V • H221Y
RT Other Mutations: P4H • V21I • V35T • T39M • V60I • T69N • K122E • D123N • I132IL • I135T • K173S • Q174K • V179I • E194EK • T200A • I202V • Q207E • R211RK • F214L • V245E • D250E • A554S

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

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

RT comments

NRTI

- **D67N** is a non-polymorphic TAM associated with low-level resistance to AZT.
- T215Y/F are TAMs that causes intermediate/high-level resistance to AZT and potentially low-level resistance to ABC and TDF. **T215S/C/D/E/I/V/N/A/L** do not reduce NRTI susceptibility but arise from viruses that once contained T215Y/F. The presence of one of these revertant mutations suggests that the patient may have once been infected with a virus containing T215Y/F.
- **K219E/Q/N/R** are accessory TAMS that usually occur in combination with multiple other TAMs.

NNRTI

- **K103N** is a non-polymorphic mutation that confers high-level reductions in NVP and EFV susceptibility. It is the most commonly transmitted DRM.
- **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.
- **H221Y** is a non-polymorphic accessory mutation selected primarily by NVP, RPV, and DOR. It frequently occurs in combination with Y181C.

Other

- **T69N/S/A/I/E** are relatively non-polymorphic mutations weakly selected in persons receiving NRTIs. They may minimally contribute reduced AZT susceptibility.
- 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.
- **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.

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
D67N	5	15	15	5	0	0	5
K219Q	5	10	10	5	0	0	5
T215CL	0	10	20	10	0	0	0
Total	10	35	45	20	0	0	10

Drug resistance mutation scores of NNRTI: Download CSV

Rule	DOR	EFV	ETR	NVP	RPV
Y181V	20	30	60	60	60
Y181V + H221Y	10	0	0	0	10
H221Y	10	10	10	15	15
K103N	0	60	0	60	0
Total	40	100	70	135	85

Drug resistance interpretation: IN — HIVDB 9.5.1 (2023-11-05)

INSTI Major Mutations: None
INSTI Accessory Mutations: None
IN Other Mutations: K14KR • R20RK • V31I • I60M • L68LM • I72V • T112V • T124A • T125A • V126F • G134N • I135V • D167E • G193D • V201I • T218TS • K219N • N222K • L234V • S283SG

Integrase Strand Transfer Inhibitors	
bictegravir (BIC)	Susceptible
cabotegravir (CAB)	Susceptible
dolutegravir (DTG)	Susceptible
elvitegravir (EVG)	Susceptible
raltegravir (RAL)	Susceptible

Mutation scoring: IN — HIVDB 9.5.1 (2023-11-05)

No drug resistance mutations were found for INSTI.

Drug resistance interpretation: PR

HIVDB 9.5.1 (2023-11-05)

PI Major Mutations: None
PI Accessory Mutations: None
PR Other Mutations: K20R • M36I • R41K • I62V • L63Q • E65D • I72V

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

- **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)

No drug resistance mutations were found for PI.

Drug resistance interpretation: RT

HIVDB 9.5.1 (2023-11-05)

NRTI Mutations: S68G • L74I • M184V • L210W • T215Y
NNRTI Mutations: K101P • K103NS • E138K • V179L
RT Other Mutations: G18GD • V35T • T39K • K49ER • E53D • T58TS • V60I • D121CH • K122E • I142T • S162SN • E169D • R172RK • D177E • I178L • T200M • E203K • Q207E • R211K • P243PS • I244V • V245KT • D250E • S268C • A272P • K277R • L282C • L283I • T286A • A288T • I293V • V314VI • S319SR • Q520QA • Q524QE • A534S • A554N

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

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

RT comments

NRTI

- **S68G** is a polymorphic mutation that is often selected in combination with K65R. It partially restores the replication defect associated with K65R.
- L74V causes intermediate ABC resistance. **L74I** causes low-level ABC resistance.
- **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.
- **L210W** is a TAM that usually occurs in combination with M41L and T215Y. The combination of M41, **L210W** and T215Y causes high-level resistance to AZT and intermediate resistance to ABC and TDF.
- **T215Y/F** are TAMs that causes intermediate/high-level resistance to AZT and potentially low-level resistance to ABC and TDF.

NNRTI

- **K101P** is a non-polymorphic mutation that confers high-level resistance to NVP, EFV, RPV, and ETR. Its does not appear to reduce DOR susceptibility.
- **K103N** is a non-polymorphic mutation that confers high-level reductions in NVP and EFV susceptibility. It is the most commonly transmitted DRM.
- **K103S** is a non-polymorphic mutation that causes high-level reductions in NVP susceptibility but intermediate reductions in EFV susceptibility. Because **K103S** is a 2-bp change from the wildtype K and a 1-bp change from K103N, persons with **K103S** may be likely to have once had K103N.
- **E138K** is a non-polymorphic mutation selected in a high proportion of persons receiving RPV. It reduces RPV susceptibility 2 to 3-fold. In combination with K101E or the NRTI-resistance mutation M184I, it is sufficient to cause VF on a first-line RPV-containing regimen. **E138K** causes low-level cross-resistance to ETR.
- **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.

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
L74I	15	0	0	60	0	0	5
M184V	15	-10	-10	10	60	60	-10
L210W	5	15	15	10	0	0	5
L210W + T215Y	10	10	10	10	0	0	10
T215Y	10	60	40	15	0	0	10
Total	55	75	55	105	60	60	20

Drug resistance mutation scores of NNRTI: Download CSV

Rule	DOR	EFV	ETR	NVP	RPV
K101P	10	60	60	60	60
E138K	5	10	10	10	45
K103NS	0	60	0	60	0
V179L	0	10	10	10	15
Total	15	140	80	140	120

Drug resistance interpretation: IN — HIVDB 9.5.1 (2023-11-05)

INSTI Major Mutations: T66I • G118R • E138K

INSTI Accessory Mutations: L74M

IN Other Mutations: S17N • L63V • I72V • E87ED • L101I • T112V • I113V • S119ST • T124A • T125A • V126M • K156G • K173R • V176VL • I182V • G193N • S195C • V201I • L234I

Integrase Strand Transfer Inhibitors

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

IN comments

Major

- **T66A/I** are non-polymorphic mutations selected in persons receiving EVG, RAL, and DTG usually in combination with other INSTI-resistance mutations. They cause moderate reductions in EVG susceptibility but do not appear to reduce susceptibility to other INSTIs.
- **G118R** is a nonpolymorphic mutation reported in a significant proportion of persons with VF and emergent HIVDR in persons receiving a DTG-containing regimen. It has occasionally been reported in persons receiving other INSTIs. It is associated with 5-10-fold reduced susceptibility to RAL, EVG, DTG and CAB, and 2-3 fold reduced susceptibility to BIC.
- **E138K/A/T** are common nonpolymorphic accessory resistance mutations selected in patients receiving RAL, EVG, CAB, and DTG. Alone they do not reduce INSTI susceptibility. However, they contribute to reduced susceptibility in combination with other mutations particularly those at position 148.

Accessory

- **L74M** is a common polymorphic INSTI-resistance mutation. It has a prevalence between 1% and 5% among INSTI-naive persons depending on subtype. It appears to be selected by each of the INSTIs. Alone it does not reduce INSTI susceptibility. However, in combination with other INSTI-resistance mutations, it contributes reduced susceptibility to each of the INSTIs.
- There is evidence for high-level **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
T66I	5	10	5	60	15
L74M + G118R	10	10	10	10	10
G118R	30	60	50	60	60
G118R + E138K	10	10	10	10	10
E138K	10	10	10	15	15
Total	65	100	85	155	110