

PI Major Mutations:

M46I

100%  
cons:6,802

•

I50V

100%  
cons:6,802

•

I54V

100%  
cons:7,322

•

V82VA

100%  
cons:12,802

PI Accessory Mutations:

None

PR Other Mutations:

L10I

0.00%  
cons:1,042

•

L15V

100%  
cons:2,002

•

L19I

100%  
cons:2,008

•

K20R

100%  
cons:2,805

•

E35D

100%  
cons:3,808

•

M36I

100%  
cons:3,808

•

R41K

100%  
cons:6,252

•

I62V

100%  
cons:8,022

•

L63S

100%  
cons:8,022

•

I64V

100%  
cons:8,022

•

A71T

100%  
cons:15,008

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)	High-Level Resistance
nelfinavir (NFV)	High-Level Resistance
saquinavir/r (SQV/r)	High-Level Resistance
tipranavir/r (TPV/r)	Low-Level 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.
- I50V is a nonpolymorphic mutation selected by FPV, LPV and DRV. It reduces susceptibility to LPV and DRV.
- I54V is a non-polymorphic PI-selected mutation that contributes reduced susceptibility to each of the PIs except DRV.
- V82A is a non-polymorphic mutation selected primarily by IDV and LPV. It is associated with reduced susceptibility to LPV and to a lesser extent ATV. It increases DRV susceptibility.

Other

- L10I/V are polymorphic, PI-selected accessory mutations that increase the replication of viruses with other PI-resistance mutations.
- K20R is a highly polymorphic PI-selected accessory mutation that increases replication fitness in viruses with PI-resistance mutations.
- A71V/T are polymorphic, PI-selected accessory mutations that increase the replication of viruses with other PI-resistance mutations.

- 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:

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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
M46I + V82VA	10	0	10	10	10	10	10	0
I54V	15	0	10	15	15	20	15	20
I54V + V82VA	10	0	10	10	10	10	10	0
V82VA	15	0	15	30	30	30	15	0
I50V	0	20	60	0	30	15	15	-5
Total	60	20	115	75	105	115	75	20

Drug resistance interpretation: RT

HIVDB 9.5.1 (2023-11-05)

NRTI Mutations:

D67G

100%  
cons:1,277

•

S68G

100%  
cons:1,278

•

K70R

100%  
cons:1,762

•

M184V

100%  
cons:2,362

•

T215FY

0.00%  
cons:2,362

•

K219E

100%  
cons:3,100

NNRTI Mutations:

K101E

100%  
cons:3,705

•

G190C

100%  
cons:2,802

RT Other Mutations:

P4T

100%  
cons:11,001

•

E28K

100%  
cons:6,807

•

K32E

100%  
cons:11,002

•

V35T

100%  
cons:12,700

•

T39TA

0.00%  
cons:2,800

•

E40ED

0.00%  
cons:2,802

•

K49R

100%  
cons:2,802

•

V60I

100%  
cons:3,805

•

V118V

0.00%  
cons:3,277

•

T139TA

0.00%  
cons:2,802

•

E169D

100%  
cons:3,802

•

D177E

100%  
cons:1,262

•

G196S

100%  
cons:12,000

•

E203K

100%  
cons:2,573

•

Q207E

100%  
cons:3,809

•

R211K

100%  
cons:12,002

•

V245K

100%  
cons:6,100

•

D250E

100%  
cons:12,072

•

A272P

100%  
cons:12,000

•

K277R

100%  
cons:1,807

•

Q278H

100%  
cons:1,802

•

L282C

100%  
cons:6,809

•

L283I

100%  
cons:6,809

•

I293V

100%  
cons:6,172

•

E297D

100%  
cons:1,807

•

A534S

100%  
cons:1903

•

A554N

100%  
cons:12,000

Nucleoside Reverse Transcriptase Inhibitors		Non-nucleoside Reverse Transcriptase Inhibitors	
abacavir (ABC)	High-Level Resistance	doravirine (DOR)	Low-Level Resistance
zidovudine (AZT)	High-Level Resistance	efavirenz (EFV)	High-Level Resistance
stavudine (D4T)	High-Level Resistance	etravirine (ETR)	Low-Level Resistance
didanosine (DDI)	High-Level Resistance	nevirapine (NVP)	High-Level Resistance
emtricitabine (FTC)	High-Level Resistance	rilpivirine (RPV)	Intermediate Resistance
lamivudine (3TC)	High-Level Resistance		
tenofovir (TDF)	Intermediate Resistance		

RT comments

NRTI

- **D67N** is a non-polymorphic TAM associated with low-level resistance to AZT. **D67G/E/S/T/H** are non-polymorphic NRTI-selected mutations that generally occur in viruses with multiple TAMs.
- **S68G** is a polymorphic mutation that is often selected in combination with K63R. It partially restores the replication defect associated with K63R.
- **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.
- **T215V/F** are TAMs that causes intermediate/high-level resistance to AZT and potentially low-level resistance to ABC and TDF.
- **K219E/Q/N/R** are accessory TAMs that usually occur in combination with multiple other TAMs.

NNRTI

- **K101E** is a non-polymorphic accessory mutation that confers intermediate resistance to NVP and RPV and low-level reductions in susceptibility to EFV, ETR, and DOR when it occurs with other NNRTI-resistance mutations.
- **G190C/T/V** are rare non-polymorphic mutations that confer high-level resistance to NVP and EFV. Their effects on ETR, RPV, and DOR susceptibility are not known.

Other

- **V118I** is a polymorphic accessory NRTI-resistance mutation that often occurs in combination with multiple TAMs.
- This virus is predicted to have intermediate-level reduced susceptibility to **RPV**. The use of the combination of CAB/**RPV** should be considered to be contraindicated.

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 ↕
<u>D67G</u>	5	15	10	5	0	0	5
<u>D67G + K70R + M184V + K219E</u>	10	0	0	0	0	0	0
<u>D67G + K70R + K219E</u>	10	15	10	10	10	10	10
<u>D67G + T215FY + K219E</u>	5	5	5	5	0	0	5
<u>K70R</u>	5	30	15	10	0	0	5
<u>M184V</u>	15	-10	-10	10	60	60	-10
<u>T215FY</u>	10	60	40	15	0	0	10
<u>K219E</u>	5	10	10	5	0	0	5
<u>K70R + T215FY</u>	0	0	5	5	0	0	0
Total	65	125	85	65	70	70	30

Drug resistance mutation scores of NNRTI: Download CSV

Rule	DOR ↕	EFV ↕	ETR ↕	NVP ↕	RPV ↕
<u>K101E</u>	15	15	15	30	45
<u>G190C</u>	10	60	10	60	10
Total	25	75	25	90	55

Drug resistance interpretation: IN

HIVDB 9.5.1 (2023-11-05)

INSTI Major Mutations: [G118R](#) <sup>100%</sup><sub>seen:148</sub> • [E138K](#) <sup>100%</sup><sub>seen:183</sub> • [R263K](#) <sup>99%</sup><sub>seen:1,107</sub>  
INSTI Accessory Mutations: [L74LM](#) <sup>1</sup><sub>seen:707</sub> <sup>1</sup><sub>seen:149</sub> • [G149A](#) <sup>10%</sup><sub>seen:470</sub>  
IN Other Mutations: [KTR](#) <sup>100%</sup><sub>seen:1,030</sub> • [S17N](#) <sup>100%</sup><sub>seen:385</sub> • [M50LV](#) <sup>1</sup><sub>seen:402</sub> <sup>1</sup><sub>seen:1,011</sub> • [L63LI](#) <sup>1</sup><sub>seen:402</sub> <sup>1</sup><sub>seen:1,011</sub> • [G94GA](#) <sup>1</sup><sub>seen:402</sub> <sup>1</sup><sub>seen:1,011</sub> • [L101I](#) <sup>10%</sup><sub>seen:1,011</sub> • [T112I](#) <sup>10%</sup><sub>seen:385</sub> • [T124A](#) <sup>100%</sup><sub>seen:385</sub> • [T125A](#) <sup>10%</sup><sub>seen:404</sub> • [V126VA](#) <sup>1</sup><sub>seen:108</sub> <sup>1</sup><sub>seen:1,011</sub> • [I135IL](#) <sup>1</sup><sub>seen:707</sub> <sup>1</sup><sub>seen:1,011</sub> • [K156N](#) <sup>10%</sup><sub>seen:385</sub> • [V201I](#) <sup>100%</sup><sub>seen:1,107</sub> • [K211Q](#) <sup>10%</sup><sub>seen:1,107</sub> • [Q216QR](#) <sup>1</sup><sub>seen:1,107</sub> <sup>1</sup><sub>seen:1,107</sub> • [L234V](#) <sup>100%</sup><sub>seen:1,107</sub> • [D256E](#) <sup>10%</sup><sub>seen:1,107</sub> • [E287A](#) <sup>100%</sup><sub>seen:1,107</sub>

Integrase Strand Transfer Inhibitors	
<b>bictegravir (BIC)</b>	High-Level Resistance
<b>cabotegravir (CAB)</b>	High-Level Resistance
<b>dolutegravir (DTG)</b>	High-Level Resistance
<b>elvitegravir (EVG)</b>	High-Level Resistance
<b>raltegravir (RAL)</b>	High-Level Resistance

IN comments

Major

- **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.
- **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

- **L74M** is a common polymorphic INSTI-resistance mutation. It has a prevalence between 1% and 5% among INSTI-naïve 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.
- **G149A** is an accessory nonpolymorphic mutation that has been reported primarily in combination with Q148 mutations. It appears to have no effect by itself but in combination with mutations at positions 140 and 148, it leads to contributes reduced susceptibility to DTG, CAB, and BIC.

- There is evidence for high-level **DTG** resistance. If **DTG** is used, it should be administered twice daily.

Drug resistance mutation scores of INSTI:

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Rule	BIC ⚡	CAB ⚡	DTG ⚡	EVG ⚡	RAL ⚡
<u>L74LM + G118R</u>	10	10	10	10	10
<u>G118R</u>	30	60	50	60	60
<u>G118R + E138K</u>	10	10	10	10	10
<u>E138K</u>	10	10	10	15	15
<u>R263K</u>	30	30	30	30	25
Total	90	120	110	125	120