

PI Major Mutations:

PI Accessory Mutations:

PI Other Mutations:

M46I93%
cov=38,172

•

I54V93%
cov=35,707

•

L76V93%
cov=23,249

•

V82A94%
cov=20,426

L33F93%
cov=40,545

L10V94%
cov=31,160

•

I13V99%
cov=31,557

•

L19V93%
cov=33,373

•

R41K98%
cov=39,000

•

K55R92%
cov=35,386

•

R57K94%
cov=31,381

•

L63V93%
cov=27,989

•

I64V94%
cov=27,995

•

T74A90%
cov=24,487

•

V77I93%
cov=23,176

•

L89M97%
cov=19,435

•

T91S93%
cov=16,806

Protease Inhibitors	
atazanavir/r (ATV/r)	High-Level Resistance
darunavir/r (DRV/r)	Low-Level Resistance
lopinavir/r (LPV/r)	High-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.
- I54V is a non-polymorphic PI-selected mutation that contributes reduced susceptibility to each of the PIs except DRV.
- L76V is a non-polymorphic mutation selected by IDV, LPV and DRV and reduces susceptibility to LPV and 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.

Accessory

- L33F is a relatively non-polymorphic accessory mutation selected by each of the PIs. In combination with other PI-resistance mutations, it is associated with reduced susceptibility to LPV, ATV, and DRV.

Other

- L10I/V 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.

Drug resistance mutation scores of PI:

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Rule

ATV/r ⚡

DRV/r ⚡

LPV/r ⚡

L33F	5	5	5
M46I	10	0	10
M46I + V82A	10	0	10
I54V	15	0	15
I54V + V82A	10	0	10
V82A	15	0	30
L76V	0	20	30
M46I + L76V	0	0	10
Total	65	25	120

NRTI Mutations:

M41L 95% cov=18,934 • D67N 93% cov=19,720 • K70R 96% cov=19,912 • V75M 95% cov=19,870 • M184V 97% cov=22,526 • L210W 96% cov=24,032 • T215Y 98% cov=23,605 • K219E 95% cov=25,401

NNRTI Mutations:

V108V I: 67%, V: 33% • Y188L 95% cov=22,927

RT Other Mutations:

P4PS P: 80%, S: 18% • V8T 94% cov=20,120 • V35M 95% cov=20,262 • K49R 97% cov=20,266 • V60I 98% cov=20,962 • D121H 97% cov=24,617 • K122E 98% cov=24,686 • K166Q 98% cov=24,686 • E169KR R: 73%, R: 21% • K173E 93% cov=22,886 • Q174R 93% cov=22,884 • D177E 98% cov=21,833 • I178L 91% cov=21,845 • T200TI T: 73%, I: 23% • Q207E 97% cov=22,263 • R211K 97% cov=24,035 • L228H 96% cov=26,275 • V245K 96% cov=27,090 • D250E 97% cov=28,111 • A272P 98% cov=28,084 • V276T 90% cov=28,303 • K277KR R: 58%, R: 38% • K281R 99% cov=28,035 • L282C 97% cov=28,005 • L283I 96% cov=28,067 • T286A 97% cov=32,170 • I293V 98% cov=33,675

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

RT comments

NRTI

- **M41L** is a TAM that usually occurs with T215Y. In combination, **M41L** plus T215Y confer intermediate / high-level resistance to AZT and d4T and contribute to reduced ddI, ABC and TDF susceptibility.
- **D67N** is a non-polymorphic TAM associated with low-level resistance to AZT.
- **K70R** is a TAM that confers intermediate resistance to AZT and contributes to reduced ABC and TDF susceptibility in combination with other TAMs.
- **V75T/M/A/S** are nonpolymorphic accessory NRTI-selected mutations. They appear to have minimal phenotypic effects on AZT, 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.
- **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.
- **K219E/Q/N/R** are accessory TAMS that usually occur in combination with multiple other TAMs.

NNRTI

- **V108I** is a relatively non-polymorphic accessory mutation selected in vitro and/or in vivo with each of the NNRTIs. It appears to contribute to reduced susceptibility to most NNRTIs only in combination with other NNRTI-resistance mutations.
- **Y188L** is a non-polymorphic mutation that confers high-level resistance to NVP, EFV, RPV, and DOR, and potentially low-level resistance to ETR.

Drug resistance mutation scores of NRTI:

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Rule	ABC ↕	AZT ↕	FTC ↕	3TC ↕	TDF ↕
<u>M41L</u>	5	15	0	0	5
<u>M41L + D67N + T215Y</u>	5	5	0	0	5
<u>M41L + M184V + T215Y</u>	10	0	0	0	0
<u>M41L + L210W</u>	10	10	0	0	10
<u>M41L + L210W + T215Y</u>	10	0	15	15	10
<u>M41L + T215Y</u>	10	10	5	5	10
<u>D67N</u>	5	15	0	0	5
<u>D67N + K70R + M184V + K219E</u>	10	0	0	0	0
<u>D67N + K70R + K219E</u>	10	15	10	10	10
<u>D67N + T215Y + K219E</u>	5	5	0	0	5
<u>K70R</u>	5	30	0	0	5
<u>M184V</u>	15	-10	60	60	-10
<u>L210W</u>	5	15	0	0	5
<u>L210W + T215Y</u>	10	10	0	0	10
<u>T215Y</u>	10	60	0	0	10
<u>K219E</u>	5	10	0	0	5
<u>V75M</u>	0	10	0	0	0
<u>K70R + T215Y</u>	0	0	0	0	0
Total	130	200	90	90	85

Drug resistance mutation scores of NNRTI:

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Rule	DOR ↕	EFV ↕	ETR ↕	NVP ↕	RPV ↕
<u>V108VI</u>	10	10	0	15	0
<u>Y188L</u>	60	60	10	60	60
Total	70	70	10	75	60