Drug resistance interpretation: PR

HIVDB 9.5.1 (2023-11-05)

PI Major Mutations: M46I · I54V · L76V · V82A
PI Accessory Mutations: L33F
PR Other Mutations: L10X · V11N · T12A · I13S · K14T · I15D · G16R · L19V · K20Q · R41K · K55R · R57K · L63V · I64V · T74A · V77I · L89M · T91S

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)	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.
- **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.
- 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
L33F	5	5	10	5	5	10	5	10
M46I	10	0	10	10	10	30	10	5
M46I + V82A	10	0	10	10	10	10	10	0
I54V	15	0	10	15	15	20	15	20
I54V + V82A	10	0	10	10	10	10	10	0
V82A	15	0	15	30	30	30	15	0
L76V	0	20	60	30	30	10	0	-5
M46I + L76V	0	0	10	10	10	10	0	0
Total	65	25	135	120	120	130	65	30

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

NRTI Mutations: M41L · D67N · K70R · V75M · L210W · T215Y

NNRTI Mutations: V108I · Y188L

RT Other Mutations: V8T · V35M · K49R · N57H · V60I · D121H · K122E · Q145P · K166H · E169S · F171L · R172E · Q174E · N175T · P176Q · D177N · V179G · Q182H · Y183M · M184W · D185M · D186I · I195X · T200* · K201N · Δ202 · L205D · R206* · Q207G · R211K · Δ219 · K220X · H221* · Q222H · K223Q · E224K · P225N · P226S · L228H · Y232M · Δ233 · L234X · H235S · P236S · D237* · K238Q · P243R · V245I · P247L · K249* · D250K · S251L · W252D · T253C · V254H · N255D · D256Y · I257R · Q258R · K259S

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

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

- **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.

Other

- V179D/E are somewhat polymorphic accessory NNRTI-selected mutation. In combination with other NNRTI DRMs, they appear to contribute low-levels of reduced susceptibility to each of the NNRTIs. In particular, the combinations of K103R/V179D and V106I/V179D act synergistically to reduce NVP and EFV susceptibility. V179F is a non-polymorphic mutation selected in combination with Y181C in persons receiving ETR. Alone it has little effect on NNRTI susceptibility, however in combination with Y181C it is associated with high-level reductions in ETR and RPV susceptibility. V179T is a rare non-polymorphic mutation occasionally selected in persons receiving NNRTIs. It is associated with minimal, if any, reduction in ETR and RPV susceptibility. 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. **V179G** is an unusual mutation at this position.
- 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. **M184W** is a highly unusual mutation at this position.
- K219E/Q/N/R are accessory TAMS that usually occur in combination with multiple other TAMs. K219W is an uncommon NRTI-selected mutation. **K219del** is an unusual mutation at this position.
- 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. **P225N** is a highly unusual mutation at this position.
- P236L is a rare mutation selected commonly by DLV, which appears to have little if any effect on current NNRTIs. **P236S** is a highly unusual mutation at this position.
- K238T/N are uncommon non-polymorphic mutations selected in persons receiving NVP and EFV usually in combination with K103N. Alone, K238T/N appear to have minimal effects on NNRTI susceptibility. **K238Q** is a highly unusual mutation at this position.

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
M41L	5	15	15	10	0	0	5
M41L + D67N + T215Y	5	5	5	5	0	0	5
M41L + L210W	10	10	10	10	0	0	10
M41L + L210W + T215Y	10	0	0	0	15	15	10
M41L + T215Y	10	10	10	10	5	5	10
D67N	5	15	15	5	0	0	5
K70R	5	30	15	10	0	0	5
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
V75M	0	10	30	15	0	0	0
K70R + T215Y	0	0	5	5	0	0	0
Total	75	180	170	105	20	20	75

Drug resistance mutation scores of NNRTI: Download CSV

Rule	DOR	EFV	ETR	NVP	RPV
V108I	10	10	0	15	0
Y188L	60	60	10	60	60
Total	70	70	10	75	60