Drug resistance interpretation: PR

HIVDB 9.5.1 (2023-11-05)

PI Major Mutations: M46MI • G48V • I54T • V82A
PI Accessory Mutations: K43T
PR Other Mutations: L10I • K20KR • E35D • M36I • L63P • I64V

Protease Inhibitors	
atazanavir/r (ATV/r)	High-Level Resistance
darunavir/r (DRV/r)	Susceptible
fosamprenavir/r (FPV/r)	Intermediate 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.
- **G48V** is a nonpolymorphic mutation selected by SQV and less often by IDV and LPV. It confers intermediate resistance to ATV but has little if any effect on LPV susceptibility.
- **I54A/T/S** are non-polymorphic PI-selected mutations that occur almost exclusively in viruses with multiple PI-resistance mutations. **I54A/T/S** are associated with 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.

Accessory

- **K43T** is a nonpolymorphic accessory mutation selected by ATV and LPV. Its phenotypic effect on currently used PIs is uncertain.

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.

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
M46MI	10	0	10	10	10	30	10	5
M46MI + V82A	10	0	10	10	10	10	10	0
G48V	30	0	0	10	10	30	60	0
I54T	15	0	10	15	15	20	15	20
I54T + V82A	10	0	10	10	10	10	10	0
V82A	15	0	15	30	30	30	15	0
K43T	0	0	0	0	0	10	0	10
Total	90	0	55	85	85	140	120	35

Drug resistance interpretation: RT

HIVDB 9.5.1 (2023-11-05)

NRTI Mutations: M41L • E44D • D67N • T69D • M184V • L210W • T215Y • K219KN
NNRTI Mutations: A98G • K103N • Y181C
RT Other Mutations: E6D • T39A • K43EQ • V118VI • K122E • I142T • K166R • G196E • Q197QK • I202V • R211K

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)	High-Level Resistance
lamivudine (3TC)	High-Level Resistance
tenofovir (TDF)	High-Level Resistance

Non-nucleoside Reverse Transcriptase Inhibitors	
doravirine (DOR)	Intermediate Resistance
efavirenz (EFV)	High-Level Resistance
etravirine (ETR)	Intermediate 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.
- **E44D** is a relatively non-polymorphic accessory mutation; E44A is a nonpolymorphic accessory mutation. Each usually occurs with multiple TAMs.
- **D67N** is a non-polymorphic TAM associated with low-level resistance to AZT.
- **T69D** is a nonpolymorphic mutation selected by early NRTIs that does not appear to reduce AZT, ABC, or TDF susceptibility.
- **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

- **A98G** is a non-polymorphic accessory mutation associated with low-level reduced susceptibility to each of the NNRTIs.
- **K103N** is a non-polymorphic mutation that confers high-level reductions in NVP and EFV susceptibility. It is the most commonly transmitted DRM.
- **Y181C** is a non-polymorphic mutation selected in persons receiving NVP, ETR and RPV. It confers high-level resistance to NVP, intermediate resistance to ETR and RPV, and low-level resistance to EFV. It does not significantly reduce DOR susceptibility.

Other

- **V118I** is a polymorphic accessory NRTI-resistance mutation that often occurs in combination with multiple TAMs.

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 + E44D + L210W + T215Y	5	5	5	5	0	0	5
M41L + D67N + T215Y	5	5	5	5	0	0	5
M41L + M184V + T215Y	10	0	0	0	0	0	0
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
D67N + T215Y + K219KN	5	5	5	5	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
K219KN	5	10	10	5	0	0	5
T69D	0	0	10	30	0	0	0
Total	110	150	140	130	80	80	75

Drug resistance mutation scores of NNRTI: Download CSV

Rule	DOR	EFV	ETR	NVP	RPV
A98G	15	15	10	30	15
A98G + Y181C	5	5	5	5	5
K103N + Y181C	5	0	0	0	0
Y181C	10	30	30	60	45
K103N	0	60	0	60	0
Total	35	110	45	155	65