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

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PI Major Mutations: None PI Accessory Mutations: None

PR Other Mutations: T12K - I13S - K14V - I15E - G16R - Q18T - L19E - L24\* - E35D - M36I - R41K - L89M

## Protease Inhibitors

Susceptible atazanavir/r (ATV/r) Susceptible darunavir/r (DRV/r) 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

Drug resistance interpretation: RT

Mutation scoring: PR

abacavir (ABC)

No drug resistance mutations were found for PI.

NRTI Mutations: M41L - S68G - M184V - T215S

NNRTI Mutations: K103N - P225H - L234I

E6A - K20R - V35T - T39N - V60I - A985 - K122E - I135T - I167X - K173S - Q174K - D177E - Y181L - Q182S - T200A - I202\* - E203R - E204V - L205E - R206T - Q207S - Δ208-209 - L210M - R211K - P217L - K219X - P226H - L228I - W229D - M230G - G231I - Y232\* - E233L - H235\* - P236Q - D237\* - K238Q - P236C - P RT Other Mutations:

Non-nucleoside Reverse Transcriptase Inhibitors

W239S - T240L - V241\* - O242S - P243C - I244R - V245K - L246E - P247A - E248D - K249C - D250H - S251D - W252Y - T253D - V254\* - N255\* - D256N

# **Nucleoside Reverse Transcriptase Inhibitors**

#### Low-Level Resistance doravirine (DOR) High-Level Resistance Low-Level Resistance High-Level Resistance efavirenz (EFV)

zidovudine (AZT) Intermediate Resistance stavudine (D4T) etravirine (ETR) Susceptible Intermediate Resistance High-Level Resistance didanosine (DDI) nevirapine (NVP) High-Level Resistance rilpivirine (RPV) Susceptible emtricitabine (FTC)

lamivudine (3TC) High-Level Resistance

tenofovir (TDF) Susceptible

#### 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 ddl, ABC and TDF susceptibility.
- \$686 is a polymorphic mutation that is often selected in combination with K65R. It partially restores the replication defect associated with K65R.
- M184V/I cause high-level in vitro resistance to ATC and FTC and low/intermediate resistance to ABC (3-fold reduced susceptibility). M184V/I are not contrained treatment with 3TC or FTC because they increase susceptibility to AZT and TDF and are associated with clinically significant reductions in HIV-1 replication.
- T215Y/F are TAMs that causes intermediate/high-level resistance to AZT and potentially low-level with a virus containing T215Y/F.

### NNRTI

K103N is a non-polymorphic mutation that confers high-level reductions in NVP and EFV susceptibility. It is the most commonly transmitted DRM.

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- 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.
- L234I is a nonpolymorphic mutation selected in persons receiving NVP and EFV. It is also selected in vitro by ETR and DOR. In combination with V106A, it is associated with high-level DOR resistance. Its effect on susceptibility when it occurs alone has not been well characterized.

# Other

- Y181C is a non-polymorphic mutation selected in persons receiving NVP, ETR and RPV, and low-level resistance to ETV. It does not significantly reduce DOR susceptibility. 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. Y181L is a highly unusual mutation at this position.
- M230L is an uncommon non-polymorphic mutation selected in persons receiving EFV, NVP, and RPV. It causes intermediate to high-level resistance to each of the NNRTIs. hypermutation resulting in viruses that are likely to be noninfectious. M2306 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. P236Q 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

Drug resistance mutation scores of NRTI:

Rule	ABC ≑	AZT ≎	D4T ≎	DDI 🗘	FTC ‡	зтс ≎	TDF 0
M41L	5	15	15	10	0	0	5
M184V	15	-10	-10	10	60	60	-10
M41L + T215S	0	10	5	5	0	0	0
T215S	0	10	20	10	0	0	0
Total	20	25	30	35	60	60	-5

Drug resistance mutation scores of NNRTI:

Rule	DOR \$	EFV \$	ETR ÷	NVP ≑	RPV ÷
K103N + P225H	10	0	0	0	0
P225H	20	45	0	45	0
L234I	45	0	0	0	0
<u>K103N</u>	0	60	0	60	0
Total	75	105	0	105	0

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