Drug resistance interpretation: RT

HIVDB 9.5.1 (2023-11-05)

NRTI Mutations: K65KR • D67DN • S68SG • M184V • K219E

NNRTI Mutations: L100I • K103N • V179T

RT Other Mutations: P4S • K11T • K20R • V21I • E28EK • K32KE • V35T • T39K • E40D • K122E • D123N • K166KN • K173S • Q174K • D177E • T200A • I202V • Q207A • R211K • P243S • V245Q

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

- **K65R** confers intermediate reductions in susceptibility to TDF, ABC, and 3TC/FTC. It increases AZT susceptibility. In NRTI-experienced, INSTI-naive patients with **K65R**, TDF+3TC+DTG is usually highly effective and more effective than AZT/3TC/DTG. However, in patients receiving TDF+3TC+DTG, there is a risk of emergent DTG resistance that does not arise in NRTI-naive patients receiving TDF+3TC+DTG.
- **D67N** is a non-polymorphic TAM associated with low-level resistance to AZT.
- **S68G** 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 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.
- **K219E/Q/N/R** are accessory TAMS that usually occur in combination with multiple other TAMs.

NNRTI

- **L100I** is a non-polymorphic mutation that usually occurs in combination with K103N. In this setting it confers high-level resistance to NVP, EFV, and RPV and intermediate resistance to ETR and DOR.
- **K103N** is a non-polymorphic mutation that confers high-level reductions in NVP and EFV susceptibility. It is the most commonly transmitted DRM.
- **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.

Mutation scoring: RT

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Drug resistance mutation scores of NRTI: Download CSV

Rule	ABC	AZT	D4T	DDI	FTC	3TC	TDF
K65KR	45	-10	60	60	30	30	50
D67DN	5	15	15	5	0	0	5
M184V	15	-10	-10	10	60	60	-10
K219E	5	10	10	5	0	0	5
K65KR + S68SG	0	0	0	0	0	0	5
Total	70	5	75	80	90	90	55

Drug resistance mutation scores of NNRTI: Download CSV

Rule	DOR	EFV	ETR	NVP	RPV
L100I	15	60	30	60	60
L100I + K103N	15	0	0	0	0
K103N	0	60	0	60	0
Total	30	120	30	120	60