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

NRTI Mutations: K65R · S68G · V75A
NNRTI Mutations: L100I · K103N · F227L
RT Other Mutations: P1K · S3R · P4R · I5V · K22N · Q23P · P25S · V35T · T39K · K43E · K49R · P55F · N57Y · R78T · Q85R · E89Q · G112S · D121Y · K122E · D123E · T128S · N137Y · T165L · P170H · D177E · I178M · M184E · G190R · T200R · K201N · I202T · E203Q · E204Q · Q207E · L210* · R211T · F214L · T216S · P217S · K219* · E224E_T · P226I · L228V · W229R · K238Q · V241A · Q242P · P243L · I244S · V245* · K249* · D250G · S251R · W252L · T253D · V254C · N255* · D256L · I257N · Q258I

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

Non-nucleoside Reverse Transcriptase Inhibitors	
doravirine (DOR)	High-Level 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.
- **S68G** is a polymorphic mutation that is often selected in combination with K65R. It partially restores the replication defect associated with K65R.
- **V75T/M/A/S** are nonpolymorphic accessory NRTI-selected mutations. They appear to have minimal phenotypic effects on AZT, ABC, and TDF.

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.
- **F227L** is a non-polymorphic mutation that usually occurs in combination with V106A. It is selected in vivo and in vitro with both NVP and DOR. In this context it is associated with high-level reductions in NVP and DOR susceptibility and intermediate reductions in EFV susceptibility. F227I/V are extremely rare mutations that have been selected in vitro by DOR.

Other

- 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. **M184E** 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
K65R	45	-10	60	60	30	30	50
V75A	0	10	30	15	0	0	0
K65R + S68G	0	0	0	0	0	0	5
Total	45	0	90	75	30	30	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
F227L	60	15	0	30	0
K103N	0	60	0	60	0
Total	90	135	30	150	60