Drug resistance interpretation: PR

HIVDB 9.5.1 (2023-11-05)

PI Major Mutations: None
PI Accessory Mutations: None
PR Other Mutations: I13V • K14R • G16E • K20I • E35N • M36I • R41K • I62V • L63S • I64L • H69K • K70KR • T74S • L89M

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

PR comments

Other

- **K20I** is the consensus amino acid in subtype G and CRF02_AG. In subtypes B and C, **K20I** is a PI-selected mutation of uncertain effects on currently used PIs.
- **T74S** is a PI-selected accessory mutation that is polymorphic in most non-B subtypes.

Mutation scoring: PR

HIVDB 9.5.1 (2023-11-05)

No drug resistance mutations were found for PI.

Drug resistance interpretation: RT

HIVDB 9.5.1 (2023-11-05)

NRTI Mutations: K65R • S68SG • M184V
NNRTI Mutations: K103S • V106VI • V179T • Y181YC • G190A
RT Other Mutations: I5IV • K11Q • K20KR • E28A • V35T • T39D • A98AS • K122E • D123N • I135T • I142V • K173ST • Q174K • D177E • V189VI • T200A • I202V • Q207A • P243T • V245Q • A554S • I556V • K558KR

Nucleoside Reverse Transcriptase Inhibitors	
abacavir (ABC)	High-Level Resistance
zidovudine (AZT)	Susceptible
stavudine (D4T)	Intermediate 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)	High-Level 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.
- **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.

NNRTI

- **K103S** is a non-polymorphic mutation that causes high-level reductions in NVP susceptibility but intermediate reductions in EFV susceptibility. Because **K103S** is a 2-bp change from the wildtype K and a 1-bp change from K103N, persons with **K103S** may be likely to have once had K103N.
- **V106I** occurs in 1% to 2% of viruses from untreated persons. It contributes to reduced NNRTI susceptibility only in combination with other NNRTI-resistance mutations. It is commonly selected in persons receiving DOR in combination with mutations at position 227.
- **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.
- **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.
- **G190A** is a non-polymorphic mutation that causes high-level resistance to NVP and intermediate resistance to EFV. It does not significantly reduce susceptibility to RPV, ETR, or DOR.

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
M184V	15	-10	-10	10	60	60	-10
K65R + S68SG	0	0	0	0	0	0	5
Total	60	-20	50	70	90	90	45

Drug resistance mutation scores of NNRTI: Download CSV

Rule	DOR	EFV	ETR	NVP	RPV
V106VI	10	0	10	10	10
V106VI + Y181YC	5	0	0	0	10
Y181YC	10	30	30	60	45
Y181YC + G190A	10	0	10	0	10
K103S	0	45	0	60	0
G190A	0	45	10	60	15
V179T + Y181YC	0	0	10	0	10
Total	35	120	70	190	100

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

INSTI Major Mutations: E138K • G140A • Q148K

INSTI Accessory Mutations: None

IN Other Mutations: K14R • V31I • D41N • I60M • Q62QE • I72V • V79VI • Q95HR • T112TIS • I113V • T124A • T125A • V126F • G134D • K136Q • K156KN • D167E • K173R • V201I • Q221S • L234V • S283G

Integrase Strand Transfer Inhibitors	
bictegravir (BIC)	High-Level Resistance
cabotegravir (CAB)	High-Level Resistance
dolutegravir (DTG)	High-Level Resistance
elvitegravir (EVG)	High-Level Resistance
raltegravir (RAL)	High-Level Resistance

IN comments

Major

- **E138K/A/T** are common nonpolymorphic accessory resistance mutations selected in patients receiving RAL, EVG, CAB, and DTG. Alone they do not reduce INSTI susceptibility. However, they contribute to reduced susceptibility in combination with other mutations particularly those at position 148.
- **G140S/A/C** are non-polymorphic mutations that usually occur with Q148 mutations. Alone, they have minimal effects on INSTI susceptibility. However, in combination with Q148 mutations they are associated with high-level resistance to RAL and EVG and intermediate reductions in DTG and BIC susceptibility.
- **Q148H/K/R** are nonpolymorphic mutations reported in persons receiving RAL, EVG, CAB, and DTG. They nearly always occur in combination with G140A/S or E138K. In this setting they are associated with near complete resistance to RAL and EVG, high-levels of reduction in CAB susceptibility, and low-to-intermediate reductions in DTG and BIC susceptibility.

- There is evidence for high-level **DTG** resistance. If **DTG** is used, it should be administered twice daily.

Mutation scoring: IN — HIVDB 9.5.1 (2023-11-05)

Drug resistance mutation scores of INSTI: Download CSV

Rule	BIC	CAB	DTG	EVG	RAL
E138K	10	10	10	15	15
E138K + G140A	10	15	10	15	15
E138K + Q148K	10	20	10	0	0
G140A	10	10	10	30	30
G140A + Q148K	10	20	10	0	0
Q148K	30	50	30	60	60
Total	80	125	80	120	120