

Drug resistance interpretation: PR

HNDB 9.5.1 (2023-11-05)

PI Major Mutations:None

PI Accessory Mutations:None

PR Other Mutations:

L10I

100%
seen:1,585

•

I13V

100%
seen:1,405

•

G16E

100%
seen:1,247

•

M36I

100%
seen:1,058

•

P39Q

100%
seen:1,011

•

R41K

100%
seen:1,112

•

I62IV

91.62%
seen:2,587

•

L63A

100%
seen:2,022

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

- L10I/V are polymorphic, PI-selected accessory mutations that increase the replication of viruses with other PI-resistance mutations.

Mutation scoring: PR

HNDB 9.5.1 (2023-11-05)

No drug resistance mutations were found for PI.

Drug resistance interpretation: RT

HNDB 9.5.1 (2023-11-05)

NRTI Mutations:

D67N

100%
seen:3,011

•

M184V

100%
seen:1,740

•

T215Y

77%
seen:2,011

•

K219E

100%
seen:2,352

NNRTI Mutations:

Y188L

100%
seen:1,126

RT Other Mutations:

I2V

100%
seen:1,016

•

V35T

100%
seen:492

•

T39A

100%
seen:492

•

V60I

100%
seen:393

•

I94L

87%
seen:2,717

•

D121H

100%
seen:1,401

•

K122E

100%
seen:1,401

•

I135T

100%
seen:2,001

•

I142IV

91.40%
seen:2,244

•

D177E

100%
seen:1,400

•

V179VI

91.40%
seen:1,351

•

T200A

100%
seen:1,707

•

Q207E

100%
seen:1,707

•

R211K

100%
seen:1,301

•

V245Q

100%
seen:341

•

D250E

100%
seen:179

•

A554N

100%
seen:19

Nucleoside Reverse Transcriptase Inhibitors				Non-nucleoside Reverse Transcriptase Inhibitors			
abacavir (ABC)	Intermediate Resistance			doravirine (DOR)	High-Level Resistance		
zidovudine (AZT)	High-Level Resistance			efavirenz (EFV)	High-Level Resistance		
stavudine (D4T)	High-Level Resistance			etravirine (ETR)	Potential Low-Level Resistance		
didanosine (DDI)	Intermediate Resistance			nevirapine (NVP)	High-Level Resistance		
emtricitabine (FTC)	High-Level Resistance			rilpivirine (RPV)	High-Level Resistance		
lamivudine (3TC)	High-Level Resistance						
tenofovir (TDF)	Low-Level Resistance						

RT comments

NRTI

- D67N is a non-polymorphic TAM associated with low-level resistance to AZT.
- M184V/I cause high-level in vitro resistance to 3TC 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.
- 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

- Y188L is a non-polymorphic mutation that confers high-level resistance to NVP, EFV, RPV, and DOR, and potentially low-level resistance to ETR.

Other

- V179I is a polymorphic mutation that is frequently selected in persons receiving ETR and RPV. However, it has little, if any, direct effect on NNRTI susceptibility.

Mutation scoring: RT

HNDB 9.5.1 (2023-11-05)

Drug resistance mutation scores of NRTI:

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Rule	ABC	AZT	D4T	DDI	FTC	3TC	TDF
D67N	5	15	15	5	0	0	5
D67N + T215Y + K219E	5	5	5	5	0	0	5
M184V	15	-10	-10	10	60	60	-10
T215Y	10	60	40	15	0	0	10
K219E	5	10	10	5	0	0	5
Total	40	80	60	40	60	60	15

Drug resistance mutation scores of NNRTI:

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Rule	DOR	EFV	ETR	NVP	RPV
Y188L	60	60	10	60	60

INSTI Major Mutations: **R263K** 100%
seen:242

INSTI Accessory Mutations: None

IN Other Mutations: **S17N** 100%
seen:235 • **M50I** 94%
seen:120 • **L101I** 100%
seen:276 • **K111KR** 6.43%
seen:229 • **T112IV** 1.10%
seen:137 • **S119T** 94%
seen:120 • **T124N** 100%
seen:229 • **T125A** 94%
seen:129 • **I133V** 100%
seen:186 • **Q137L** 100%
seen:187 • **V163I** 94%
seen:186 • **V201I** 100%
seen:189 • **T206S** 94%
seen:189 • **D207E** 100%
seen:189 • **L234I** 100%
seen:182

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

IN comments

Major

- R263K** is a nonpolymorphic mutation selected in vitro by EVG, DTG, BIC, and CAB. It occurs in a high proportion of persons who develop VF and emergent HIVDR while receiving DTG. Alone, it reduces DTG, BIC, and CAB susceptibility about 2-fold.

Other

- M50I** is a highly polymorphic mutation, which has a prevalence of 3% to 34% in INSTI-naïve persons depending on subtype. It has been selected in vitro by DTG and BIC in combination with R263K. It may contribute to reduced DTG and CAB susceptibility in combination with R263K.
- This virus is predicted to have intermediate-level reduced susceptibility to **CAB**. The use of the combination of **CAB**/RPV should be considered to be contraindicated.
- There is evidence for intermediate **DTG** resistance. If **DTG** is used, it should be administered twice daily.

Drug resistance mutation scores of INSTI:

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Rule	BIC ⚡	CAB ⚡	DTG ⚡	EVG ⚡	RAL ⚡
<u>R263K</u>	30	30	30	30	25

PI Major Mutations:None

PI Accessory Mutations:[L33LF](#)<sup>(P: 84%, Q: 33%,
cons=1,312)</sup>•[F53FL](#)<sup>(L: 84%, P: 28%,
cons=1,403)</sup>

PR Other Mutations:[L10I](#)<sup>(95%,
cons=682)</sup>•[I13V](#)<sup>(95%,
cons=630)</sup>•[G16E](#)<sup>(95%,
cons=716)</sup>•[V32VA](#)<sup>(L: 84%, V: 33%,
cons=1,207)</sup>•[E35D](#)<sup>(95%,
cons=1,298)</sup>•[M36I](#)<sup>(100%,
cons=1,298)</sup>•[R41K](#)<sup>(98%,
cons=1,358)</sup>•[I66IF](#)<sup>(P: 37%, Q: 23%,
cons=1,464)</sup>•[H69K](#)<sup>(93%,
cons=1,408)</sup>•[K70R](#)<sup>(93%,
cons=1,408)</sup>•[A71AV](#)<sup>(L: 80%, V: 17%,
cons=1,431)</sup>•[L89M](#)<sup>(100%,
cons=1,111)</sup>

Protease Inhibitors	
atazanavir/r (ATV/r)	Low-Level Resistance
darunavir/r (DRV/r)	Susceptible
fosamprenavir/r (FPV/r)	Potential Low-Level Resistance
indinavir/r (IDV/r)	Susceptible
lopinavir/r (LPV/r)	Susceptible
nelfinavir (NFV)	Low-Level Resistance
saquinavir/r (SQV/r)	Low-Level Resistance
tipranavir/r (TPV/r)	Potential Low-Level Resistance

PR comments

Accessory

- L33F** is a relatively non-polymorphic accessory mutation selected by each of the PIs. In combination with other PI-resistance mutations, it is associated with reduced susceptibility to LPV, ATV, and DRV.
- F53L** is a nonpolymorphic accessory mutation selected primarily by SQV, IDV, ATV and LPV. In combination with other mutations, it is associated with reduced susceptibility to ATV and possibly LPV. F53Y is an uncommon nonpolymorphic accessory PI-selected mutation that has not been well studied.

Other

- L10I/V** are polymorphic, PI-selected accessory mutations that increase the replication of viruses with other PI-resistance mutations.
- V32I is a non-polymorphic mutation selected by LPV, ATV, and DRV which is associated with reduced susceptibility to each of these PIs. **V32A** is a highly unusual mutation at this position.
- A71V/T** are polymorphic, PI-selected accessory mutations that increase the replication of viruses with other PI-resistance mutations.

Drug resistance mutation scores of PI:

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Rule	ATV/r ⇅	DRV/r ⇅	FPV/r ⇅	IDV/r ⇅	LPV/r ⇅	NFV ⇅	SQV/r ⇅	TPV/r ⇅
L33LF	5	5	10	5	5	10	5	10
F53FL	10	0	0	0	0	10	15	0
Total	15	5	10	5	5	20	20	10

NRTI Mutations:[V75M](#)<sup>(95%,
cons=682)</sup>•[F77L](#)<sup>(100%,
cons=628)</sup>•[M184V](#)<sup>(95%,
cons=638)</sup>

NNRTI Mutations:[K103N](#)<sup>(100%,
cons=611)</sup>•[E138Q](#)<sup>(100%,
cons=782)</sup>

RT Other Mutations:[E5D](#)<sup>(95%,
cons=1,207)</sup>•[TTTA](#)<sup>(L: 80%, T: 20%,
cons=1,264)</sup>•[V35T](#)<sup>(100%,
cons=1,207)</sup>•[T39A](#)<sup>(95%,
cons=1,077)</sup>•[K102N](#)<sup>(100%,
cons=881)</sup>•[K122KE](#)<sup>(L: 80%, K: 17%,
cons=1,111)</sup>•[D123N](#)<sup>(77%,
cons=638)</sup>•[I135T](#)<sup>(100%,
cons=764)</sup>•[P157PA](#)<sup>(P: 84%, A: 12%,
cons=1,235)</sup>•[S162A](#)<sup>(95%,
cons=684)</sup>•[K173S](#)<sup>(95%,
cons=619)</sup>•[Q174K](#)<sup>(100%,
cons=619)</sup>•[D177E](#)<sup>(100%,
cons=612)</sup>•[V179I](#)<sup>(95%,
cons=638)</sup>•[T200A](#)<sup>(100%,
cons=612)</sup>•[Q207A](#)<sup>(100%,
cons=864)</sup>•[R211S](#)<sup>(100%,
cons=1,008)</sup>•[V245EK](#)<sup>(L: 80%, K: 19%,
cons=1,263)</sup>•[E248D](#)<sup>(95%,
cons=1,030)</sup>•[A272P](#)<sup>(100%,
cons=638)</sup>•[T286A](#)<sup>(95%,
cons=617)</sup>•[E291D](#)<sup>(95%,
cons=1,00)</sup>•[V292I](#)<sup>(95%,
cons=1,00)</sup>•[I293V](#)<sup>(100%,
cons=1,00)</sup>•[K527KS](#)<sup>(L: 80%, S: 42%,
cons=62)</sup>•[K530R](#)<sup>(98%,
cons=1,171)</sup>•[A534S](#)<sup>(95%,
cons=601)</sup>•[A554NS](#)<sup>(L: 80%, S: 12%,
cons=1,431)</sup>

Nucleoside Reverse Transcriptase Inhibitors		Non-nucleoside Reverse Transcriptase Inhibitors	
abacavir (ABC)	Low-Level Resistance	doravirine (DOR)	Susceptible
zidovudine (AZT)	Potential Low-Level Resistance	efavirenz (EFV)	High-Level Resistance
stavudine (D4T)	Intermediate Resistance	etravirine (ETR)	Potential Low-Level Resistance
didanosine (DDI)	Intermediate Resistance	nevirapine (NVP)	High-Level Resistance
emtricitabine (FTC)	High-Level Resistance	rilpivirine (RPV)	Low-Level Resistance
lamivudine (3TC)	High-Level Resistance		
tenofovir (TDF)	Susceptible		

RT comments

NRTI

- V75T/M/A/S** are nonpolymorphic accessory NRTI-selected mutations. They appear to have minimal phenotypic effects on AZT, ABC, and TDF.
- F77L** usually occurs in combination with the multi-NRTI resistance mutation Q151M. When it occurs alone, its clinical significance is uncertain.
- 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

- K103N** is a non-polymorphic mutation that confers high-level reductions in NVP and EFV susceptibility. It is the most commonly transmitted DRM.
- E138Q/G** are non-polymorphic accessory mutations selected by ETR occasionally NVP and EFV. They cause low-level reductions in susceptibility to NVP, RPV, and ETR.

Other

- V179I** is a polymorphic mutation that is frequently selected in persons receiving ETR and RPV. However, it has little, if any, direct effect on NNRTI susceptibility.
- This virus is predicted to have low-level reduced susceptibility to **RPV**. The use of the combination of CAB/**RPV** should be considered to be relatively contraindicated.

Drug resistance mutation scores of NRTI:

Download CSV

Rule	ABC	AZT	D4T	DDI	FTC	3TC	TDF
<u>F77L</u>	5	10	10	10	5	5	5
<u>M184V</u>	15	-10	-10	10	60	60	-10
<u>V75M</u>	0	10	30	15	0	0	0
Total	20	10	30	35	65	65	-5

Drug resistance mutation scores of NNRTI:

Download CSV

Rule	DOR	EFV	ETR	NVP	RPV
<u>K103N</u>	0	60	0	60	0
<u>E138Q</u>	0	10	10	10	15
Total	0	70	10	70	15

INSTI Major Mutations: None

INSTI Accessory Mutations: None

IN Other Mutations: E13ED 100%
seen=1,228 • K14KR 100%
seen=1,329 • S17SN 100%
seen=1,346 • D25E 100%
seen=1,382 • V31I 100%
seen=1,712 • M50I 88%
seen=18,562 • I84L 10%
seen=1,814 • F100Y 10%
seen=1,897 • L101I 100%
seen=1,905 • T112V 10%
seen=1,329 • T124A 10%
seen=1,394 • T125A 10%
seen=1,393 • K136Q 10%
seen=1,216 • V201I 10%
seen=1,312 • I203M 10%
seen=1,261 • I220V 10%
seen=1,312 • N222K 10%
seen=1,395 • Y227F 10%
seen=1,216 • L234I 10%
seen=1,343 • S255N 10%
seen=1,362 • D256E 10%
seen=1,340

Integrase Strand Transfer Inhibitors	
bictegravir (BIC)	Susceptible
cabotegravir (CAB)	Susceptible
dolutegravir (DTG)	Susceptible
elvitegravir (EVG)	Susceptible
raltegravir (RAL)	Susceptible

IN comments

Other

- M50I is a highly polymorphic mutation, which has a prevalence of 3% to 34% in INSTI-naïve persons depending on subtype. It has been selected in vitro by DTG and BIC in combination with R263K. It may contribute to reduced DTG and CAB susceptibility in combination with R263K.

No drug resistance mutations were found for INSTI.