

**ANRS - AC 43: RESISTANCE GROUP
GENOTYPE INTERPRETATION FOR HIV-2**

GENOTYPE INTERPRETATION: NUCLEOSIDE AND NUCLEOTIDE REVERSE TRANSCRIPTASE INHIBITORS [1]

	Mutations associated with resistance	Mutations associated with « possible resistance »
ZDV	<ul style="list-style-type: none"> • Q151M • S215A/C/F/L/Y + 1 mutation among K65R, N69S/T, K70R, Y115F, K223R 	<ul style="list-style-type: none"> • S215A/C/F/L/Y
3TC/FTC	<ul style="list-style-type: none"> • M184I/V 	<ul style="list-style-type: none"> • K65R
ABC	<ul style="list-style-type: none"> • K65R • Q151M • M184I/V + 1 mutation among: L74V, Y115F 	<ul style="list-style-type: none"> • 2 mutations among: D67N, K70N/R, M184V/I, S215A/C/F/L/Y
TDF/TAF	<ul style="list-style-type: none"> • K65R • Q151M + V111I 	

ZDV: zidovudine, 3TC: lamivudine, FTC: emtricitabine, ABC: abacavir, TDF: tenofovir, TAF: tenofovir alafenamide

Didanosine and stavudine are not recommended

GENOTYPE INTERPRETATION: PROTEASE INHIBITORS [1]

	Mutations associated with resistance	Mutations associated with « possible resistance »
LPV	<ul style="list-style-type: none">• 2 mutations among: I82F, I84V, L90M• I54M• V47A	<ul style="list-style-type: none">• V62A + L99F• 1 mutation among: I82F, I84V, L90M
DRV	<ul style="list-style-type: none">• I50V• I54M• I84V + L90M	<ul style="list-style-type: none">• 1 mutation among: I84V, L90M

LPV: lopinavir, DRV: darunavir

For indinavir and saquinavir refer to previous rules (See Archives, Version 27, September 2017)
Atazanavir and tipranavir are not recommended

GENOTYPE INTERPRETATION: INTEGRASE STRAND TRANSFER INHIBITORS [1-5]

	Mutations associated with resistance	Mutations associated with « possible resistance »
RAL	<ul style="list-style-type: none"> • N155H/R • Q148K/R/H [3,4,5] • E92Q + T97A • Y143C/G/R + 1 mutation among: E92Q, T97A • Insertion at codon 231 [5] 	<ul style="list-style-type: none"> • E92Q • Y143C/G/R
EVG	<ul style="list-style-type: none"> • E92G/Q • Q148K/R/H [3,4,5] • N155H • T97A + Y143C • Insertion at codon 231 [5] 	<ul style="list-style-type: none"> • Y143C
DTG	<ul style="list-style-type: none"> • Q148K • G140S + Q148R/H [3,4,5] • E92Q + N155H • T97A + N155H • Insertion at codon 231 [5] 	<ul style="list-style-type: none"> • Q148R/H [3] • N155H • E92Q • T97A + Y143C
CAB*	<ul style="list-style-type: none"> • Q148K • G140S + Q148R/H [3,4,5] • E92Q + N155H • T97A + N155H • Insertion at codon 231 [5] 	<ul style="list-style-type: none"> • Q148R/H [3] • N155H • E92Q • T97A + Y143C
BIC*	<ul style="list-style-type: none"> • Q148K • G140S + Q148R/H [5] • E92Q + N155H • T97A + N155H 	<ul style="list-style-type: none"> • Q148R/H • N155H • E92Q • T97A + Y143C • Insertion at codon 231 [5]

RAL: raltegravir, EVG: elvitegravir, DTG: dolutegravir, CAB: cabotegravir, BIC: bictegravir

***Due to the very close structures of dolutegravir and cabotegravir, rules for dolutegravir are transposed to cabotegravir with the exception of the insertion at codon 231 for bictegravir**

NON-NUCLEOSIDE REVERSE TRANSCRIPTASE INHIBITORS
<ul style="list-style-type: none">• Naturally resistant to all NNRTI [2]
FUSION INHIBITOR
<ul style="list-style-type: none">• Naturally resistant to enfuvirtide [2]
ATTACHEMENT INHIBITOR
<ul style="list-style-type: none">• Naturally resistant to fostemsavir [6]

REFERENCES

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- 3/ Smith RA et al. Three main mutational pathways in HIV-2 lead to high-level raltegravir and elvitegravir resistance: implications for emerging HIV-2 treatment regimens. PLoS ONE, 2012; 7.
- 4/ Smith RA, In vitro antiviral activity of cabotegravir against HIV-2. Antimicrob Agents Chemother. 2018 Jul 16. pii: AAC.01299-18. doi: 10.1128/AAC.01299-18.
- 5/ Le Hingrat Q et al. A 5 amino-acid insertion in the C-terminal region of HIV-2 integrase impacts phenotypic susceptibility to the five integrase inhibitors. 16th European Meeting on HIV & Hepatitis Treatment Strategies & Antiviral Drug Resistance, May 2018, Roma, Italy, Abstract 4.
- 6/ Lataillade M et al. Viral drug resistance through 48 weeks, in a phase 2b, randomized, controlled trial of the HIV-1 attachment inhibitor prodrug, Fostemsavir. J Acquir Immune Defic Syndr. 2018 Mar 1;77(3):299-30