

ANRS – MIE VIROLOGY NETWORK 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 [1-6]

	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] • G118R [6] • R263K [6,7] 	<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] • G118R [6] • R263K [6,7] 	<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] • G118R [6] • R263K [6,7] 	<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] • G118R [6] • R263K [6,7] 	<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 • G118R [6] • R263K [6,7] 	<ul style="list-style-type: none"> • Q148R/H • N155H • E92Q • T97A + Y143C • Insertion at codon 231 [5]

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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 [8]

ANRS – MIE VIROLOGY NETWORK: RESISTANCE GROUP

GENOTYPE INTERPRETATION: CAPSID INHIBITORS

	Mutations associated with resistance	Mutations associated with « possible resistance »
LEN	<ul style="list-style-type: none"> • N73D [9] 	<ul style="list-style-type: none"> • Q66H [9] • R69K [9] • A76V [9]

LEN: lenacapavir

REFERENCES

- 1/ Charpentier C et al. HIV-2EU-Supporting Standardized HIV-2 Drug-Resistance Interpretation in Europe: An Update. *Clin Infect Dis*. 2015 Jul 17. pii: civ572
- 2/ Witvrouw E et al. Susceptibility of HIV-2, SIV and SHIV to various anti-HIV-1 compounds: implications for treatment and postexposure prophylaxis. *Antivir Ther* 2004; 9(1): 57-65.
- 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/ Smith RA, Wu VH, Song J, et al. Spectrum of Activity of Raltegravir and Dolutegravir Against Novel Treatment-Associated Mutations in HIV-2 Integrase: A Phenotypic Analysis Using an Expanded Panel of Site-Directed Mutants. *J Infect Dis*. 2022 Aug 26;226(3):497-509. doi: 10.1093/infdis/jjac037.
- 7/ Requena S, Lozano AB, Caballero E, et al. Clinical experience with integrase inhibitors in HIV-2-infected individuals in Spain. *J Antimicrob Chemother*. 2019 May 1;74(5):1357-1362.
- 8/ 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
- 9/ Bertine M. et al. Rapid Selection of HIV-2 Capsid Mutations After Failure of a Lenacapavir-Containing Regimen, CROI 2024, Abstr. 682