

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

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

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

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

Didanosine and stavudine are not recommended

**GENOTYPE INTERPRETATION: PROTEASE INHIBITORS [1]**

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

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

**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

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

## REFERENCES

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- 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.
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- 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