**Katholieke Universiteit Leuven**
**Rega Institute for Medical Research and University Hospitals Leuven**
Microbiology and Immunology
Clinical and Epidemiological Virology

Kristel Van Laethem and Anne-Mieke Vandamme

www.kuleuven.ac.be/rega/cev/links/
kristel.vanlaethem@uz.kuleuven.ac.be

**Algorithm for the use of genotypic resistance data**
**Rega v6.1, October 2, 2003**

| | **Criteria to consider an isolate resistant** [a,b,c,d] | **Criteria to consider an isolate intermediate resistant** [b,c,d] |
|---|---|---|
| **NRTI** | | |
| zidovudine | [at least 1 mutation of (**T69X-XX**,**Q151M**)]<br>*or* (**T215F/Y** and not M184I/V)<br>*or* [at least 2 mutations of (M41L,D67N,T69A/N,K70R,L210W,**T215F/Y**,K219E/Q) and not M184I/V]<br>*or* [at least 2 mutations of (M41L,D67N,T69A/N,K70R,L210W,**T215F/Y**,K219E/Q) and M184I/V and G333D/E]<br>*or* [at least 3 mutations of (M41L,D67N,T69A/N,K70R,L210W,**T215F/Y**,K219E/Q) and M184I/V] | [1 mutation of (M41L,D67N,T69A/N,K70R,L210W,K219E/Q) and not M184I/V]<br>*or* [1 mutation of (M41L,D67N,T69A/N,K70R,L210W,T215F/Y,K219E/Q) and M184I/V and G333D/E]<br>*or* [2 mutations of (M41L,D67N,T69A/N,K70R,L210W,T215F/Y,K219E/Q) and M184I/V] |
| zalcitabine | at least 1 mutation of (**K65R**,**D67G**,**Δ67**,**T69D/G/N/S**,**T69X-XX**,**L74V**,**V75T**,**Q151M**) | M184I/V<br>*or* [at least 4 mutations of (M41L,D67N,T69A,K70R,L210W,T215F/Y,K219E/Q)] |
| didanosine | at least 1 mutation of (**K65R**,**T69G/N**,**T69X-XX**,**L74V**,**Q151M**) | [at least 1 mutation of (V75T,M184I/V)]<br>*or* [at least 4 mutations of (M41L,D67N,T69A/D,K70R,L210W,T215F/Y,K219E/Q)] |
| lamivudine | **M184I/V**<br>*or* (K65R and Q151M) | [at least 1 mutation of (Δ67,T69X-XX)]<br>*or* [1 mutation of (K65R,Q151M)]<br>*or* {[at least 1 mutation of (E44A/D,V118I)] and [at least 2 mutations of (M41L,D67N,T69A/N,K70R,L210W,T215F/Y,K219E/Q)]} |
| stavudine | [at least 1 mutation of (**Δ67**,**T69G**,**T69X-XX**,**V75A/M/S/T**,**Q151M**)]<br>*or* [at least 4 mutations of (M41L,D67N,T69A/D/N,K70R,L210W,T215F/Y,K219E/Q)] | 3 mutations of (M41L,D67N,T69A/D/N,K70R,L210W,T215F/Y,K219E/Q) |

| | | |
|---|---|---|
| abacavir | [at least 1 mutation of (**Δ67**,**T69G**)]<br>*or* [at least 2 mutations of (K65R,T69X-XX,L74V,Y115F,Q151M,M184I/V,T215F/Y)]<br>*or* {[at least 1 mutation of (K65R,T69X-XX,L74V,Y115F,Q151M,M184I/V)] and [at least 3 mutations of (M41L,E44A/D,D67N,T69A/D/N,K70R,V75T,V118I,L210W,K219E/Q)]}<br>*or* [at least 6 mutations of (M41L,E44A/D,D67N,T69A/D/N,K70R,V75T,V118I,L210W,T215F/Y,K219E/Q)] | [at least 4 mutations of (M41L,E44A/D,D67N,T69A/D/N,K70R,V75T,V118I,L210W,T215F/Y,K219E/Q)]<br>*or* (M41L and T215F/Y)<br>*or* [1 mutation of (K65R,T69X-XX,L74V,Y115F,Q151M,M184I/V)] |
| **NtRTI** | | |
| tenofovir | [at least 1 mutation of (**K65R**,**T69X-XX**)] | [at least 1 mutation of (L74V,Q151M)]<br>*or* [M41L and at least 2 mutations of (D67N,K70R,L210W,T215Y/F,K219E/N/Q)]<br>*or* [L210W and at least 2 mutations of (M41L,D67N,K70R,T215Y/F,K219E/N/Q)]<br>*or* [T215Y/F and at least 2 mutations of (M41L,D67N,K70R,L210W,K219E/N/Q)] |
| **NNRTI** | | |
| nevirapine | [at least 1 mutation of (**L100I**,**K103N**,**V106A**,**Y181C/I**,**Y188C/H/L**,**G190A/E/S**,**M230L**)]<br>*or* [at least 2 mutations of (A98G,K101E/Q,V106I,V108I,V179D)] | 1 mutation of (A98G,K101E/Q,V106I,V108I,V179D) |
| delavirdine | [at least 1 mutation of (**L100I**,**K103N**,**V106A**,**Y181C/I**,**Y188L**,**G190E**,**M230L**,**P236L**)]<br>*or* [at least 2 mutations of (A98G,K101E/Q,V106I,V108I,V179D,Y188C/H)] | 1 mutation of (A98G,K101E/Q,V106I,V108I,V179D,Y188C/H) |
| efavirenz | [at least 1 mutation of (**K103N**,**Y188L**,**G190S**,**M230L**)]<br>*or* [at least 2 mutations of (L100I,K101E/Q,V106A/I,V108I,V179D,Y181C/I,Y188C/H,G190A/E/T,P225H)] | 1 mutation of (A98G,L100I,K101E/Q,V106A/I,V108I,V179D,Y181C/I,Y188C/H,G190A/E/T,P225H) |
| **PI**[e] | | |
| saquinavir (/r) | {(**G48V** and **L90M**) and [at least 2 mutations of (L10F/I/R/V,K20M/R,M46I/L,I54L/V,L63P,A71I/T/V,G73S,V82A/F/S/T,I84V)]}<br>*or* {[1 mutation of (**G48V**,**L90M**)] and [at least 3 mutations of (L10F/I/R/V,K20M/R,M46I/L,I54L/V,L63P,A71I/T/V,G73S,V82A/F/S/T,I84V)]}<br>*or* [at least 6 mutations of (L10F/I/R/V,K20M/R,M46I/L,I54L/V,L63P,A71I/T/V,G73S,V82A/F/S/T,I84V)] | (**G48V** and **L90M**)<br>*or* {[at least 1 mutation of (**G48V**,**L90M**)] and [at least 1 mutation of (L10F/I/R/V,K20M/R,M46I/L,I54L/V,L63P,A71I/T/V,G73S,V82A/F/S/T,I84V)]}<br>*or* [at least 4 mutations of (L10F/I/R/V,K20M/R,M46I/L,I54L/V,L63P,A71I/T/V,G73S,V82A/F/S/T,I84V)] |
| ritonavir | [at least 2 mutations of (**M46I/L**,**V82A/F/S/T**,**I84V**)]<br>*or* {[at least 1 mutation of (**M46I/L**,**V82A/F/S/T**,**I84V**)] and [at least 1 mutation of (L10F/I/R/V,K20M/R,L24I,L33F,M36I,G48V,I54L/V,L63P,A71I/T/V,G73S,N88S,L90M)]}<br>*or* [at least 4 mutations of (L10F/I/R/V,K20M/R,L24I,L33F,M36I,G48V,I54L/V,L63P,A71I/T/V,G73S,N88S, L90M)] | [1 mutation of (M46I/L,V82A/F/S/T,I84V)]<br>*or* [3 mutations of (L10F/I/R/V,K20M/R,L24I,L33F,M36I,G48V,I54L/V,L63P,A71I/T/V,G73S,N88S,L90M)] |

| | | |
|---|---|---|
| indinavir<br>(/r) | {(**M46I/L** and **V82A/F/S/T** and **I84V**) and [at least 1 mutation of (L10F/I/R/V,K20M/R,L24I,L33F,M36I,G48V,I54L/V,L63P,A71I/T/V,G73S,N88S,L90M)]}<br>*or* {[at least 2 mutations of (**M46I/L**,**V82A/F/S/T**,**I84V**)] and [at least 2 mutations of (L10F/I/R/V,K20M/R,L24I,L33F,M36I,G48V,I54L/V,L63P,A71I/T/V,G73S,N88S,L90M)]}<br>*or* {[at least 1 mutation of (**M46I/L**,**V82A/F/S/T**,**I84V**)] and [at least 3 mutations of (L10F/I/R/V,K20M/R,L24I,L33F,M36I,G48V,I54L/V,L63P,A71I/T/V,G73S,N88S,L90M)]}<br>*or* [at least 6 mutations of (L10F/I/R/V,K20M/R,L24I,L33F,M36I,G48V,I54L/V,L63P,A71I/T/V,G73S,N88S, L90M)] | [at least 2 mutations of (**M46I/L**,**V82A/F/S/T**,**I84V**)]<br>*or* {[at least 1 mutation of (**M46I/L**,**V82A/F/S/T**,**I84V**)] and [at least 1 mutation of (L10F/I/R/V,K20M/R,L24I,L33F,M36I,G48V,I54L/V,L63P,A71I/T/V,G73S,N88S,L90M)]}<br>*or* [at least 4 mutations of (L10F/I/R/V,K20M/R,L24I,L33F,M36I,G48V,I54L/V,L63P,A71I/T/V,G73S,N88S, L90M)] |
| nelfinavir | [at least 2 mutations of (**D30N**,**V82A**,**L90M**)]<br>*or* {[at least 1 mutation of (**D30N**,**V82A**,**L90M**)] and [at least 1 mutation of (M36I,M46I/L,G48V,I54L/V,L63P,A71I/T/V,V77I,V82F/S/T,I84V,N88D/S)]}<br>*or* [at least 4 mutations of (M36I,M46I/L,G48V,I54L/V,L63P,A71I/T/V,V77I,V82F/S/T,I84V,N88D/S)] | [1 mutation of (D30N,V82A,L90M)]<br>*or* [3 mutations of (M36I,M46I/L,G48V,I54L/V,L63P,A71I/T/V,V77I,V82F/S/T,I84V,N88D/S)] |
| amprenavir<br>(/r) | {**I50V** and [at least 3 mutations of (L10F/I/R/V,K20M/R,V32I,L33F,M46I/L,I47V,I54L/M/V,L63P,V82A/F/S/T,I84V,L90M)]}<br>*or* [at least 6 mutations of (L10F/I/R/V,K20M/R,V32I,L33F,M46I/L,I47V,I54L/M/V,L63P,V82A/F/S/T,I84V,L90M)] | {**I50V** and [at least 1 mutation of (L10F/I/R/V,K20M/R,V32I,L33F,M46I/L,I47V,I54L/M/V,L63P,V82A/F/S/T,I84V,L90M)]}<br>*or* [at least 4 mutations of (L10F/I/R/V,K20M/R,V32I,L33F,M46I/L,I47V,I54L/M/V,L63P,V82A/F/S/T,I84V,L90M)] |
| lopinavir/r | at least 6 mutations of (L10F/I/R/V,K20M/R,L24I,L33F,M46I/L,I47V,G48V,I50V,F53L,I54A/L/M/S/T/V,L63P, A71I/L/T/V,V82A/F/S/T,I84V,L90M) | at least 4 mutations of (L10F/I/R/V,K20M/R,L24I,L33F,M46I/L,I47V,G48V,I50V,F53L,I54A/L/M/S/T/V,L63P, A71I/L/T/V,V82A/F/S/T,I84V,L90M) |
| atazanavir | {(**I50L** or **A71V**) and [at least 3 mutations of (L10F/I/Y,K20I/R/T,L24I,V32I,L33F/I/MV,M36I/L/V,K45R,M46I/L/V,G48V,I54V,L63A/P/T, A71T,G73A/C/S/T,V77I,V82A/M/T,I84V,N88D/S,L89M,L90M)]}<br>*or* {(**I50L** and **A71V**) and [at least 1 mutation of (L10F/I/Y,K20I/R/T,L24I,V32I,L33F/I/MV,M36I/L/V,K45R,M46I/L/V,G48V,I54V,L63A/P/T, A71T,G73A/C/S/T,V77I,V82A/M/T,I84V,N88D/S,L89M,L90M)]}<br>*or* [at least 7 mutations of (L10F/I/Y,K20I/R/T,L24I,V32I,L33F/I/MV,M36I/L/V,K45R,M46I/L/V,G48V,I54V,L63A/P/T, A71T,G73A/C/S/T,V77I,V82A/M/T,I84V,N88D/S,L89M,L90M)] | {(**I50L** or **A71V**) and [at least 2 mutations of (L10F/I/Y,K20I/R/T,L24I,V32I,L33F/I/MV,M36I/L/V,K45R,M46I/L/V,G48V,I54V,L63A/P/T, A71T,G73A/C/S/T,V77I,V82A/M/T,I84V,N88D/S,L89M,L90M)]}<br>*or* (**I50L** and **A71V**)<br>*or* [at least 4 mutations of (L10F/I/Y,K20I/R/T,L24I,V32I,L33F/I/MV,M36I/L/V,K45R,M46I/L/V,G48V,I54V,L63A/P/T, A71T,G73A/C/S/T,V77I,V82A/M/T,I84V,N88D/S,L89M,L90M)] |

| **EI** | | |
|---|---|---|
| enfuvirtide | at least 2 mutations of (G36D/E/S/V,I37V,V38A/E/M/V,Q40H,N42D/E/K/T,N43D/K/S,L44M,L45M) | 1 mutation of (G36D/E/S/V,I37V,V38A/E/M/V,Q40H,N42D/E/K/T,N43D/K/S,L44M,L45M) |

[a] Primary or key mutations are indicated in bold, secondary or accessory mutations are in plain text.
[b] T69X-XX**,** either T69S-SS, T69S-SG, T69S-AG, T69S-SA or T69T-SG. Δ67, deletion of amino acid 67. A, alanine; R, arginine; N, asparagine; D, aspartic acid; C, cysteine; Q, glutamine; E, glutamic acid; G, glycine; H, histidine; I, isoleucine; L, leucine; K, lysine; M, methionine; F, phenylalanine; P, proline; S, serine; T, threonine; W, tryptophan; Y, tyrosine and V, valine.
[c] If more mutations are present at a certain position (e.g. T215Y and T215F), they are only counted as one mutation in the rules.
[d] If none of the criteria to consider an isolate resistant towards a particular drug are full-filled, proceed to the criteria to consider an isolate intermediate resistant. If none of the latter criteria are full-filled, the isolate can be scored susceptible to that particular drug.
[e] /r, PI boosted with baby dose of ritonavir.
NRTI, nucleoside reverse transcriptase inhibitor; NtRTI, nucleotide reverse transcriptase inhibitor; NNRTI, non-nucleoside reverse transcriptase inhibitor; PI, protease inhibitor; EI, entry inhibitor.