**Table S1**. Frequency of major mutations in the RT gene associated with resistance to RTIs.1

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Type of Inhibitor** | **RT position**2 | **Substitution** | **Mutant**3 | **Wild type**3 | **Other amino acid**3,4 |
| NRTI | M41 | L | 18,3 | 81,5 | 0,0 |
| A62 | V | 2,8 | 96,9 | 0,2 |
| K65 | R | 2,1 | 97,7 | 0,0 |
| E | 0,1 |
| N | 0,1 |
| D67 | N | 14,6 | 81,6 | 0,6 |
| K70 | R | 18,0 | 80,7 | 0,6 |
| E | 0,2 |
| L74 | V | 1,8 | 96,2 | 0,0 |
| V75 | I | 4,4 | 93,2 | 0,9 |
| F77 | L | 0,6 | 99,4 | 0,0 |
| Y115 | F | 0,8 | 99,2 | 0,0 |
| F116 | Y | 1,5 | 98,2 | 0,2 |
| Q151 | M | 2,1 | 97,9 | 0,0 |
| M184 | V | 86,9 | 11,1 | 0,0 |
| I | 2,8 |
| L210 | W | 9,4 | 89,9 | 0,5 |
| T215 | Y | 19,0 | 63,5 | 1,2 |
| F | 16,2 |
| K219 | Q | 8,3 | 82,5 | 2,1 |
| E | 7,0 |
| NNRTI | V90I | I | 15,6 | 84,3 | 0,0 |
| A98 | G | 15,9 | 79,4 | 3,7 |
| L100 | I | 0,9 | 99,0 | 0,0 |
| K101 | P | 0,3 | 79,6 | 5,9 |
| E | 10,8 |
| H | 1,4 |
| K103 | N | 49,7 | 47,0 | 1,6 |
| S | 1,9 |
| V106 | M | 1,8 | 90,0 | 0,2 |
| I | 2,8 |
| A | 5,1 |
| V108 | I | 15,3 | 84,7 | 0,1 |
| E138 | A | 2,6 | 92,6 | 0,6 |
| G | 0,5 |
| K | 0,5 |
| Q | 3,8 |
| R | 0,0 |
| V179 | D | 0,7 | 81,9 | 13,9 |
| F | 0,2 |
| T | 0,8 |
| L | 0,3 |
| Y181 | C | 31,9 | 66,2 | 0,1 |
| I | 0,5 |
| V | 1,4 |
| Y188 | C | 0,5 | 93,6 | 0,5 |
| L | 4,8 |
| H | 0,5 |
| G190 | S | 1,4 | 80,7 | 0,4 |
| A | 17,5 |
| H221 | Y | 16,0 | 83,5 | 0,2 |
| P225 | H | 6,9 | 92,6 | 0,2 |
| F227 | C | 0,0 | 94,9 | 0,0 |
| M230 | I | 0,0 | 95,3 | 0,1 |
| L | 3,9 |

1Mutations from the IAS-USA list 2015.

2Mutations that are selected by the drug regimen (AZT/d4T + 3TC + NVP/EFV) accordingly to the IAS-USA 2014 list are underlined.

3Percentage of 1303 treatment-experienced individuals

4Exludes ambiguities.

**Table S3.** Associations of additional non-polymorphic mutations with known major RTI resistance mutations1

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Mutations2** | | **Single Mutant3** | **Double Mutant** | **Subtypes4** | **Countries4** | ***p*-value** | | |
| **Benjamini-Hochberg** | **Holm** | **Bonferroni** |
| I94L  (N=14) | M41L | 4 (0.38%, N=1059) | 10 (4.24%, N=236) | CRF02 | BF, CM, TG | 0,0006 | 0,0044 | 0,0045 |
| L210W | 5 (0.43%, N=1168) | 9 (7.44%, N=121) | CRF02 | BF, CM, TG | <0,0001 | 0,0001 | 0,0001 |
| T215Y | 0 (0%, N=827) | 10 (4.07%, N=246) | N/A | N/A | <0,0001 | 0,0001 | 0,0001 |
| T215F | 0 (0%, N=827) | 5 (2.38%, N=210) | N/A | N/A | 0,0071 | 0,0816 | 0,0852 |
| L109I  (N=31) | M41L | 13 (1.23%, N=1056) | 18 (7.66%, N=235) | C, CRF02 | CM, TG | <0,0001 | 0,0001 | 0,0002 |
| V106M | 18 (1.54%, N=1168) | 4 (19.05%, N=21) | C, CRF02, G | CM | 0,0086 | 0,1064 | 0,1116 |
| V106A | 18 (1.54%, N=1168) | 7 (10.94%, N=64) | CRF02 | CM, TG | 0,0040 | 0,0420 | 0,0437 |
| V108I | 14 (1.28%, N=1098) | 17 (8.72%, N=195) | C, CRF02 | CM, TG | <0,0001 | 0,0001 | 0,0001 |
| L210W | 18 (1.55%, N=1163) | 13 (10.66%, N=122) | C, CRF02, G | CM, TG | <0,0001 | 0,0003 | 0,0003 |
| T215Y | 5 (0.61%, N=826) | 17 (6.97%, N=244) | CRF02 | CM, TG | <0,0001 | <0,0001 | <0,0001 |
| T215F | 5 (0.61%, N=826) | 11 (5.29%, N=208) | CRF02 | CM, TG | 0,0008 | 0,0073 | 0,0076 |
| T139R  (N=31) | Y181C | 8 (0.97%, N=823) | 23 (6.07 %, N=379) | C, CRF02 | CM, TG | <0,0001 | 0,0002 | 0,0002 |
| T215F | 10 (1.3%, N=772) | 13 (6.5%, N=200) | CRF02 | CM, TG | 0,0035 | 0,0337 | 0,0349 |
| T165L  (N= 34) | M41L | 19 (1.87%, N=1018) | 15 (6.44%, N=233) | CRF02, G | BF, CM, SN, TG | 0,0086 | 0,1148 | 0,1209 |

1Associations with a *p* value <0.01 (corrected with Benjamini-Hochberg procedures); mutations from the IAS-USA list 2015.

2NNRTIS mutation are underlined

3Prevalence of the non-polymorphic RTI-selected mutation in the wild group for the respective known RTI-selected mutation. The percentage of the non-polymorphic RTI-selected mutation and the size of the group are given in parentheses.

4Subtypes/CRFs (A, C, D, CRF01, CRF02, F, G) or countries (Codes ISO 3166-1 alpha-2) that intersect in the categories.

**Table S3.** Prevalence of RTI-selected mutations associated with HIV-1 group M subtypes and CRFs

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Type of Inhibitor** | **Major Mutation** | **Subtype A**  **(N=83)** | **Subtype C**  **(N=65)** | **CRF02 (N=595)** | **CRF06 (N=82)** | **Subtype G (N=64)** | **Type of Association**2 | ***p*-value** | | |
| **Benjamini-Hochberg** | **Holm** | **Bonferroni** |
| NNRTI | M41L | 10 (12%) | 7 (11%) | 101 (17%) | **30** (**37%)** | 17 (27%) | CRF06 ↑ | <0,0001 | <0,0001 | <0,0001 |
| NNRTI | V106M | 0 (0%) | **8** (**12%)** | 9 (2%) | 0 (0%) | 2 (3%) | C ↑ | <0,0001 | <0,0001 | <0,0001 |
| G190A | 22 (27%) | 19 (29%) | **83** (**14%)** | 20 (24%) | 10 (16%) | CRF02 ↓ | 0,023 | 0,0686 | 0,069 |

1Associations with a *p* value <0.05 (corrected with Benjamini-Hochberg procedures); mutations from the IAS-USA list 2015.