

Supplementary Table S1. Rilpivirine IC₅₀, Fold-Change and Resistance Category, and Reverse Transcriptase Genotype for Each Plasma-Derived HIV-1 from Individuals on Failing First-Line Non-Nucleoside Reverse Transcriptase Inhibitor-Based Antiretroviral Therapy

| Sample | FC ^a | IC ₅₀ (ng/mL) | Protein Adjusted IC ₉₀ | Major NRTI ^b | Major NNRTI ^b |
|--------|-----------------|-----------------------------|---|----------------------------------|----------------------------|
| 1 | 0.36 | 0.04 | 1.6 | A62AV,L74IL,M184V | K101E,V106M,E138A,G190A |
| 2 | 0.58 | 0.07 | 2.6 | D67N,K70R,M184V,T215Y,K219Q | V106M,F227L,N348I |
| 3 | 0.74 | 0.09 | 3.3 | K65R,L74I,Y115F,M184V | K103N,V106M |
| 4 | 0.76 | 0.09 | 3.3 | D67N, K70E, M184V | V106M, G190A, H221Y, F227L |
| 5 | 0.84 | 0.10 | 3.7 | None | V106MV,G190AG |
| 6 | 0.87 | 0.10 | 3.8 | None | K103N |
| 7 | 0.95 | 0.11 | 4.2 | K70E,L74IL,Y115F,M184V | A98G,V106M,Y188C |
| 8 | 1.0 | 0.12 | 4.3 | None | K103N |
| 9 | 1.0 | 0.12 | 4.4 | T69NT | K103N |
| 10 | 1.1 | 0.13 | 4.8 | M41L,D67N,V75I,M184V,L210W,T215Y | K103N,V106M,F227FL |
| 11 | 1.2 | 0.14 | 5.3 | V75M,M184V | V106M,E138A,G190A |
| 12 | 1.2 | 0.15 | 5.5 | M41L,M184V,T215F | V106M,G190A |
| 13 | 1.2 | 0.15 | 5.5 | M184V | K103N,N348I |
| 14 | 1.4 | 0.16 | 6.0 | A62V,K65R,L74I,Y115F,M184V | V106M,Y188C,G190A |
| 15 | 1.5 | 0.18 | 6.7 | A62V,K65R,M184V | K103S,V106M |
| 16 | 1.6 | 0.20 | 7.2 | A62V,K65R,L74IL,M184V | K103N,G190A |
| 17 | 1.6 | 0.20 | 7.3 | M184V | V106M,G190A,H221Y |
| 18 | 1.6 | 0.20 | 7.3 | M184V | K101HKNQ,K103N,G190A |
| 19 | 1.7 | 0.21 | 7.6 | L74V,Y115F,M184V | K103Q,V106M,Y188F,F227L |
| 20 | 1.8 | 0.22 | 8.0 | K65R,M184V | V106M,Y188C |
| 21 | 1.8 | 0.22 | 8.1 | K65R,M184V | V106M,V179D |
| 22 | 1.9 | 0.22 | 8.3 | M41L,D67N,K70E,M184V,T215F | K101H,V106M,G190A,F227L |
| 23 | 2.0 | 0.24 | 8.7 | K65R,M184V | V106M,V179D,M230L |
| 24 | 2.0 | 0.24 | 8.8 | L74IL,Y115F,F116FY,M184V,K219EK | V106M,Y188C |

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| 25 | 2.0 | 0.24 | 8.9 | L74I,M184V | K103N |
| 26 | 2.1 | 0.25 | 9.1 | D67N,T69N,K70R,L74IL,M184V,T215IV,K219E | K103N,P225H |
| 27 | 2.1 | 0.25 | 9.1 | K65R,D67G,Y115F,M184V,K219E | V106M,Y181C,G190A |
| 28 | 2.1 | 0.25 | 9.2 | M41L,D67N,K70R,L74I,M184V,T215Y,K219Q | K101E,G190A,P225H |
| 29 | 2.2 | 0.26 | 9.6 | L74IL,M184V | K103S,V106M |
| 30 | 2.2 | 0.26 | 9.6 | K65R,L74I,M184V,K219E | K103N,V106M |
| 31 | 2.2 | 0.27 | 9.8 | K65R,L74I,Y115F,M184V,K219E | V90I,V106M,E138G,V179E,F227L |
| 32 | 2.5 | 0.30 | 11 | M184V | K103N,N348I |
| 33 | 2.6 | 0.31 | 11 | M184V,T215F | A98G,K103N,V108I |
| 34 | 2.6 | 0.31 | 12 | D67N,K70R,M184V,K219Q | K103N,V106M,E138AEKT,N348I |
| 35 | 2.7 | 0.32 | 12 | M41LM,K65R,M184V | V106M,E138A,V179D |
| 36 | 2.8 | 0.33 | 12 | M41L,D67N,M184V,T215F,K219W | A98G,K101E,G190A |
| 37 | 2.8 | 0.33 | 12 | M184V | K103N,E138A,P225H |
| 38 | 2.9 | 0.34 | 13 | M184V | K103N,V106M,E138Q,N348IN |
| 39 | 2.9 | 0.35 | 13 | M41L,D67N,T69D,K70R,M184V,T215F,K219Q | K101H,V106M,G190A,F227L |
| 40 | 3.1 | 0.37 | 14 | None | K101EK,K103KN,V106M,V108IV,G190AG |
| 41 | 3.2 | 0.38 | 14 | T69N,K70R,M184V | V106M,V179D |
| 42 | 3.3 | 0.39 | 14 | D67N,K70G,M184V,K219Q | K103NS,V106M,G190A,N348I |
| 43 | 3.4 | 0.40 | 15 | A62AV,K65R,M184I | V90I,A98G,K103N,Y181C,G190A |
| 44 | 3.5 | 0.41 | 15 | M184MV | K103N,E138A,P225H |
| 45 | 3.5 | 0.42 | 15 | M41L,L74I,M184V,T215F | K103N,V108I |
| 46 | 3.5 | 0.42 | 15 | L74V,V75L,M184V,K219N | G190E |
| 47 | 3.8 | 0.45 | 17 | M41LM,M184V,T215Y | K103N,V108I |
| 48 | 4.0 | 0.47 | 18 | K65R,Y115F,M184V | L100M,K101EK,V106M,E138K,V179DV,F227L |
| 49 | 4.0 | 0.48 | 18 | K70E,Y115F,M184V | V106M,V179D |
| 50 | 4.1 | 0.49 | 18 | L74IL,M184V,T215NSTY | K101EK,K103N,V108IV,P225H,M230LM |
| 51 | 4.3 | 0.52 | 19 | L74V,Y115F,M184V | K103S,G190A,Y318F |
| 52 | 4.6 | 0.54 | 20 | K70EK,L74V,M184V | L100I,K103N,V106MV |
| 53 | 4.6 | 0.55 | 20 | K65R,L74IL,Y115F,M184V | K103N,P225H |
| 54 | 4.9 | 0.59 | 22 | A62AV,K65KR,K70EK,M184V | K103N,Y181C |

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| 55 | 5.1 | 0.61 | 22 | M41LM,V75M,M184V,T215Y | A98G,V106M,F227L |
| 56 | 5.2 | 0.61 | 23 | M41L,D67N,T69D,K70R,M184V,T215F,K219Q | K103N,V106M,E138A,F227L |
| 57 | 5.4 | 0.65 | 24 | L74V,M184V | V179D,Y188L,N348IT |
| 58 | 6.2 | 0.74 | 27 | M184V | Y181C |
| 59 | 6.2 | 0.74 | 27 | None | K103N,E138EG,P225H |
| 60 | 6.5 | 0.77 | 28 | K219KR | K103N,P225H |
| 61 | 7.5 | 0.89 | 33 | M41L,K65R,T69V,K70T,M184V | K101E,V106M,Y181C,G190A,H221Y,F227L |
| 62 | 7.6 | 0.90 | 33 | M184V | Y181C,N348IT |
| 63 | 10 | 1.2 | 44 | K65R,L74IL,M184V | K103NS,V106MV,M230L |
| 64 | 10 | 1.2 | 45 | K65R | V106M,V179D,Y181C |
| 65 | 11 | 1.3 | 49 | V75M, F77L, M184V, T215Y | V106A, G190A, F227L |
| 66 | 13 | 1.5 | 57 | T69NT,K70KR,M184V | K103N,P225H,N348I |
| 67 | 13 | 1.6 | 58 | K65R,M184V | L100I,K103N |
| 68 | 14 | 1.7 | 61 | K70EK,M184V,T215FIST | V90IV,K103N,V108IV,Y181CY,G190AG,K238KT,N348IN |
| 69 | 14 | 1.7 | 62 | D67N, K70E, V75T, M184V | A98AG, K103N, V106IM, V108IV, Y181C, G190A, H221Y |
| 70 | 15 | 1.7 | 64 | A62AV,V75IT,M184I | K103N,P225HP,M230L |
| 71 | 18 | 2.1 | 78 | K65R,M184V | V106M,E138A,V179D,M230L |
| 72 | 23 | 2.8 | 103 | K65R,T69 deletion | K101E,K103KN,E138AT,Y181C,G190AT |
| 73 | 25 | 3.0 | 109 | A62V,K65R,M184I | V106M,V179D,M230L |
| 74 | 26 | 3.1 | 114 | M41L, V75I, M184V, T215Y | Y188L, H221Y, N348IN |
| 75 | 27 | 3.2 | 117 | M41L,T69AD,T215Y,K219KR | A98G,Y181C,G190S |
| 76 | 27 | 3.2 | 118 | M41L, D67N, T69D, M184I, L210W, T215Y | V90I, L100I, K103N |
| 77 | 30 | 3.6 | 132 | K65R,V75I,M184V,K219E | V90I,V108I,V179D,Y181C,G190A |
| 78 | 32 | 3.8 | 140 | K65R,M184V | L100I,K103N |
| 79 | 33 | 3.9 | 145 | K65R,K70KT,M184V | A98G,K101E,V106I,V108IV,Y181C,G190A |
| 80 | 33 | 4.0 | 148 | K65R,M184V | L100I,K103N |
| 81 | 41 | 4.9 | 181 | M184V,K219E | L100I,K103N |
| 82 | 44 | 5.2 | 193 | K65R,L74I,M184V | L100I,K103N |
| 83 | 47 | 5.6 | 207 | K70KN,L74V,Y115F,M184V | A98G,Y181C,H221Y,Y318F |
| 84 | 48 | 5.7 | 211 | M41L,D67N,K70KNRS,L74I,M184V,T215F,K219Q | A98G,K103N,P225H,K238N |

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|-----|----|-----|-----|--|--------------------------------------|
| 85 | 51 | 6.1 | 224 | K65R,K70KT,L74IL,M184V,K219KQ | K103NS,V106M,M230L |
| 86 | 64 | 7.6 | 280 | L74V,M184V | L100I,K103N,V108I,H221HY |
| 87 | 67 | 8.0 | 295 | D67N, T69D, K70R, M184V, T215V, K219Q | A98G, K103N, P225H |
| 88 | 72 | 8.6 | 318 | K65R, T69 deletion, K70KN, L74LV, Y115F, K219R | K101E, V106M, Y181C, G190A, H221Y |
| 89 | 73 | 8.6 | 320 | None | A98AG,K103N,V106MV,V179DINV,Y188FHLY |
| 90 | 77 | 9.2 | 339 | T69N,K70R,M184V,T215I,K219Q | A98G,K103N,V108I,M230L |
| 91 | 77 | 9.2 | 339 | K70E,M184V | L100I,K103N,V108IV,E138K,P225HP |
| 92 | 77 | 9.2 | 339 | D67G,M184V | L100IL,Y188L |
| 93 | 77 | 9.2 | 339 | M41L,D67N,K70KR,M184V,L210LW,T215Y,K219E | A98G,V179DV,Y188L |
| 94 | 77 | 9.2 | 339 | K65R,V75M,M184I | K103N,V106M,M230L |
| 95 | 77 | 9.2 | 339 | D67N,K70R,M184V,T215FI,K219E | K103N,V108I,V179E,N348I |
| 96 | 77 | 9.2 | 339 | K65R,T69 deletion | K103N,V179E,Y181C |
| 97 | 77 | 9.2 | 339 | K65R,K70KT,M184V | K103N,V179T,Y188L |
| 98 | 77 | 9.2 | 339 | K65R,L74V,M184V | L100I,K103N,M230L |
| 99 | 77 | 9.2 | 339 | A62AV,K65R,Y115FY,M184V | L100I,K103N |
| 100 | 77 | 9.2 | 339 | K65R,M184V,K219E | L100I,K103N,M230L,Y318F |

^a Fold-change resistance (FC) was calculated by dividing the IC₅₀ generated for each patient derived virus by a composite IC₅₀ from 12 treatment naïve patient derived viruses collected from the same geographical region.

^b Genotypic information was obtained through HIVdb v7.0 (Stanford University). Major NRTI and NNRTI resistance mutations are reported directly as determined by HIVdb v7.0.