

Supplemental Table 1. Summary of Baseline Resistance-Associated Substitutions in B/F/TAF-treated Participants

Baseline Genotype of Participants, % (n/N)	Pooled B/F/TAF n=2034
PR/RT data available (historical and/or proviral)	90 (1825/2034)
NRTI-R ^a	16 (288/1825)
M184V/I	10 (182/1825)
K65R/N	1 (18/1825)
≥1 TAM	9 (167/1825)
NNRTI-R ^b	22 (397/1825)
RPV-R ^c	9 (170/1825)
K103N/S	11 (205/1825)
PI-R ^d	11 (201/1825)
IN data available (historical and/or proviral)	85 (1731/2034)
Primary INSTI-R ^e	2 (30/1731)

- a. Nucleoside reverse transcriptase inhibitor resistance (NRTI-R) substitutions were K65R/E/N, T69 insertions, K70E, L74V/I, Y115F, Q151M, M184V/I, and thymidine analog mutations (TAMs; M41L, D67N, K70R, L210W, T215F/Y, and K219E/N/Q/R) in reverse transcriptase.
- b. Nonnucleoside reverse transcriptase inhibitor resistance (NNRTI-R) substitutions were L100I, K101E/P, K103N/S, V106M/A, V108I, E138A/G/K/Q/R, V179L, Y181C/I/V, Y188C/H/L, G190A/E/Q/S, H221Y, P225H, F227C and M230L/I in reverse transcriptase.
- c. Rilpivirine resistance (RPV-R) substitutions were L100I, K101E/P, E138A/G/K/Q/R, V179L, Y181C/I/V, Y188L, H221Y, F227C, and M230I/L in RT.
- d. Protease inhibitor resistance (PI-R) substitutions were D30N, V32I, M46I/L, I47V/A, G48V, I50V/L, I54M/L, Q58E, T74P, L76V, V82A/F/L/S/T, N83D, I84V, N88S and L90M in protease.
- e. Primary integrase strand transfer inhibitor resistance (INSTI-R) substitutions were T66I/A/K, E92Q/G, F121Y, Y143R/H/C, S147G, Q148H/K/R, N155H/S and R263K in integrase.

Supplemental Table 2. Detection of Baseline M184V/I by Historical or Baseline DNA Genotype and Viral Suppression at Last Visit Among B/F/TAF-treated Participants

Participants, % (n/N)	Historical Genotype n=956		Baseline DNA Genotype n=1712	
	Detection Frequency	HIV-1 RNA <50 copies/mL at Last Visit [median B/F/TAF duration, weeks]	Detection Frequency	HIV-1 RNA <50 copies/mL at Last Visit [median B/F/TAF duration, weeks]
M184V/I	4% (38/956)	100% (38/38) [55]	10% (167/1712)	98% (164/167) [71]
M184V only	4% (35/956)	100% (35/35) [56]	9% (148/1712)	99% (146/148) [71]
M184I	<1% (2/956)	100% (2/2) [62]	1% (10/1712)	100% (10/10) [94]
M184V and M184I mixture	<1% (1/956)	100% (1/1) [40]	1% (9/1712)	89% (8/9) [47]
M184V/I alone (no other resistance substitution)	1% (9/956)	100% (9/9) [60]	2% (34/1712)	97% (33/34) [71]
M184V/I + ≥1 other resistance substitution	3% (29/956)	100% (29/29) [54]	8% (133/1712)	98% (131/133) [71]
M184V/I + other NRTI-R	1% (13/956)	100% (13/13) [54]	5% (81/1712)	99% (80/81) [64]
M184V/I + K65R/N	<1% (3/956)	100% (3/3) [50]	<1% (7/1712)	100% (7/7) [53]
M184V/I + ≥1 TAM	1% (10/956)	100% (10/10) [55]	4% (68/1712)	99% (67/68) [64]
M184V/I + 1-2 TAMs	1% (8/956)	100% (8/8) [56]	2% (29/1712)	97% (28/29) [69]
M184V/I + ≥3 TAMs	<1% (2/956)	100% (2/2) [53]	2% (39/1712)	100% (39/39) [62]
M184V/I + K70E, L74V/I, Y115F, and/or Q151M	1% (6/956)	100% (6/6) [56]	1% (23/1712)	10% (23/23) [70]
M184V/I + NNRTI-R	3% (25/956)	100% (25/25) [54]	5% (85/1712)	99% (84/85) [72]
M184V/I + K103N	2% (15/956)	100% (15/15) [51]	3% (58/1712)	98% (57/58) [72]
M184V/I + RPV-R	1% (11/956)	100% (11/11) [58]	3% (45/1712)	100% (45/45) [72]
M184V/I + E138A/G/K/Q/R	1% (5/956)	100% (5/5) [51]	<1% (8/1712)	100% (8/8) [88]
M184V/I + PI-R	1% (8/956)	100% (8/8) [67]	3% (46/1712)	100% (46/46) [64]
M184V/I + Primary INSTI-R	0	NA	<1 % (4/1712)	100% (4/4) [63]

Supplemental Table 3. Discovery of M184V/I by Retrospective Baseline DNA Genotyping by M184V/I Enrollment Criteria

A. All Studies (M184V/I n=182)

Baseline DNA Genotype, % (n)	Historical Genotype at Enrollment			Total n=1825
	M184V/I n=38	Wild-type M184 n=918	No data n=869	
M184V/I	61% (23)	3% (31)	13% (113)	9% (167)
Wild-type M184	24% (9)	85% (780)	87% (756)	85% (1545)
No data	16% (6)	12% (107)	0	6% (113)

B. Studies 4030 and 4580 only (M184V/I n=97): M184V/I Allowed

Baseline DNA Genotype, % (n)	Historical Genotype at Enrollment			Total n=705
	M184V/I n=37	Wild-type M184 n=338	No data n=330	
M184V/I	59% (22)	5% (17)	13% (43)	12% (82)
Wild-type M184	24% (9)	81% (273)	87% (287)	81% (569)
No data	16% (6)	14% (48)	0	54% (8)

C. Studies 1844, 1878, 4449, and 1474 only (M184V/I n=85): M184V/I Excluded if Known Prior to Switch

Baseline DNA Genotype, % (n)	Historical Genotype at Enrollment			Total n=1120
	M184V/I n=1	Wild-type M184 n=580	No data n=539	
M184V/I	100% (1)	2% (14)	13% (70)	8% (85)
Wild-type M184	0	87% (507)	87% (469)	87% (976)
No data	0	10% (59)	0	5% (59)

Supplemental Table 4. Demographics, Clinical Characteristics, and Resistance at Baseline for Participants With and Without Preexisting M184V/I

	M184V/I n=216	Wild-type M184V/I n=216	P-value^a
From USA, % (n)	80% (173)	70% (1311)	0.003 ^b
Median age, years (IQR)	52.5 (47.75–59)	48 (38–56)	<0.0001
<50 years, % (n)	35% (76)	54% (1014)	
≥50 years, % (n)	65% (140)	46% (849)	<0.0001
Sex at birth, % (n)			
Male	78% (168)	82% (1534)	
Female	22% (48)	18% (329)	0.100
Race/ethnicity			
Black or African decent	47% (100)	37% (678)	0.003 ^b
Hispanic/Latino	19% (41)	14% (264)	0.049 ^b
Baseline BMI, % (n)			
Underweight & normal: <25 kg/m ²	32% (69)	35% (654)	
Overweight: ≥25–<30 kg/m ²	40% (87)	37% (683)	0.634
Obese: ≥30 kg/m ²	28% (60)	28% (526)	
Baseline CKD stage (based on eGFR [CG]), % (n)			
Stage 1: ≥90 mL/min	58% (125)	68% (1263)	
Stage 2: ≥60–<90 mL/min	36% (78)	29% (534)	
Stage 3A: ≥45–<60 mL/min	6% (13)	3% (55)	
Stage 3B: ≥30–<45 mL/min	0	<1% (11)	0.004
Stage 4: ≥15–<30 mL/min	0	0	
Stage 5: <15 mL/min	0	0	
Median CD4 count, cells/μL (IQR)	638.5 (460–839.5)	681 (495–884)	0.038
CD4 <500 cells/μL, % (n)	34% (73)	25% (473)	
CD4 ≥500 cells/μL, % (n)	66% (143)	75% (1390)	0.008
Baseline HIV-1 RNA, % (n)			
<50 copies/mL	97% (210)	98% (1823)	
≥50 copies/mL	3% (6)	2% (40)	0.551
HIV acquisition factor, % (n)			
Injection drug use	8% (18)	3% (61)	0.0002 ^b
Homosexual sex	55% (119)	65% (1210)	0.004 ^b
Heterosexual sex	38% (81)	31% (586)	0.072 ^b
HIV disease status, % (n)			
Symptomatic or AIDS	23% (50)	15% (280)	
Asymptomatic	77% (166)	85% (1583)	0.002
Median time since ART start, years (IQR)	19.0 (11.1–22.4)	7.3 (3.9–13.6)	<0.0001

	M184V/I n=216	Wild-type M184V/I n=216	P-value^a
Median duration of baseline ARV regimen (IQR)	2.1 (1.0–4.1)	1.7 (1.0–3.4)	0.127
Median number of prior third agents (IQR)	3.0 (2.0–4.0)	2.0 (1.0–2.0)	<0.0001
Median number of prior third agent classes (IQR)	2.0 (1.0–3.0)	1.0 (1.0–2.0)	<0.0001
Prior third agents, % (n)			
Any INSTI	63% (137)	67% (1242)	0.340 ^b
DTG	52% (112)	54% (999)	0.621 ^b
EVG	13% (29)	17% (325)	0.137 ^b
RAL	20% (44)	10% (178)	<0.0001 ^b
Any NNRTI	48% (103)	38% (704)	0.005 ^b
Any PI	79% (171)	52% (973)	<0.0001 ^b
Baseline resistance substitutions, % (n)			
NRTI-R (other than M184V/I)	49% (105)	7% (132)	<0.0001 ^b
≥1 TAM	40% (87)	6% (119)	<0.0001 ^b
NNRTI-R	54% (116)	18% (344)	<0.0001 ^b
RPV-R	27% (59)	8% (144)	<0.0001 ^b
PI-R	27% (59)	9% (169)	<0.0001 ^b
Primary INSTI-R	2% (5)	1% (26)	0.324 ^b
Secondary INSTI-R ^c	41% (86)	51% (890)	0.007 ^b
Clinical trial, % (n)			
Study 4030	38% (81)	21% (389)	<0.0001
Study 4580	24% (51)	23% (422)	
Study 1844	8% (17)	27% (511)	
Study 1878	30% (64)	25% (460)	
Study 4449	1% (3)	4% (81)	

- P-value derived from the CMH test for categorical data (general association statistic was used for nominal data; row mean scores differ statistic was used for ordinal data) or the 2-sided Wilcoxon rank sum test for continuous data.
 - Versus not from USA, non-Black race, not Hispanic or Latino ethnicity, no injection drug use, no homosexual or heterosexual sex, no prior treatment with listed third agents, or no baseline resistance to listed drug classes, as applicable.
 - Secondary INSTI-R substitutions are M50I, H51Y, L68V/I, V72A/N/T, L74M, Q95K/R, T97A, G118R, S119P/R/T, F121C, A128T, E138K/A, G140A/C/S, P145S, Q146R/I/K/L/P, V151L/A, S153A/F/Y, E157K/Q, G163K/R and E170A in integrase.
- ART, antiretroviral treatment; BMI, body mass index; CDK, chronic kidney disease; DTG, dolutegravir; eGFR (CG), estimated glomerular filtration rate by Cockcroft-Gault; EVG, elvitegravir; IQR, interquartile range; R, resistance; RAL, raltegravir; RPV, rilpivirine;