Table, Supplemental Digital Content 1. Frequency distribution of neuropathologic outcomes within antiretroviral therapy predictors and covariates.

n (%) within predictor or covariate	Neuronal phospho-tau pathology: present, absent	
	Frontal cortex	**Putamen**
Predictors		
NRTI drug use		
Abacavir (ABC)		
Yes	21 (48.8), 22 (51.2)	13 (43.3), 17 (56.7) *
No	53 (41.4), 75 (58.6)	20 (26), 57 (74)
Emtricitabine (FTC)		
Yes	21 (39.6), 32 (60.4)	10 (32.3), 21 (67.7)
No	53 (44.9), 65 (55.1)	23 (30.3), 53 (69.7)
Lamivudine (3TC)		
Yes	42 (45.7), 50 (54.3)	16 (26.2), 45 (73.8)
No	32 (40.5), 47 (59.5)	17 (37), 29 (63)
Tenofovir DF (TDF)		
Yes	30 (37.5), 50 (62.5) *	18 (32.7), 37 (67.3)
No	44 (48.4), 47 (51.6)	15 (28.8), 37 (71.2)
NNRTI drug use		
Efavirenz (EFV)		
Yes	18 (47.4), 20 (52.6)	5 (25), 15 (75)
No	56 (42.1), 77 (57.9)	28 (32.2), 59 (67.8)
PI drug use		
Atazanavir (ATV)		
Yes	11 (44), 14 (56)	7 (38.9), 11 (61.1)
No	63 (43.2), 83 (56.8)	26 (29.2), 63 (70.8)
Darunavir (DRV)		
Yes	6 (46.2), 7 (53.8)	7 (77.8), 2 (22.2) ****
No	68 (43), 90 (57)	26 (26.5), 72 (73.5)
Lopinavir (LPV)		
Yes	18 (43.9), 23 (56.1)	8 (30.8), 18 (69.2)
No	56 (43.1), 74 (56.9)	25 (30.9), 56 (69.1)
Ritonavir (RTV)		
Yes	37 (42.5), 50 (57.5)	19 (35.2), 35 (64.8)
No	37 (44), 47 (56)	14 (26.4), 39 (73.6)
INSTI drug use		
Raltegravir (RAL)		
Yes	6 (75), 2 (25) **	3 (75), 1 (25) **
No	68 (41.7), 95 (58.3)	30 (29.1), 73 (70.9)
CPE score: median [IQR, *n*]	8 [6.75−10, 74], 7 [6−9, 97] *	7 [6−9.5, 33], 8 [6−9, 74]
Covariates		
Age at death (years): median [IQR, *n*]	48.5 [40.75−56, 74], 47 [41−55, 97]	46 [39.5−54, 33], 46.5 [39.75−55, 74]
Sex		
Female	19 (52.8), 17 (47.2)	4 (22.2), 14 (77.8)
Male	55 (40.7), 80 (59.3)	29 (32.6), 60 (67.4)
Race/ethnicity		
White	32 (39), 50 (61)	16 (34), 31 (66)
Black	19 (52.8), 17 (47.2)	5 (22.7), 17 (77.3)
Hispanic	21 (46.7), 24 (53.3)	10 (31.3), 22 (68.8)
Others	2 (25), 6 (75)	2 (33.3), 4 (66.7)
APOE ε4 carrier status[a]		
Yes	12 (34.3), 23 (65.7)	11 (42.3), 15 (57.7)
No	51 (45.1), 62 (54.9)	18 (26.9), 49 (73.1)
APOE ε2 carrier status[a]		
Yes	4 (33.3), 8 (66.7)	1 (12.5), 7 (87.5)
No	59 (43.4), 77 (56.6)	28 (32.9), 57 (67.1)
Hepatitis C virus serostatus		
Yes	17 (34.7), 32 (65.3)	11 (34.4), 21 (65.6)
No	26 (40), 39 (60)	13 (24.1), 41 (75.9)

Diabetes mellitus		
Yes	5 (27.8), 13 (72.2)	5 (35.7), 9 (64.3)
No	41 (41), 59 (59)	23 (31.1), 51 (68.9)
Hypertension		
Yes	12 (31.6), 26 (68.4)	5 (17.9), 23 (82.1) **
No	36 (43.9), 46 (56.1)	23 (37.7), 38 (62.3)
Hyperlipidemia		
Yes	8 (33.3), 16 (66.7)	6 (42.9), 8 (57.1)
No	37 (42), 51 (58)	19 (27.9), 49 (72.1)
Lifetime alcohol dependence		
Yes	23 (44.2), 29 (55.8)	8 (29.6), 19 (70.4)
No	42 (48.8), 44 (51.2)	17 (32.1), 36 (67.9)
Lifetime cannabis dependence		
Yes	6 (37.5), 10 (62.5)	2 (28.6), 5 (71.4)
No	59 (48.4), 63 (51.6)	23 (31.5), 50 (68.5)
Lifetime psychostimulant dependence		
Yes	6 (27.3), 16 (72.7) **	2 (14.3), 12 (85.7)
No	59 (50.9), 57 (49.1)	23 (34.8), 43 (65.2)
Lifetime cigarette smoking		
Yes	19 (47.5), 21 (52.5) **	10 (37), 17 (63)
No	17 (28.8), 42 (71.2)	15 (28.3), 38 (71.7)
Lower last-visit CD4+ T-cell count[b]		
Yes	52 (40.9), 75 (59.1)	26 (35.1), 48 (64.9) *
No	20 (50), 20 (50)	6 (19.4), 25 (80.6)
	2.699 [2.314−4.751, 73],	3.347 [2.521−4.875, 33],
Last-visit PVL: median [IQR, *n*]	4.116 [2.308−5.005, 92] *	3.535 [2.542−4.871, 71]
Longer postmortem interval[c]		
Yes	29 (42), 40 (58)	14 (32.6), 29 (67.4)
No	45 (44.1), 57 (55.9)	19 (29.7), 45 (70.3)
HIV encephalitis or white matter lesions		
Yes	14 (45.2), 17 (54.8)	4 (18.2), 18 (81.8) *
No	60 (42.9), 80 (57.1)	29 (34.1), 56 (65.9)
Opportunistic brain diseases		
Yes	3 (21.4), 11 (78.6) **	3 (33.3), 6 (66.7)
No	71 (45.2), 86 (54.8)	30 (30.6), 68 (69.4)
NNTC site		
CNTN	13 (20.3), 51 (79.7) ****	17 (27.4), 45 (72.6)
NNAB	31 (53.4), 27 (46.6)	16 (35.6), 29 (64.4)
TNRC	15 (60), 10 (40)	No samples
MHBB	15 (62.5), 9 (37.5)	No samples

Iba1, ionized calcium-binding adapter molecule-1; GFAP, glial fibrillary acidic protein; CSVD, cerebral small vessel disease; NRTI, nucleoside reverse transcriptase inhibitor; NNRTI, non-nucleoside reverse transcriptase inhibitor; PI, protease inhibitor; INSTI, integrase strand transfer inhibitor; CPE, central nervous system penetration-effectiveness; IQR, interquartile range; *APOE*, apolipoprotein-E gene; PVL, plasma HIV-1 RNA ($\log_{10}$ copies/mL); NNTC, National NeuroAIDS Tissue Consortium; CNTN, California NeuroAIDS Tissue Network; NNAB, National Neurological AIDS Bank; TNRC, Texas NeuroAIDS Research Center; MHBB, Manhattan HIV Brain Bank.
[a]With one or two *APOE* ε2 or ε4 alleles, excluding *APOE* ε2/ε4 carrying cases.
[b]Fewer than 200 cells/μL.
[c]Longer than 12 hours.
*$P<0.2$, **$P<0.1$, ***$P<0.05$, ****$P<0.01$ (two-tailed, Fisher's exact test for categorical predictors and covariates, Mann-Whitney U-test for continuous predictor and covariates).

Table, Supplemental Digital Content 1. Continued.

n (%) within predictor or covariate	β-Amyloid plaque deposition: present, absent	
	Frontal cortex	**Putamen**
Predictors		
NRTI drug use		
Abacavir (ABC)		
Yes	14 (32.6), 29 (67.4)	3 (9.4), 29 (90.6)
No	34 (26.6), 94 (73.4)	14 (16.1), 73 (83.9)
Emtricitabine (FTC)		
Yes	16 (30.2), 37 (69.8)	8 (23.5), 26 (76.5) **
No	32 (27.1), 86 (72.9)	9 (10.6), 76 (89.4)
Lamivudine (3TC)		
Yes	27 (29.3), 65 (70.7)	10 (14.7), 58 (85.3)
No	21 (26.6), 58 (73.4)	7 (13.7), 44 (86.3)
Tenofovir DF (TDF)		
Yes	18 (22.5), 62 (77.5) *	12 (19.4), 50 (80.6) *
No	30 (33), 61 (67)	5 (8.8), 52 (91.2)
NNRTI drug use		
Efavirenz (EFV)		
Yes	9 (23.7), 29 (76.3)	5 (23.8), 16 (76.2) *
No	39 (29.3), 94 (70.7)	12 (12.2), 86 (87.8)
PI drug use		
Atazanavir (ATV)		
Yes	6 (24), 19 (76)	4 (19), 17 (81)
No	42 (28.8), 104 (71.2)	13 (13.3), 85 (86.7)
Darunavir (DRV)		
Yes	3 (23.1), 10 (76.9)	2 (22.2), 7 (77.8)
No	45 (28.5), 113 (71.5)	15 (13.6), 95 (86.4)
Lopinavir (LPV)		
Yes	12 (29.3), 29 (70.7)	8 (26.7), 22 (73.3) ***
No	36 (27.7), 94 (72.3)	9 (10.1), 80 (89.9)
Ritonavir (RTV)		
Yes	21 (24.1), 66 (75.9)	11 (18), 50 (82)
No	27 (32.1), 57 (67.9)	6 (10.3), 52 (89.7)
INSTI drug use		
Raltegravir (RAL)		
Yes	2 (25), 6 (75)	2 (50), 2 (50) **
No	46 (28.2), 117 (71.8)	15 (13), 100 (87)
CPE score: median [IQR, n]	8 [7−9, 48], 7 [6−10, 123]	8 [6−13, 17], 7 [6−9, 102]
Covariates		
Age at death (years): median [IQR, n]	54 [47−58.5, 48], 46 [39−54, 123] ****	57 [44−59, 17], 46 [39−54, 102] ***
Sex		
Female	8 (22.2), 28 (77.8)	2 (9.5), 19 (90.5)
Male	40 (29.6), 95 (70.4)	15 (15.3), 83 (84.7)
Race/ethnicity		
White	24 (29.3), 58 (70.7)	8 (15.7), 43 (84.3)
Black	9 (25), 27 (75)	3 (12.5), 21 (87.5)
Hispanic	12 (26.7), 33 (73.3)	6 (16.7), 30 (83.3)
Others	3 (37.5), 5 (62.5)	0 (0), 8 (100)
APOE ε4 carrier status[a]		
Yes	17 (48.6), 18 (51.4) ****	7 (25), 21 (75)
No	26 (23), 87 (77)	10 (13.7), 63 (86.3)
APOE ε2 carrier status[a]		
Yes	3 (25), 9 (75)	2 (25), 6 (75)
No	40 (29.4), 96 (70.6)	15 (16.1), 78 (83.9)
Hepatitis C virus serostatus		
Yes	13 (26.5), 36 (73.5)	4 (10.5), 34 (89.5)
No	21 (32.3), 44 (67.7)	7 (12.1), 51 (87.9)

Diabetes mellitus		
Yes	2 (11.1), 16 (88.9) **	3 (20), 12 (80)
No	35 (35), 65 (65)	11 (13.3), 72 (86.7)
Hypertension		
Yes	9 (23.7), 29 (76.3)	4 (13.3), 26 (86.7)
No	29 (35.4), 53 (64.6)	10 (14.5), 59 (85.5)
Hyperlipidemia		
Yes	5 (20.8), 19 (79.2)	2 (13.3), 13 (86.7)
No	31 (35.2), 57 (64.8)	9 (11.7), 68 (88.3)
Lifetime alcohol dependence		
Yes	12 (23.1), 40 (76.9)	4 (13.3), 26 (86.7)
No	25 (29.1), 61 (70.9)	8 (14), 49 (86)
Lifetime cannabis dependence		
Yes	1 (6.3), 15 (93.8) **	1 (14.3), 6 (85.7)
No	36 (29.5), 86 (70.5)	11 (13.8), 69 (86.3)
Lifetime psychostimulant dependence		
Yes	5 (22.7), 17 (77.3)	2 (13.3), 13 (86.7)
No	32 (27.6), 84 (72.4)	10 (13.9), 62 (86.1)
Lifetime cigarette smoking		
Yes	14 (35), 26 (65)	5 (16.7), 25 (83.3) *
No	16 (27.1), 43 (72.9)	4 (6.8), 55 (93.2)
Lower last-visit CD4+ T-cell count[b]		
Yes	29 (22.8), 98 (77.2) ***	14 (16.9), 69 (83.1)
No	17 (42.5), 23 (57.5)	3 (9.1), 30 (90.9)
Last-visit PVL: median [IQR, n]	2.602 [1.869−4.199, 47], 3.963 [2.602−5.133, 118] ****	2.602 [1.838−4.840, 17], 3.843 [2.602−4.855, 97]
Longer postmortem interval[c]		
Yes	18 (26.1), 51 (73.9)	5 (10.2), 44 (89.8)
No	30 (29.4), 72 (70.6)	12 (17.1), 58 (82.9)
HIV encephalitis or white matter lesions		
Yes	6 (19.4), 25 (80.6)	2 (8), 23 (92)
No	42 (30), 98 (70)	15 (16), 79 (84)
Opportunistic brain diseases		
Yes	1 (7.1), 13 (92.9) *	1 (7.7), 12 (92.3)
No	47 (29.9), 110 (70.1)	16 (15.1), 90 (84.9)
NNTC site		
CNTN	14 (21.9), 50 (78.1) **	3 (4.1), 70 (95.9) ****
NNAB	23 (39.7), 35 (60.3)	14 (30.4), 32 (69.6)
TNRC	4 (16), 21 (84)	No samples
MHBB	7 (29.2), 17 (70.8)	No samples

Iba1, ionized calcium-binding adapter molecule-1; GFAP, glial fibrillary acidic protein; CSVD, cerebral small vessel disease; NRTI, nucleoside reverse transcriptase inhibitor; NNRTI, non-nucleoside reverse transcriptase inhibitor; PI, protease inhibitor; INSTI, integrase strand transfer inhibitor; CPE, central nervous system penetration-effectiveness; IQR, interquartile range; *APOE*, apolipoprotein-E gene; PVL, plasma HIV-1 RNA ($\log_{10}$ copies/mL); NNTC, National NeuroAIDS Tissue Consortium; CNTN, California NeuroAIDS Tissue Network; NNAB, National Neurological AIDS Bank; TNRC, Texas NeuroAIDS Research Center; MHBB, Manhattan HIV Brain Bank.
[a]With one or two *APOE* ε2 or ε4 alleles, excluding *APOE* ε2/ε4 carrying cases.
[b]Fewer than 200 cells/μL.
[c]Longer than 12 hours.
*$P<0.2$, **$P<0.1$, ***$P<0.05$, ****$P<0.01$ (two-tailed, Fisher's exact test for categorical predictors and covariates, Mann-Whitney U-test for continuous predictor and covariates).

Table, Supplemental Digital Content 1. Continued.

n (%) within predictor or covariate	Iba1 microgliosis: marked, mild	
	Frontal cortex	**Putamen**
Predictors		
NRTI drug use		
Abacavir (ABC)		
Yes	23 (53.5), 20 (46.5)	18 (56.3), 14 (43.8)
No	62 (48.4), 66 (51.6)	41 (47.1), 46 (52.9)
Emtricitabine (FTC)		
Yes	28 (52.8), 25 (47.2)	18 (52.9), 16 (47.1)
No	57 (48.3), 61 (51.7)	41 (48.2), 44 (51.8)
Lamivudine (3TC)		
Yes	42 (45.7), 50 (54.3)	31 (45.6), 37 (54.4)
No	43 (54.4), 36 (45.6)	28 (54.9), 23 (45.1)
Tenofovir DF (TDF)		
Yes	40 (50), 40 (50)	29 (46.8), 33 (53.2)
No	45 (49.5), 46 (50.5)	30 (52.6), 27 (47.4)
NNRTI drug use		
Efavirenz (EFV)		
Yes	17 (44.7), 21 (55.3)	9 (42.9), 12 (57.1)
No	68 (51.1), 65 (48.9)	50 (51), 48 (49)
PI drug use		
Atazanavir (ATV)		
Yes	13 (52), 12 (48)	9 (42.9), 12 (57.1)
No	72 (49.3), 74 (50.7)	50 (51), 48 (49)
Darunavir (DRV)		
Yes	6 (46.2), 7 (53.8)	3 (33.3), 6 (66.7)
No	79 (50), 79 (50)	56 (50.9), 54 (49.1)
Lopinavir (LPV)		
Yes	19 (46.3), 22 (53.7)	16 (53.3), 14 (46.7)
No	66 (50.8), 64 (49.2)	43 (48.3), 46 (51.7)
Ritonavir (RTV)		
Yes	44 (50.6), 43 (49.4)	33 (54.1), 28 (45.9)
No	41 (48.8), 43 (51.2)	26 (44.8), 32 (55.2)
INSTI drug use		
Raltegravir (RAL)		
Yes	4 (50), 4 (50)	1 (25), 3 (75)
No	81 (49.7), 82 (50.3)	58 (50.4), 57 (49.6)
CPE score: median [IQR, *n*]	8 [6−9, 85], 7 [6−9.25, 86]	7 [6−9, 59], 7 [6−9, 60]
Covariates		
	45 [39.5−53.5, 85],	46 [40−53, 59],
Age at death (years): median [IQR, *n*]	52 [42.75−57, 86] ****	48.5 [40−56, 60] *
Sex		
Female	20 (55.6), 16 (44.4)	13 (61.9), 8 (38.1)
Male	65 (48.1), 70 (51.9)	46 (46.9), 52 (53.1)
Race/ethnicity		
White	41 (50), 41 (50)	26 (51), 25 (49)
Black	19 (52.8), 17 (47.2)	12 (50), 12 (50)
Hispanic	20 (44.4), 25 (55.6)	16 (44.4), 20 (55.6)
Others	5 (62.5), 3 (37.5)	5 (62.5), 3 (37.5)
APOE ε4 carrier status[a]		
Yes	22 (62.9), 13 (37.1) **	20 (71.4), 8 (28.6) ****
No	49 (43.4), 64 (56.6)	27 (37), 46 (63)
APOE ε2 carrier status[a]		
Yes	4 (33.3), 8 (66.7)	3 (37.5), 5 (62.5)
No	67 (49.3), 69 (50.7)	44 (47.3), 49 (52.7)
Hepatitis C virus serostatus		
Yes	26 (53.1), 23 (46.9)	18 (47.4), 20 (52.6)
No	29 (44.6), 36 (55.4)	30 (51.7), 28 (48.3)

Diabetes mellitus		
Yes	5 (27.8), 13 (72.2) **	6 (40), 9 (60)
No	52 (52), 48 (48)	46 (55.4), 37 (44.6)
Hypertension		
Yes	13 (34.2), 25 (65.8) ***	13 (43.3), 17 (56.7) *
No	47 (57.3), 35 (42.7)	41 (59.4), 28 (40.6)
Hyperlipidemia		
Yes	10 (41.7), 14 (58.3)	8 (53.3), 7 (46.7)
No	47 (53.4), 41 (46.6)	44 (57.1), 33 (42.9)
Lifetime alcohol dependence		
Yes	31 (59.6), 21 (40.4) *	16 (53.3), 14 (46.7)
No	40 (46.5), 46 (53.5)	25 (43.9), 32 (56.1)
Lifetime cannabis dependence		
Yes	8 (50), 8 (50)	5 (71.4), 2 (28.6)
No	63 (51.6), 59 (48.4)	36 (45), 44 (55)
Lifetime psychostimulant dependence		
Yes	16 (72.7), 6 (27.3) ***	6 (40), 9 (60)
No	55 (47.4), 61 (52.6)	35 (48.6), 37 (51.4)
Lifetime cigarette smoking		
Yes	24 (60), 16 (40)	15 (50), 15 (50)
No	31 (52.5), 28 (47.5)	35 (59.3), 24 (40.7)
Lower last-visit CD4+ T-cell count[b]		
Yes	66 (52), 61 (48)	40 (48.2), 43 (51.8)
No	16 (40), 24 (60)	16 (48.5), 17 (51.5)
Last-visit PVL: median [IQR, n]	4.199 [2.602−5.428, 81], 2.652 [1.875−4.548, 84] ****	4.018 [2.602−5.250, 56], 2.958 [2.561−4.710, 58] **
Longer postmortem interval[c]		
Yes	39 (56.5), 30 (43.5) *	27 (55.1), 22 (44.9)
No	46 (45.1), 56 (54.9)	32 (45.7), 38 (54.3)
HIV encephalitis or white matter lesions		
Yes	20 (64.5), 11 (35.5) **	16 (64), 9 (36) *
No	65 (46.4), 75 (53.6)	43 (45.7), 51 (54.3)
Opportunistic brain diseases		
Yes	10 (71.4), 4 (28.6) *	10 (76.9), 3 (23.1) ***
No	75 (47.8), 82 (52.2)	49 (46.2), 57 (53.8)
NNTC site		
CNTN	43 (67.2), 21 (32.8) ****	50 (68.5), 23 (31.5) ****
NNAB	18 (31), 40 (69)	9 (19.6), 37 (80.4)
TNRC	17 (68), 8 (32)	No samples
MHBB	7 (29.2), 17 (70.8)	No samples

Iba1, ionized calcium-binding adapter molecule-1; GFAP, glial fibrillary acidic protein; CSVD, cerebral small vessel disease; NRTI, nucleoside reverse transcriptase inhibitor; NNRTI, non-nucleoside reverse transcriptase inhibitor; PI, protease inhibitor; INSTI, integrase strand transfer inhibitor; CPE, central nervous system penetration-effectiveness; IQR, interquartile range; *APOE*, apolipoprotein-E gene; PVL, plasma HIV-1 RNA ($\log_{10}$ copies/mL); NNTC, National NeuroAIDS Tissue Consortium; CNTN, California NeuroAIDS Tissue Network; NNAB, National Neurological AIDS Bank; TNRC, Texas NeuroAIDS Research Center; MHBB, Manhattan HIV Brain Bank.
[a]With one or two *APOE* ε2 or ε4 alleles, excluding *APOE* ε2/ε4 carrying cases.
[b]Fewer than 200 cells/µL.
[c]Longer than 12 hours.
*$P<0.2$, **$P<0.1$, ***$P<0.05$, ****$P<0.01$ (two-tailed, Fisher's exact test for categorical predictors and covariates, Mann-Whitney U-test for continuous predictor and covariates).

Table, Supplemental Digital Content 1. Continued.

n (%) within predictor or covariate	GFAP astrogliosis: marked, mild	
	Frontal cortex	**Putamen**
Predictors		
NRTI drug use		
Abacavir (ABC)		
Yes	21 (48.8), 22 (51.2)	18 (56.3), 14 (43.8)
No	64 (50), 64 (50)	41 (47.1), 46 (52.9)
Emtricitabine (FTC)		
Yes	28 (52.8), 25 (47.2)	17 (50), 17 (50)
No	57 (48.3), 61 (51.7)	42 (49.4), 43 (50.6)
Lamivudine (3TC)		
Yes	44 (47.8), 48 (52.2)	35 (51.5), 33 (48.5)
No	41 (51.9), 38 (48.1)	24 (47.1), 27 (52.9)
Tenofovir DF (TDF)		
Yes	38 (47.5), 42 (52.5)	30 (48.4), 32 (51.6)
No	47 (51.6), 44 (48.4)	29 (50.9), 28 (49.1)
NNRTI drug use		
Efavirenz (EFV)		
Yes	19 (50), 19 (50)	9 (42.9), 12 (57.1)
No	66 (49.6), 67 (50.4)	50 (51), 48 (49)
PI drug use		
Atazanavir (ATV)		
Yes	10 (40), 15 (60)	13 (61.9), 8 (38.1)
No	75 (51.4), 71 (48.6)	46 (46.9), 52 (53.1)
Darunavir (DRV)		
Yes	6 (46.2), 7 (53.8)	3 (33.3), 6 (66.7)
No	79 (50), 79 (50)	56 (50.9), 54 (49.1)
Lopinavir (LPV)		
Yes	19 (46.3), 22 (53.7)	12 (40), 18 (60)
No	66 (50.8), 64 (49.2)	47 (52.8), 42 (47.2)
Ritonavir (RTV)		
Yes	40 (46), 47 (54)	31 (50.8), 30 (49.2)
No	45 (53.6), 39 (46.4)	28 (48.3), 30 (51.7)
INSTI drug use		
Raltegravir (RAL)		
Yes	4 (50), 4 (50)	1 (25), 3 (75)
No	81 (49.7), 82 (50.3)	58 (50.4), 57 (49.6)
CPE score: median [IQR, *n*]	7 [6−9, 85], 8 [6−9, 86]	8 [6−9, 59], 7 [6−9, 60]
Covariates		
Age at death (years): median [IQR, *n*]	47 [40.5−55, 85], 49.5 [41−56, 86]	47 [41−55, 59], 45 [39−54, 60]
Sex		
Female	16 (44.4), 20 (55.6)	9 (42.9), 12 (57.1)
Male	69 (51.1), 66 (48.9)	50 (51), 48 (49)
Race/ethnicity		
White	48 (58.5), 34 (41.5) *	30 (58.8), 21 (41.2) *
Black	15 (41.7), 21 (58.3)	12 (50), 12 (50)
Hispanic	18 (40), 27 (60)	12 (33.3), 24 (66.7)
Others	4 (50), 4 (50)	5 (62.5), 3 (37.5)
APOE ε4 carrier status[a]		
Yes	17 (48.6), 18 (51.4)	18 (64.3), 10 (35.7) **
No	54 (47.8), 59 (52.2)	31 (42.5), 42 (57.5)
APOE ε2 carrier status[a]		
Yes	6 (50), 6 (50)	4 (50), 4 (50)
No	65 (47.8), 71 (52.2)	45 (48.4), 48 (51.6)
Hepatitis C virus serostatus		
Yes	22 (44.9), 27 (55.1)	19 (50), 19 (50)
No	36 (55.4), 29 (44.6)	29 (50), 29 (50)

Diabetes mellitus		
Yes	9 (50), 9 (50)	7 (46.7), 8 (53.3)
No	55 (55), 45 (45)	44 (53), 39 (47)
Hypertension		
Yes	19 (50), 19 (50)	13 (43.3), 17 (56.7)
No	45 (54.9), 37 (45.1)	39 (56.5), 30 (43.5)
Hyperlipidemia		
Yes	11 (45.8), 13 (54.2)	8 (53.3), 7 (46.7)
No	51 (58), 37 (42)	41 (53.2), 36 (46.8)
Lifetime alcohol dependence		
Yes	29 (55.8), 23 (44.2) *	16 (53.3), 14 (46.7)
No	37 (43), 49 (57)	28 (49.1), 29(50.9)
Lifetime cannabis dependence		
Yes	10 (62.5), 6 (37.5)	5 (71.4), 2 (28.6)
No	56 (45.9), 66 (54.1)	39 (48.8), 41 (51.3)
Lifetime psychostimulant dependence		
Yes	15 (68.2), 7 (31.8) **	8 (53.3), 7 (46.7)
No	51 (44), 65 (56)	36 (50), 36 (50)
Lifetime cigarette smoking		
Yes	16 (40), 24 (60) ***	13 (43.3), 17 (56.7) *
No	36 (61), 23 (39)	36 (61), 23 (39)
Lower last-visit CD4+ T-cell count[b]		
Yes	59 (46.5), 68 (53.5) *	36 (43.4), 47 (56.6) ***
No	24 (60), 16 (40)	22 (66.7), 11 (33.3)
	3.451 [1.875−4.928, 81],	3.948 [2.480−4.943, 56],
Last-visit PVL: median [IQR, n]	3.547 [2.602−4.875, 84]	3.070 [2.602−4.741, 58]
Longer postmortem interval[c]		
Yes	37 (53.6), 32 (46.4)	28 (57.1), 21 (42.9) *
No	48 (47.1), 54 (52.9)	31 (44.3), 39 (55.7)
HIV encephalitis or white matter lesions		
Yes	16 (51.6), 15 (48.4)	11 (44), 14 (56)
No	69 (49.3), 71 (50.7)	48 (51.1), 46 (48.9)
Opportunistic brain diseases		
Yes	6 (42.9), 8 (57.1)	7 (53.8), 6 (46.2)
No	79 (50.3), 78 (49.7)	52 (49.1), 54 (50.9)
NNTC site		
CNTN	40 (62.5), 24 (37.5) **	44 (60.3), 29 (39.7) ****
NNAB	23 (39.7), 35 (60.3)	15 (32.6), 31 (67.4)
TNRC	10 (40), 15 (60)	No samples
MHBB	12 (50), 12 (50)	No samples

Iba1, ionized calcium-binding adapter molecule-1; GFAP, glial fibrillary acidic protein; CSVD, cerebral small vessel disease; NRTI, nucleoside reverse transcriptase inhibitor; NNRTI, non-nucleoside reverse transcriptase inhibitor; PI, protease inhibitor; INSTI, integrase strand transfer inhibitor; CPE, central nervous system penetration-effectiveness; IQR, interquartile range; *APOE*, apolipoprotein-E gene; PVL, plasma HIV-1 RNA ($\log_{10}$ copies/mL); NNTC, National NeuroAIDS Tissue Consortium; CNTN, California NeuroAIDS Tissue Network; NNAB, National Neurological AIDS Bank; TNRC, Texas NeuroAIDS Research Center; MHBB, Manhattan HIV Brain Bank.
[a]With one or two *APOE* ε2 or ε4 alleles, excluding *APOE* ε2/ε4 carrying cases.
[b]Fewer than 200 cells/μL.
[c]Longer than 12 hours.
*$P<0.2$, **$P<0.1$, ***$P<0.05$, ****$P<0.01$ (two-tailed, Fisher's exact test for categorical predictors and covariates, Mann-Whitney U-test for continuous predictor and covariates).

Table, Supplemental Digital Content 1. Continued.

n (%) within predictor or covariate	CSVD: present, absent Forebrain white matter
Predictors	
NRTI drug use	
Abacavir (ABC)	
Yes	14 (70), 6 (30) *
No	48 (84.2), 9 (15.8)
Emtricitabine (FTC)	
Yes	20 (100), 0 (0) ****
No	42 (73.7), 15 (26.3)
Lamivudine (3TC)	
Yes	32 (78), 9 (22)
No	30 (83.3), 6 (16.7)
Tenofovir DF (TDF)	
Yes	33 (84.6), 6 (15.4)
No	29 (76.3), 9 (23.7)
NNRTI drug use	
Efavirenz (EFV)	
Yes	12 (80), 3 (20)
No	50 (80.6), 12 (19.4)
PI drug use	
Atazanavir (ATV)	
Yes	10 (83.3), 2 (16.7)
No	52 (80), 13 (20)
Darunavir (DRV)	
Yes	2 (100), 0 (0)
No	60 (80), 15 (20)
Lopinavir (LPV)	
Yes	13 (86.7), 2 (13.3)
No	49 (79), 13 (21)
Ritonavir (RTV)	
Yes	30 (85.7), 5 (14.3)
No	32 (76.2), 10 (23.8)
INSTI drug use	
Raltegravir (RAL)	
Yes	0 (0), 0 (0)
No	62 (80.5), 15 (19.5)
CPE score: median [IQR, *n*]	7 [6−8, 62], 8 [5−9, 15]
Covariates	
Age at death (years): median [IQR, *n*]	45.5 [39.75−53.25, 62], 47 [39−54, 15]
Sex	
Female	12 (80), 3 (20)
Male	50 (80.6), 12 (19.4)
Race/ethnicity	
White	33 (82.5), 7 (17.5)
Black	10 (71.4), 4 (28.6)
Hispanic	14 (87.5), 2 (12.5)
Others	5 (71.4), 2 (28.6)
APOE ε4 carrier status[a]	
Yes	13 (86.7), 2 (13.3)
No	36 (83.7), 7 (16.3)
APOE ε2 carrier status[a]	
Yes	4 (80), 1 (20)
No	45 (84.9), 8 (15.1)
Hepatitis C virus serostatus	
Yes	21 (80.8), 5 (19.2)
No	28 (77.8), 8 (22.2)

Diabetes mellitus	
Yes	9 (100), 0(0) *
No	51 (77.3), 15 (22.7)
Hypertension	
Yes	17 (77.3), 5 (22.7)
No	43 (81.1), 10 (18.9)
Hyperlipidemia	
Yes	8 (72.7), 3 (27.3)
No	52 (81.3), 12 (18.8)
Lifetime alcohol dependence	
Yes	23 (92), 2 (8) **
No	21 (70), 9 (30)
Lifetime cannabis dependence	
Yes	5 (100), 0 (0)
No	39 (78), 11 (22)
Lifetime psychostimulant dependence	
Yes	9 (75), 3 (25)
No	35 (81.4), 8 (18.6)
Lifetime cigarette smoking	
Yes	15 (75), 5 (25)
No	44 (81.5), 10 (18.5)
Lower last-visit CD4+ T-cell count[b]	
Yes	42 (77.8), 12 (22.2)
No	19 (86.4), 3 (13.6)
Last-visit PVL: median [IQR, n]	3.553 [2.210−4.899, 59], 4.211 [3.898−4.732, 14]
Longer postmortem interval[c]	
Yes	35 (87.5), 5 (12.5)
No	27 (73), 10 (27)
HIV encephalitis or white matter lesions	
Yes	19 (95), 1 (5) **
No	43 (75.4), 14 (24.6)
Opportunistic brain diseases	
Yes	8 (66.7), 4 (33.3)
No	54 (83.1), 11 (16.9)
NNTC site	
CNTN	62 (80.5), 15 (19.5)
NNAB	No samples
TNRC	No samples
MHBB	No samples

Iba1, ionized calcium-binding adapter molecule-1; GFAP, glial fibrillary acidic protein; CSVD, cerebral small vessel disease; NRTI, nucleoside reverse transcriptase inhibitor; NNRTI, non-nucleoside reverse transcriptase inhibitor; PI, protease inhibitor; INSTI, integrase strand transfer inhibitor; CPE, central nervous system penetration-effectiveness; IQR, interquartile range; *APOE*, apolipoprotein-E gene; PVL, plasma HIV-1 RNA ($\log_{10}$ copies/mL); NNTC, National NeuroAIDS Tissue Consortium; CNTN, California NeuroAIDS Tissue Network; NNAB, National Neurological AIDS Bank; TNRC, Texas NeuroAIDS Research Center; MHBB, Manhattan HIV Brain Bank.

[a]With one or two *APOE* ε2 or ε4 alleles, excluding *APOE* ε2/ε4 carrying cases.
[b]Fewer than 200 cells/μL.
[c]Longer than 12 hours.
*$P<0.2$, **$P<0.1$, ***$P<0.05$, ****$P<0.01$ (two-tailed, Fisher's exact test for categorical predictors and covariates, Mann-Whitney U-test for continuous predictor and covariates).

Table, Supplemental Digital Content 2. Results of logistic regression models testing associations between biological covariates and neuropathologic outcomes, after adjusting for the two technical covariates.

P value	Neuronal phospho-tau pathology[a]		β-Amyloid plaque deposition[a]	
	Frontal cortex	**Putamen**	**Frontal cortex**	**Putamen**
Age at death (each year increase)	0.855	0.694	**<0.0005 (+)**	**0.070 (+)**
Female (vs. male)	0.331	0.420	0.417	0.567
Race/ethnicity (vs. white)				
Black	0.245	0.261	0.382	0.389
Hispanic	0.374	0.696	0.329	0.481
Others	0.876	0.781	0.397	0.536
APOE ε4 carrier status[c]	0.438	**0.176 (+)**	**0.005 (+)**	0.261
APOE ε2 carrier status[c]	0.373	0.292	0.768	0.356
Hepatitis C virus serostatus	0.434	0.312	0.469	0.894
Diabetes mellitus	**0.105 (−)**	0.945	**0.004 (−)**	0.921
Hypertension	**0.113 (−)**	**0.039 (−)**	**0.119 (−)**	0.642
Hyperlipidemia	**0.124 (−)**	0.342	**0.156 (−)**	0.883
Lifetime alcohol dependence	0.913	0.964	0.702	0.762
Lifetime cannabis dependence	0.293	0.930	**0.083 (−)**	0.679
Lifetime psychostimulant dependence	**0.114 (−)**	**0.185 (−)**	0.907	0.755
Lifetime cigarette smoking	0.810	0.986	0.676	0.641
Lower last-visit CD4+ T-cell count (<200 cells/μL)	0.211	**0.107 (+)**	**0.023 (−)**	0.259
Last-visit plasma HIV-1 RNA (log$_{10}$ copies/mL)	**0.096 (−)**	0.852	**0.014 (−)**	0.825
HIV encephalitis or white matter lesions	0.272	**0.173 (−)**	0.281	0.696
Opportunistic brain diseases	0.477	0.572	**0.107 (−)**	0.595

[a]Presence (with reference to absence).
[b]Marked gliosis (with reference to mild gliosis).
[c]With one or two *APOE* ε2 or ε4 alleles, excluding *APOE* ε2/ε4 carrying cases.
Model for CSVD: outcome = biological covariate.
Models for the other eight outcomes: outcome = biological covariate + technical covariates (NNTC site and PMI).
Covariates having *P*<0.20 (in boldface, with direct (+) or inverse (−) association) were subsequently included in the initial logistic regression models with antiretroviral therapy predictors.
Iba1, ionized calcium-binding adapter molecule-1; GFAP, glial fibrillary acidic protein; CSVD, cerebral small vessel disease; *APOE*, apolipoprotein-E gene; NNTC, National NeuroAIDS Tissue Consortium; PMI, longer postmortem interval (>12 hours).

Table, Supplemental Digital Content 2. Continued.

P value	Iba1 microgliosis[b]		GFAP astrogliosis[b]	
	Frontal cortex	**Putamen**	**Frontal cortex**	**Putamen**
Age at death (each year increase)	**0.009 (−)**	0.635	0.611	**0.054 (+)**
Female (vs. male)	0.271	**0.172 (+)**	0.542	0.475
Race/ethnicity (vs. white)				
Black	0.311	0.480	**0.102 (−)**	0.669
Hispanic	0.541	0.685	**0.040 (−)**	**0.073 (−)**
Others	0.929	0.997	0.393	0.970
APOE ε4 carrier status[c]	**0.040 (+)**	**<0.0005 (+)**	0.959	**0.025 (+)**
APOE ε2 carrier status[c]	0.393	0.584	0.839	0.916
Hepatitis C virus serostatus	0.286	0.585	0.248	0.944
Diabetes mellitus	**0.160 (−)**	0.807	0.993	0.916
Hypertension	**0.021 (−)**	0.227	0.736	0.250
Hyperlipidemia	0.311	0.853	0.429	0.840
Lifetime alcohol dependence	0.662	0.744	0.211	0.974
Lifetime cannabis dependence	0.423	0.215	**0.198 (+)**	0.353
Lifetime psychostimulant dependence	**0.183 (+)**	0.265	**0.045 (+)**	0.938
Lifetime cigarette smoking	**0.041 (+)**	0.281	0.238	0.368
Lower last-visit CD4+ T-cell count (<200 cells/μL)	0.209	0.904	**0.154 (−)**	**0.020 (−)**
Last-visit plasma HIV-1 RNA (log$_{10}$ copies/mL)	**0.002 (+)**	0.379	0.406	0.589
HIV encephalitis or white matter lesions	**0.172 (+)**	0.308	0.855	0.229
Opportunistic brain diseases	0.223	0.366	0.247	0.754

[a]Presence (with reference to absence).
[b]Marked gliosis (with reference to mild gliosis).
[c]With one or two *APOE* ε2 or ε4 alleles, excluding *APOE* ε2/ε4 carrying cases.
Model for CSVD: outcome = biological covariate.
Models for the other eight outcomes: outcome = biological covariate + technical covariates (NNTC site and PMI).
Covariates having *P*<0.20 (in boldface, with direct (+) or inverse (−) association) were subsequently included in the initial logistic regression models with antiretroviral therapy predictors.
Iba1, ionized calcium-binding adapter molecule-1; GFAP, glial fibrillary acidic protein; CSVD, cerebral small vessel disease; *APOE*, apolipoprotein-E gene; NNTC, National NeuroAIDS Tissue Consortium; PMI, longer postmortem interval (>12 hours).

Table, Supplemental Digital Content 2. Continued.

P value	CSVD[a] Forebrain white matter
Age at death (each year increase)	0.922
Female (vs. male)	0.858
Race/ethnicity (vs. white)	
Black	0.356
Hispanic	0.739
Others	0.425
APOE ε4 carrier status[c]	0.896
APOE ε2 carrier status[c]	0.583
Hepatitis C virus serostatus	0.803
Diabetes mellitus	**0.134 (+)**
Hypertension	0.661
Hyperlipidemia	0.451
Lifetime alcohol dependence	**0.045 (+)**
Lifetime cannabis dependence	0.376
Lifetime psychostimulant dependence	0.563
Lifetime cigarette smoking	0.504
Lower last-visit CD4+ T-cell count (<200 cells/μL)	0.444
Last-visit plasma HIV-1 RNA ($\log_{10}$ copies/mL)	**0.152 (−)**
HIV encephalitis or white matter lesions	**0.059 (+)**
Opportunistic brain diseases	**0.181 (−)**

[a]Presence (with reference to absence).
[b]Marked gliosis (with reference to mild gliosis).
[c]With one or two *APOE* ε2 or ε4 alleles, excluding *APOE* ε2/ε4 carrying cases.
Model for CSVD: outcome = biological covariate.
Models for the other eight outcomes: outcome = biological covariate + technical covariates (NNTC site and PMI).
Covariates having *P*<0.20 (in boldface, with direct (+) or inverse (−) association) were subsequently included in the initial logistic regression models with antiretroviral therapy predictors.
Iba1, ionized calcium-binding adapter molecule-1; GFAP, glial fibrillary acidic protein; CSVD, cerebral small vessel disease; *APOE*, apolipoprotein-E gene; NNTC, National NeuroAIDS Tissue Consortium; PMI, longer postmortem interval (>12 hours).