

Supplemental Digital Content

Table S1. Major Mutations Associated With Resistance to NRTIs¹⁻³

	Discriminatory mutations ^a					TAMs						MDR mutations	
	184	65	70	74	115	41	67	70	210	215	219	69	151
Consensus	M	K	K	L	Y	M	D	K	T	T	K	T	Q
3TC	VI	R										Ins	M
FTC	VI	R										Ins	M
ABC	VI	R	E/G/N	VI	F	L			W	FY		Ins	M
TDF	***	R	E/G/N		F	L		R	W	FY		Ins	M
ZDV	***	***	*	*		L	N	R	W	FY	QE	Ins	M
ddl	VI	R	E	VI		L			W	FY		Ins	M
d4T	***	R	E			L	N	R	W	FY	QE	Ins	M

ABC, abacavir; ddl, didanosine; d4T, stavudine; FTC, emtricitabine; MDR, multidrug resistance; NRTI, nucleoside reverse transcriptase inhibitor; TAM, thymidine analogue mutation; 3TC, lamivudine; TDF, tenofovir disoproxil fumarate; ZDV, zidovudine. ^aThe asterisks indicate the level of susceptibility, with 3 asterisks indicating a higher level of susceptibility than 1 asterisk.

References:

1. Stanford University. Major nucleoside RT inhibitor (NRTI) resistance mutations. In: HIV drug resistance [database online]. Version 8.4. Palo Alto, CA: Stanford University, 2017. Updated June 16, 2017. Available at: <https://hivdb.stanford.edu/dr-summary/resistance-notes/NRTI>.
2. Rhee SY, Varghese V, Holmes SP, et al. Mutational correlates of virological failure in individuals receiving a WHO-recommended tenofovir-containing first-line regimen: an international collaboration. *EbioMedicine*. 2017;18:225–235.
3. Rhee SY, Jordan MR, Raizes E, et al. HIV-1 drug resistance mutations: potential applications for point-of-care genotypic resistance testing. *PloS One*. 2015;10(12):e0145772.

Supplemental Table 2. Clinical Studies Involving 2-Drug Regimens Containing 3TC and an NRTI, NNRTI, INI, or Boosted PI

Study	Time frame, years	Study number	Population	Enrolled and randomized, N	Primary endpoint, weeks	Treatment group	Comparator group	Study results
GARDEL	2010-2012	NCT01237444	Treatment naive	426	48	LPV/r + 3TC	LPV/r + [3TC or FTC] + 2nd NRTI	Cahn et al. <i>Lancet Infect Dis.</i> 2014;14(7):572-580.
OLE	2011-2014	NCT01471821	Treatment experienced	250	48	LPV/r + 3TC	LPV/r + 2 NRTIs	Arribas et al. <i>Lancet Infect Dis.</i> 2015;15(7):785-792.
SALT	2011-2015	NCT01307488	Treatment experienced	286	48	ATV/r + 3TC	ATV/r + 2 NRTIs	Perez-Molina et al. <i>Lancet Infect Dis.</i> 2015;15(7):775-784.
ATLAS-M	2014-2016	NCT01599364	Treatment experienced	266	48	ATV/r + 3TC	ATV/r + 2 NRTIs	Di Giambenedetto et al. <i>J Antimicrob Chemother.</i> 2017;72(4):1163-1171.
DUAL	2014-2016	NCT02159599	Treatment experienced	249	48	DRV/r + 3TC	DRV/r + [TDF/FTC or ABC/3TC]	Pulido et al. <i>Clin Infect Dis.</i> 2017 [Epub ahead of print].
PADDLE	2014-2017	NCT02211482	Treatment naive	20	48	DTG + 3TC	None	Cahn et al. <i>J Int AIDS Soc.</i> 2017;20(1):1-7.
ASPIRE	2014-2017	NCT02263326	Treatment experienced	90	48	DTG + 3TC	Current ART	NA
ACTG A5353	2015-2017	NCT02582684	Treatment naive	122	24	DTG/3TC	None	Taiwo et al. Poster MOAB1017LB. Presented at: 9th IAS Conference on HIV Science; July 23-26, 2017; Paris, France.
ANRS 167 Lamidol	2015-2017	NCT02527096	Treatment experienced	110	48	DTG + 3TC	Current ART s	Joly et al. Poster 458. Presented at: 24th Annual Conference on Retroviruses and Opportunistic Infections; February 13-16, 2017; Seattle, WA.
SIMPLE	2015-2017	NCT02581202	Treatment experienced	216	48	LPV/r + 3TC	3-Drug current ART	NA
ANDES	2015-2017	NCT02770508	Treatment naive	145	48	DRV/r + 3TC	DRV/r + TDF/FTC	24-week results only to date. Sued et al. Oral abstract MOAB0106LB. Presented at: 9th IAS Conference on HIV Science; July 23-26, 2017; Paris, France.
BASEC Nr 2016-10963	2016-2017	NCT03223402	Treatment experienced	10 (estimated)	24	NVP + 3TC	NVP + 2 NRTIs	NA
GEMINI-1	2016-2024	NCT02831673	Treatment naive	700 (estimated)	48	DTG/3TC	DTG + TDF/FTC	NA
GEMINI-2	2016-2024	NCT02831764	Treatment naive	700 (estimated)	48	DTG/3TC	DTG + TDF/FTC	NA
RALAM	Recruiting	NCT02284035	Treatment experienced	75 (estimated)	24	RAL + 3TC	Current ART	NA
DOLULAM	NA	NA	Treatment experienced	27	96	DTG + 3TC	Current ART	Reynes et al. Abstract MOPEB0322. Published at: 9th IAS Conference on HIV Science; July 23-26, 2017; Paris, France.

ABC, abacavir; ART, antiretroviral therapy; ATV, atazanavir; DRV, darunavir; DTG, dolutegravir; FTC, emtricitabine; INI, integrase inhibitor; LPV, lopinavir; NA, not available; NNRTI, non-nucleotide reverse transcriptase inhibitor; NRTI, nucleoside reverse transcriptase inhibitors; NVP, nevirapine; PI, protease inhibitor; r, ritonavir; 3TC, lamivudine; TDF, tenofovir disoproxil fumarate.