

SUPPLEMENTARY MATERIAL

Table S1. Search Strategy			
No.	Query	Facet	Results
Embase® and MEDLINE® database search strings			
1	'human immunodeficiency virus infection'/exp OR 'human immunodeficiency virus infection'	Disease	389,563
2	'human immunodeficiency virus'/exp OR 'human immunodeficiency virus' OR 'human immunodeficiency virus' OR (human NEXT/5 (immun* OR immunodeficiency OR immunodeficiency OR virus OR infection*)) OR ('human immun*' AND 'deficiency virus')		623,067
3	'hiv':ab,ti OR 'hiv-1':ab,ti OR 'hiv 1':ab,ti OR 'hiv-2':ab,ti OR 'hiv 2':ab,ti OR 'hiv1':ab,ti OR 'hiv2':ab,ti OR 'hiv-i':ab,ti OR 'hiv-ii':ab,ti OR 'hiv infection' OR 'hiv-infection' OR 'hiv infect*' OR ('hiv':ab,ti AND infect*)		408,665
4	'acquired immune deficiency syndrome'/exp		141,651
5	'aids':ab,ti OR ('acquired immun*' AND 'deficiency virus') OR (acquir* NEXT/5 (immun* OR immunodeficiency OR immunodeficiency OR virus OR infection*))		280,642
6	#1 OR #2 OR #3 OR #4 OR #5		806,834
7	'cohort analysis'/exp OR 'longitudinal study'/exp OR 'prospective study'/exp OR 'follow up'/exp OR 'major clinical study'/exp OR 'clinical article'/exp OR 'intervention study'/exp OR cohort*:ab,ti OR (((('follow up' OR followup) NEXT/1 (study OR studies)):ab,ti) OR 'retrospective study'/exp OR 'case control study'/exp OR ((case* NEXT/1 control*):ab,ti) OR 'register'/de OR regist*:ab,ti OR 'data base'/de OR database:ab,ti OR 'data base':ab,ti OR (('real world' NEXT/1 (evidence OR data OR study OR studies)):ab,ti) OR 'health care record':ab,ti OR 'healthcare record':ab,ti OR 'health care records':ab,ti OR 'healthcare records':ab,ti OR 'medical record':ab,ti OR 'medical records':ab,ti OR questionnaire OR survey* OR ((medical OR insurance) AND (claims OR claim OR 'claims database' OR 'claim database')) OR 'pragmatic clinical trial' OR 'pragmatic trials' OR ((prospective OR retrospective) NEAR/5 (observation* OR study)) OR 'case study'/exp OR 'case series' OR 'large case series' OR (case NEAR/2 (stud* OR series OR large))	Study design	10,621,840
8	'dolutegravir'/syn OR 'dolutegravir sodium' OR 'dolutegravir sodium monohydrate' OR 'gsk 1349572' OR 'gsk 1349572a' OR 'gsk 572' OR 'gsk1349572' OR 'gsk1349572a' OR 'gsk572' OR 's 1349572' OR 's 349572' OR 's gsk 1349572' OR 's gsk1349572' OR 's-349572' OR 's1349572' OR 's349572' OR 'tivicay' OR 'dtg':ab,ti OR 'juluca' OR 'triumeq' OR 'str':ab,ti	Intervention	21,642
9	#6 AND #7 AND #8	Combination	2267
10	#9 AND ([editorial]/lim OR [letter]/lim OR [note]/lim OR [review]/lim OR [short survey]/lim)	Limits	241
11	#9 AND [animals]/lim NOT ([humans]/lim AND [animals]/lim)		15
12	#10 OR #11		256
13	#9 NOT #12		2011
14	#13 AND [2013-2020]/py	Final hits	1879

Cochrane databases search strings			
1	MeSH descriptor: [HIV] explode all trees	Disease	3088
2	MeSH descriptor: [HIV Infections] explode all trees		12,626
3	hiv:ab,ti or "hiv-1":ab,ti or "hiv 1":ab,ti or "hiv-2":ab,ti or "hiv 2":ab,ti or hiv1:ab,ti or hiv2:ab,ti or "hiv-i":ab,ti or "hiv-ii":ab,ti or "hiv infection" or "hiv-infection" or "hiv infect*" or (hiv:ab,ti and infect*)		25,343
4	MeSH descriptor: [Acquired Immunodeficiency Syndrome] explode all trees		1959
5	aids:ab,ti or ("acquired immun*" and "deficiency virus") or (acquir* next/5 (immun* or immunodeficiency or immunodeficiency or virus or infection*))		13,029
6	#1 or #2 or #3 or #4 or #5		32,762
7	dolutegravir or "dolutegravir sodium" or "dolutegravir sodium monohydrate" or "gsk 1349572" or "gsk 1349572a" or "gsk 572" or "gsk1349572" or "gsk1349572a" or gsk572 or "s 1349572" or "s 349572" or "s gsk 1349572" or "s gsk1349572" or "s-349572" or s1349572 or s349572' or tivicay or dtg:ab,ti or juluca or triumeq or str:ab,ti	Intervention	1070
8	#6 and #7 (Publication Year from 2013 to 2020)	Combination (final hits)	596
PubMed platform search strings for MEDLINE® In-Process			
1	Search HIV	Disease	375,682
2	Search (hiv[Title/Abstract] OR "hiv-1"[Title/Abstract] OR "hiv 1"[Title/Abstract] OR "hiv-2"[Title/Abstract] OR "hiv 2"[Title/Abstract] OR hiv1[Title/Abstract] OR "hiv2"[Title/Abstract] OR "hiv-i"[Title/Abstract] OR "hiv-ii"[Title/Abstract] OR "hiv infection" OR "hiv-infection" OR (hiv infect*) OR (hiv[Title/Abstract] AND infect*))		359,008
3	Search (("human immunodeficiency virus infection" OR "human immunodeficiency virus" OR "human immunodeficiency virus" OR ((human immun*) AND "deficiency virus")))		97,728
4	Search "acquired immune deficiency syndrome"		6090
5	Search (aids[Title/Abstract] OR ((acquired immun*) AND (deficiency AND (virus OR infect*))))		157,100
6	Search (#1 OR #2 OR #3 OR #4 OR #5)		457,261
7	Search (Dolutegravir OR "dolutegravir sodium" OR "gsk 1349572" OR "gsk1349572" OR "tivicay" OR "triumeq")	Intervention	1300
8	Search (#6 AND #7 (inprocess[sb] OR pubstatusaheadofprint))	Combination	317
9	Search (#8 (Publication Year from 2013 to 2017))	Final hits	182

Table S2. Quality Measures of the 4 Observational Studies That Included Effectiveness Data

Source	Study design	Comparator group(s)?	Exclusion criteria	Sample size justification?	Assessment of primary effectiveness outcome	Data on adherence to medicine?	Censoring for loss to follow-up?	PWH lost to follow-up for any reason, n (%)	Description of reasons for treatment discontinuation?	Description of how missing data were handled?
Maggiolo 2018 [32]	Prospective	No	VL >50 c/mL; HBsAg positive; documented resistance to study drugs	No	No description	No	NR	17 (8)	Yes	No
Hidalgo-Tenorio 2019 (DOLAMA) [52]	Retrospective	No	VL >50 c/mL; HBV treated with tenofovir; pregnancy; resistance to study drugs	Yes	From clinical records	No	No	31 (18)	Yes	No
Baldin et al 2019 [30]	Retrospective	No	VL >50 c/mL; HBsAg positive	No	No description	No	No	110 (20)	Yes	No
Galizzi 2020 (CSLHIV) [48]	Retrospective	Yes	VL >50 c/mL	No	No description of whether virologic analyses were blinded	No	Yes	NR for DTG + 3TC population	NR for DTG + 3TC population	No

c/mL, copies/mL; DTG, dolutegravir; HBsAg, hepatitis B surface antigen; HBV, hepatitis B virus; NR, not reported; PWH, people with HIV; 3TC, lamivudine; VF, virologic failure; VL, viral load. Duplicate studies have been removed.

Table S3. Characteristics of Studies With ART-Naive PWH

Source	Study type	ART-naive PWH receiving DTG + 3TC, n	Baseline VL	PWH with available genotype at baseline (n)	Baseline resistance substitutions in PWH with available genotype at baseline, n (%)	Effectiveness outcome
Ciccullo 2020 [31]	Multicenter, prospective	10	4.84 log ₁₀ c/mL (median)	10	1 (10%) individual had resistance to NNRTIs or first-generation INSTI elvitegravir and raltegravir (Y188C and D232N)	7 PWH reached 24 wk of follow-up and all had VL <50 c/mL
Cabello Úbeda 2019 [40]	Retrospective	30	NR	0	Resistance mutations in 4 PWH (E138A, K103N, V106I, V82C)	At 12 wk, 92% of PWH had VL <50 c/mL
Stephenson 2020 [43]	Retrospective	4	2 had VL >10,000 c/mL, 2 had VL <1000 c/mL	NR	NR	By 8 wk, 100% had VL <30 c/mL
Postel 2020 [44]	Multicenter, Prospective	25	37,100 c/mL (median)	NR	NR	90% achieved VL <50 c/mL at 6 mo, no discontinuations due to VF

ART, antiretroviral therapy; c/mL, copies/mL; DTG, dolutegravir; INSTI, integrase strand transfer inhibitor; NNRTI, non-nucleoside reverse transcriptase inhibitor; NR, not reported; PWH, people with HIV; 3TC, lamivudine; VF, virologic failure; VL, viral load.

Table S4. Reported Bone Mineral Density Outcomes in PWH Receiving DTG + 3TC

Study^a	PWH on DTG + 3TC, N	Time point (wk)	% of DTG + 3TC PWH on TDF before switch	PWH with osteoporosis at BL, n (%)	PWH with osteopenia at BL, n (%)	Bone health outcomes vs BL
Ciccullo 2018 [71]	20	48	NR ^b	6 (30)	9 (45)	Significant mean increase in lumbar spine BMD of 4.3% (+0.03 g/cm ² ; 95% CI, 0.01-0.05; <i>P</i> =0.001) No significant difference in femur BMD
Piscaglia 2018 [72]	21	96 (± 4 wk)	48	NR	NR	Significant improvement in spine BMD (+3.17%; <i>P</i> <0.001) in 21 PWH receiving DTG + 3TC and having a DEXA scan within 6 mo of switch, and 96 wk after that No significant difference in hip BMD
Calza 2020 [73]	29	48	NR	4 (14)	11 (38)	No significant difference in lumbar spine BMD or femur neck BMD No change in numbers of PWH with osteopenia or osteoporosis

BL, baseline; BMD, bone mineral density; DEXA, dual-energy x-ray absorptiometry; DTG, dolutegravir; PWH, people with HIV; 3TC, lamivudine; TDF, tenofovir disoproxil fumarate.

^aCiccullo 2018 and Piscaglia 2018 contain data from different studies from the ODOACRE cohort. ^b19 (95%) PWH had previously taken TDF.

Figure S1. Proportion of PWH in switch cohorts treated with DTG + 3TC in studies reporting on resistance observed at virologic failure. PWH with resistance substitutions have been arbitrarily designated as 1 and 2. Data only included for studies reporting treatment-emergent resistance at any time point. Duplicate studies have been removed. BL, baseline; DTG, dolutegravir; INSTI, integrase strand transfer inhibitor; NRTI, nucleoside reverse transcriptase inhibitor; PWH, people with HIV; 3TC, lamivudine; VF, virologic failure. ^aResistance testing performed only on those with VF and available samples. ^bSubstitution formatted in bold to highlight the only INSTI or NRTI substitution reported at failure that was not reported at BL.

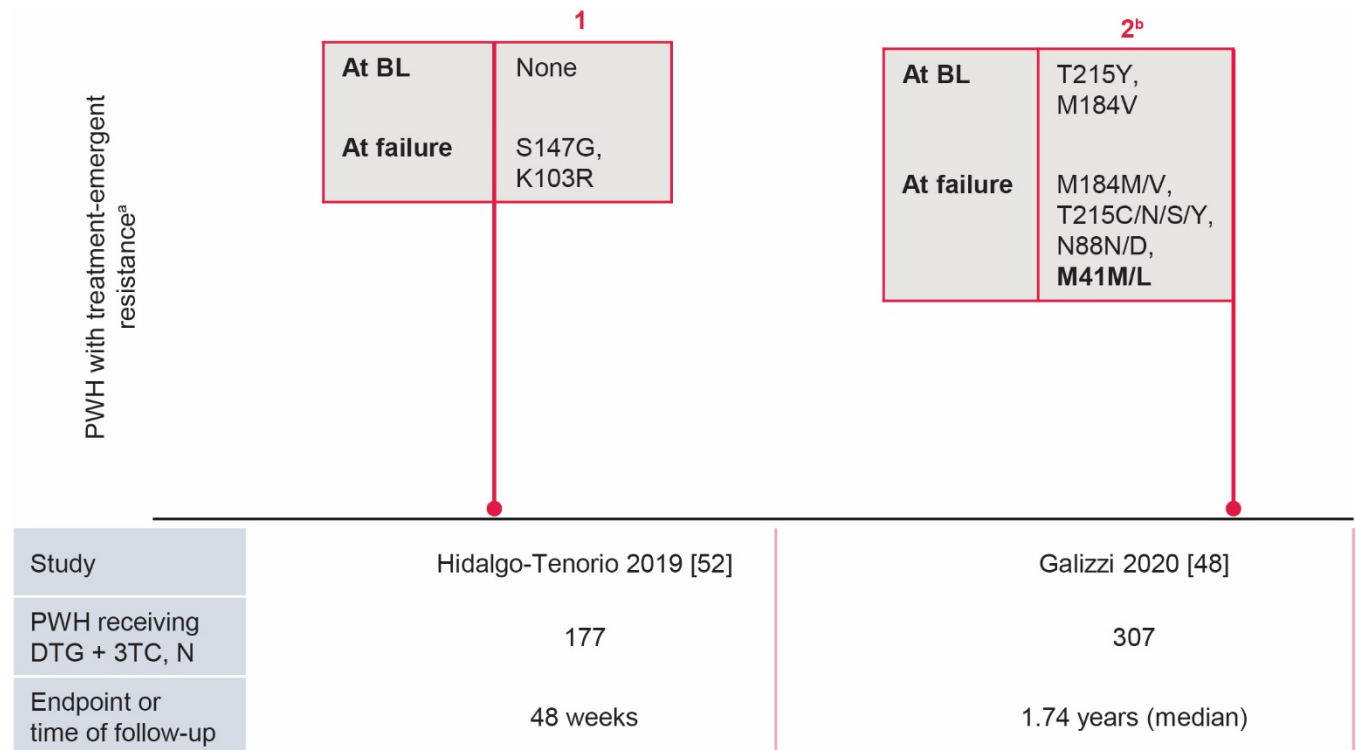


Figure S2. Proportion of PWH in switch studies treated with DTG + 3TC with discontinuation due to toxicity or adverse events. Data included for studies with N ≥100 and reporting discontinuations due to AEs at any time point. Duplicate studies have been removed. AE, adverse event; CNS, central nervous system; DTG, dolutegravir; NR, not reported; PWH, people with HIV; 3TC, lamivudine. ^aPercentage calculated based on overall N on DTG + 3TC.

