

ONLINE SUPPLEMENTARY MATERIAL

Virologic Response to Dolutegravir + Lamivudine in People With Suppressed HIV-1 and Historical M184V/I: A Meta-analysis

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Supplementary Table 1. Summary of Systematic Literature Search Strategy Criteria

Embase® and MEDLINE® database search criteria			
Number	Query	Facet	Results, n
1	'human immunodeficiency virus infection'/exp OR 'human immunodeficiency virus infection'	Disease	419,744
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')		691,876
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*)		442,502
4	'acquired immune deficiency syndrome'/exp		152,503
5	'aids':ab,ti OR ('acquired immun*' AND 'deficiency virus') OR (acquir* NEXT/5 (immun* OR immunodeficiency OR immunodeficiency OR virus OR infection*))		298,917
6	#1 OR #2 OR #3 OR #4 OR #5		896,219
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	12,061,091
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	Intervention	25,108

	's349572' OR 'tivicay' OR 'dtg':ab,ti OR 'juluca' OR 'triumeq' OR 'str':ab,ti		
9	#6 AND #7 AND #8	Combination	3487
10	#9 AND ([editorial]/lim OR [letter]/lim OR [note]/lim OR [review]/lim OR [short survey]/lim)	Limits	338
11	#9 AND [animals]/lim NOT ([humans]/lim AND [animals]/lim)		19
12	#10 OR #11		357
13	#9 NOT #12		3130
14	13 AND [2013-2022]/py	Final hits	3055

Cochrane database search criteria

Number	Query	Facet	Results, n
1	MeSH descriptor: [HIV] explode all trees	Disease	3275
2	MeSH descriptor: [HIV Infections] explode all trees		13,711
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*)		27,987
4	MeSH descriptor: [Acquired Immunodeficiency Syndrome] explode all trees		2054
5	aids:ab,ti or ("acquired immun*" and "deficiency virus") or (acquir* next/5 (immun* or immunodeficiency or immunodeficiency or virus or infection*))		14,176
6	#1 or #2 or #3 or #4 or #5		36,201
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	1362
8	#6 and #7	Combination	801
9	#8 (Publication Year from Jan 2013 to Oct 2022)	Final hits	774

MEDLINE® In-Process searched via PubMed® platform

Number	Query	Facet	Results, n
1	Search HIV	Disease	402,237
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*))		384,739
3	Search (("human immunodeficiency virus infection" OR "human immunodeficiency virus" OR "human immunodeficiency virus" OR ((human immun*) AND "deficiency virus")))		106,504
4	Search "acquired immune deficiency syndrome"		6301

5	Search (aids[Title/Abstract] OR ((acquired immun* AND (deficiency AND (virus OR infect*))))		166,474
6	Search (#1 OR #2 OR #3 OR #4 OR #5)		489,208
7	Search (Dolutegravir OR "dolutegravir sodium" OR "gsk 1349572" OR "gsk1349572" OR "tivicay" OR "trumeq")	Intervention	1735
8	Search (#6 AND #7 (inprocess[sb] OR pubstatusaheadofprint))	Combination	70
9	Search (#8 (Publication Year from Jan 2013 to Oct 2022))	Final hits	70

Supplementary Table 2. Summary of Targeted Literature Search Strategy Criteria**Embase® and MEDLINE® database search criteria**

Number	Query	Facet	Results, n
1	'human immunodeficiency virus infection'/exp OR 'human immunodeficiency virus infection'	Disease	414,164
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')		679,290
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*)		435,271
4	'acquired immune deficiency syndrome'/exp		151,240
5	'aids':ab,ti OR ('acquired immun*' AND 'deficiency virus') OR (acquir* NEXT/5 (immun* OR immunodeficiency OR immunodeficiency OR virus OR infection*))		294,721
6	#1 OR #2 OR #3 OR #4 OR #5		880,095
7	('clinical trial'/exp OR 'randomized controlled trial'/exp OR 'controlled clinical trial'/exp OR 'multicenter study'/exp OR 'phase 3 clinical trial'/exp OR 'phase 4 clinical trial'/exp OR 'randomization'/exp OR 'single blind procedure'/exp OR 'double blind procedure'/exp OR 'crossover procedure'/exp OR 'placebo'/exp OR 'randomi?ed controlled trial\$:ti,ab OR rct:ti,ab OR random\$ NEAR/2 allocat\$ OR (single AND blind\$:ti,ab) OR (double AND blind\$:ti,ab) OR (treble OR triple) NEAR/2 blind\$ OR placebo\$:ti,ab OR 'prospective study':ti,ab OR 'open label':ti,ab)	Study design	2,387,353
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 'trumeq' OR 'str':ab,ti	Intervention	24,296
9	#6 AND #7 AND #8	Combination	1121
10	#9 AND ([editorial]/lim OR [letter]/lim OR [note]/lim OR [review]/lim OR [short survey]/lim)	Limits	75
11	#9 AND [animals]/lim NOT ([humans]/lim AND [animals]/lim)		10
12	#10 OR #11		85
13	#9 NOT #12		1036

14 #13 AND [2013-2022]/py Final hits 988

Cochrane database search criteria			
Number	Query	Facet	Results, n
1	MeSH descriptor: [HIV] explode all trees	Disease	3264
2	MeSH descriptor: [HIV Infections] explode all trees		13,582
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*)		27,358
4	MeSH descriptor: [Acquired Immunodeficiency Syndrome] explode all trees		2037
5	aids:ab,ti or ("acquired immun*" and "deficiency virus") or (acquir* next/5 (immun* or immunodeficiency or immunodeficiency or virus or infection*))		13,837
6	#1 or #2 or #3 or #4 or #5		35,344
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	1298
8	#6 and #7	Combination	759
9	#8 (Publication Year from 2013 to 2017)	Final hits	163

MEDLINE® In-Process searched via PubMed® platform			
Number	Query	Facet	Results, n
1	Search HIV	Disease	396,836
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*))		379,510
3	Search (("human immunodeficiency virus infection" OR "human immunodeficiency virus" OR "human immunodeficiency virus" OR ((human immun*) AND "deficiency virus")))		105,376
4	Search "acquired immune deficiency syndrome"		6253
5	Search (aids[Title/Abstract] OR ((acquired immun*) AND (deficiency AND (virus OR infect*))))		164,545
6	Search (#1 OR #2 OR #3 OR #4 OR #5)		482,674
7	Search (Dolutegravir OR "dolutegravir sodium" OR "gsk 1349572" OR "gsk1349572" OR "tivicay" OR "trumeq")	Intervention	1639
8	Search (#6 AND #7 (inprocess[sb] OR pubstatusaheadofprint))	Combination	45
9	Search (#8 (Publication Year from 2013 to 2022))	Final hits	45

Supplementary Table 3. Meta-analysis Logit-Transformed Estimated Proportions of PWH With Historical M184V/I to Experience VF From Interventional Studies, Inclusive of All VF Definitions

Week 24						
Study	VF events, n	PWH with M184V/I, n	Proportion with VF (95% CI)	Total estimated proportion with VF (95% CI)		Heterogeneity
				Common-effects model	Random-effects model	
DOLULAM	0	17	0.00 (0.00-0.20)	0.00 (0.00-1.00)	0.00 (0.00-1.00)	$I^2 = 0\%$
TANGO	0	4	0.00 (0.00-0.60)			$\tau^2 = 0$
ART PRO	0	21	0.00 (0.00-0.16)			$P=1.00$
Week 48						
Study	VF events, n	PWH with M184V/I, n	Proportion with VF (95% CI)	Total estimated proportion with VF (95% CI)		Heterogeneity
				Common-effects model	Random-effects model	
DOLULAM	0	17	0.00 (0.00-0.20)	0.00 (0.00-1.00)	0.00 (0.00-1.00)	$I^2 = 0\%$
TANGO	0	4	0.00 (0.00-0.60)			$\tau^2 = 0$
ART PRO	0	21	0.00 (0.00-0.16)			$P=1.00$
SALSA	0	5	0.00 (0.00-0.52)			
SOLAR 3D	0	50	0.00 (0.00-0.07)			
Week 96						
Study	VF events, n	PWH with M184V/I, n	Proportion with VF (95% CI)	Total estimated proportion with VF (95% CI)		Heterogeneity
				Common-effects model	Random-effects model	
DOLULAM	0	17	0.00 (0.00-0.20)	0.00 (0.00-1.00)	0.00 (0.00-1.00)	$I^2 = 0\%$
						$\tau^2 = 0$
ART PRO	0	21	0.00 (0.00-0.16)			$P=1.00$

PWH, people with HIV-1; VF, virologic failure.

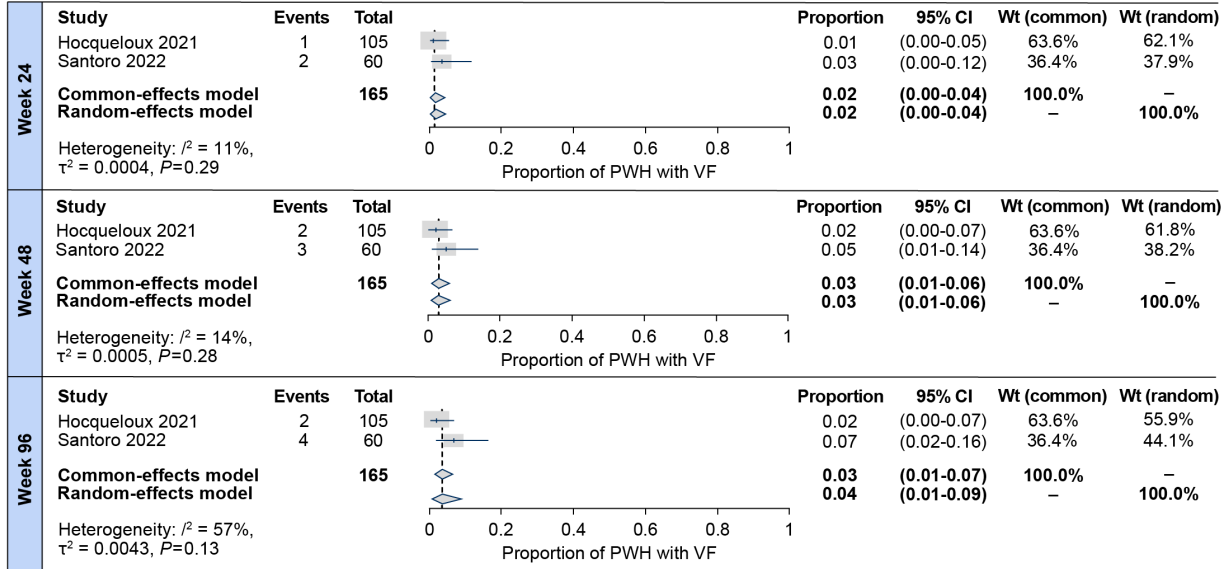
Supplementary Table 4. Meta-analysis Freeman-Tukey Double-Arcsine–Transformed Estimated Proportions of PWH With Historical M184V/I to Experience VF From Interventional Studies, Inclusive of All VF Definitions

Week 24						
Study	VF events, n	PWH with M184V/I, n	Proportion with VF (95% CI)	Total estimated proportion with VF (95% CI)		Heterogeneity
				Common-effects model	Random-effects model	
DOLULAM	0	17	0.00 (0.00-0.20)	0.00 (0.00-0.03)	0.00 (0.00-0.03)	$I^2 = 0\%$
TANGO	0	4	0.00 (0.00-0.60)			$\tau^2 = 0$
ART PRO	0	21	0.00 (0.00-0.16)			$P=0.89$
Week 48						
Study	VF events, n	PWH with M184V/I, n	Proportion with VF (95% CI)	Total estimated proportion with VF (95% CI)		Heterogeneity
				Common-effects model	Random-effects model	
DOLULAM	0	17	0.00 (0.00-0.20)	0.00 (0.00-0.00)	0.00 (0.00-0.00)	$I^2 = 0\%$
TANGO	0	4	0.00 (0.00-0.60)			$\tau^2 = 0$
ART PRO	0	21	0.00 (0.00-0.16)			$P=0.94$
SALSA	0	5	0.00 (0.00-0.52)			
SOLAR 3D	0	50	0.00 (0.00-0.07)			
Week 96						
Study	VF events, n	PWH with M184V/I, n	Proportion with VF (95% CI)	Total estimated proportion with VF (95% CI)		Heterogeneity
				Common-effects model	Random-effects model	
DOLULAM	0	17	0.00 (0.00-0.20)	0.00 (0.00-0.05)	0.00 (0.00-0.05)	$I^2 = 0\%$
ART PRO	0	21	0.00 (0.00-0.16)			$\tau^2 = 0$
						$P=0.94$

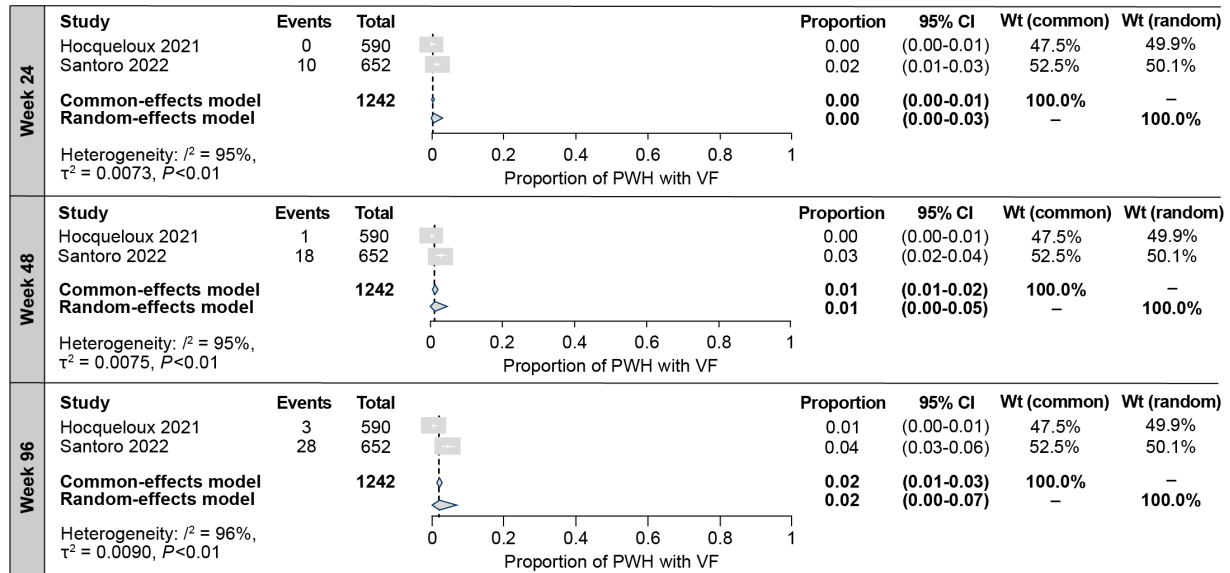
PWH, people with HIV-1; VF, virologic failure.

Supplementary Figure 1. Meta-analysis estimates of VF from base analysis RWE studies in PWH (A) with and (B) without historical M184V/I after switch to DTG + 3TC, using arcsine-transformed proportions. DTG, dolutegravir; PWH, people with HIV-1; RWE, real-world evidence; 3TC, lamivudine; VF, virologic failure; Wt, weight.

A PWH with M184V/I before switch

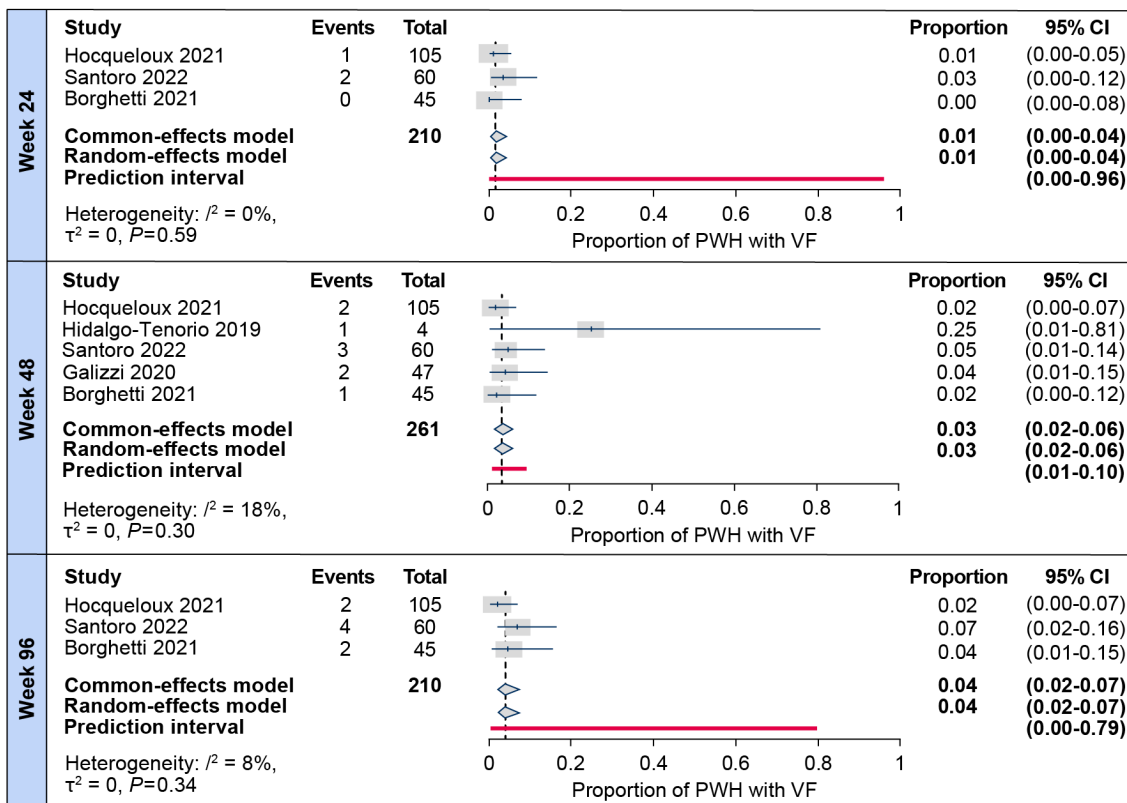


B PWH without M184V/I before switch

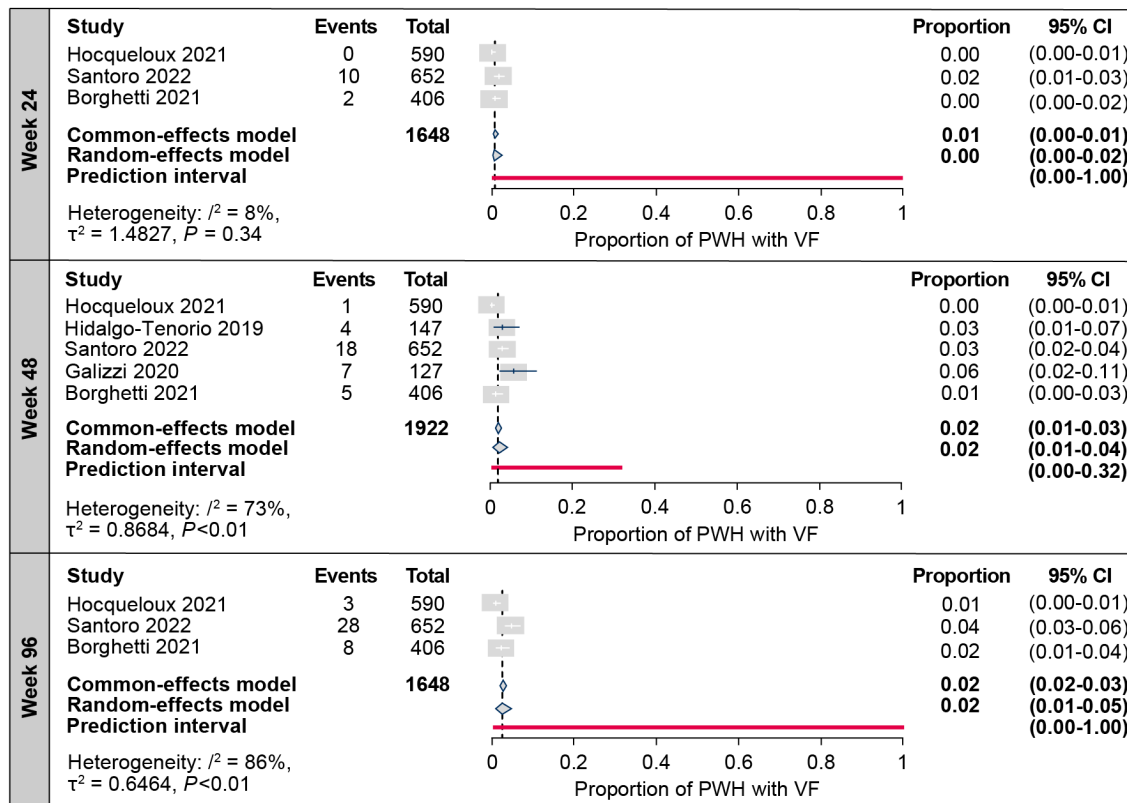


Supplementary Figure 2. Meta-analysis estimates of VF from sensitivity analysis RWE studies in PWH **(A)** with and **(B)** without historical M184V/I after switch to DTG + 3TC, using logit-transformed proportions. All studies reporting outcomes were included regardless of VF definition. DTG, dolutegravir; PWH, people with HIV-1; RWE, real-world evidence; 3TC, lamivudine; VF, virologic failure.

A PWH with M184V/I before switch

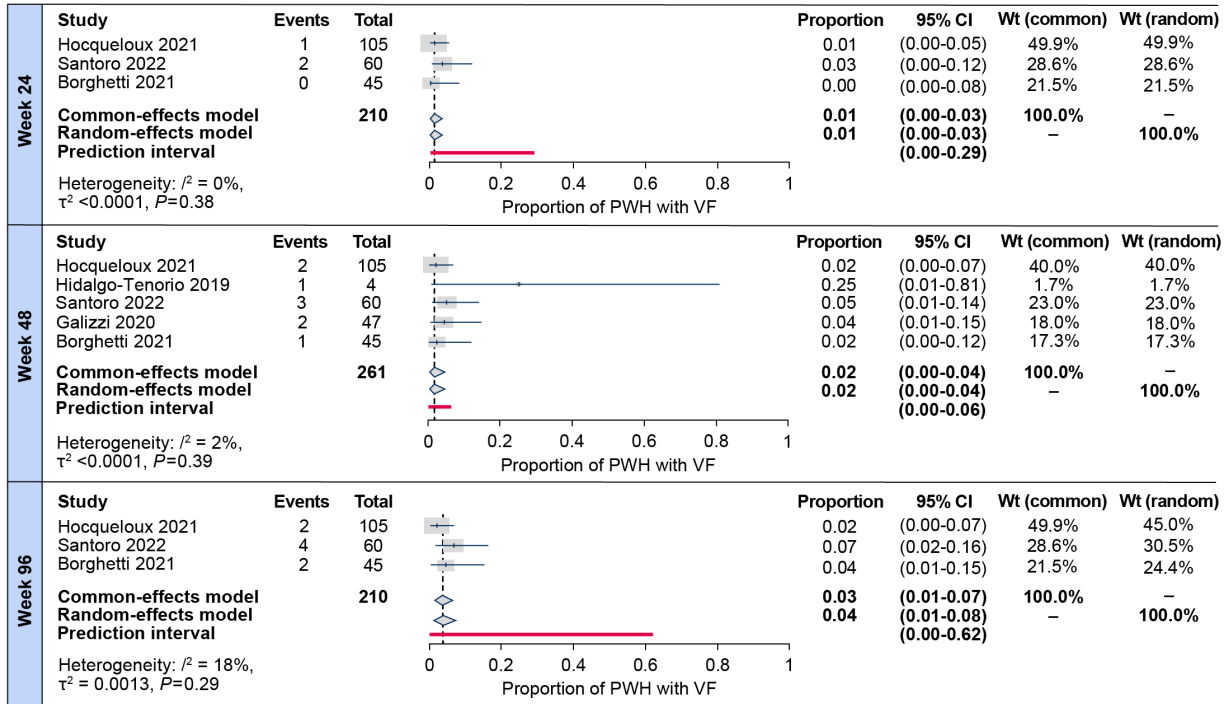


B PWH without M184V/I before switch

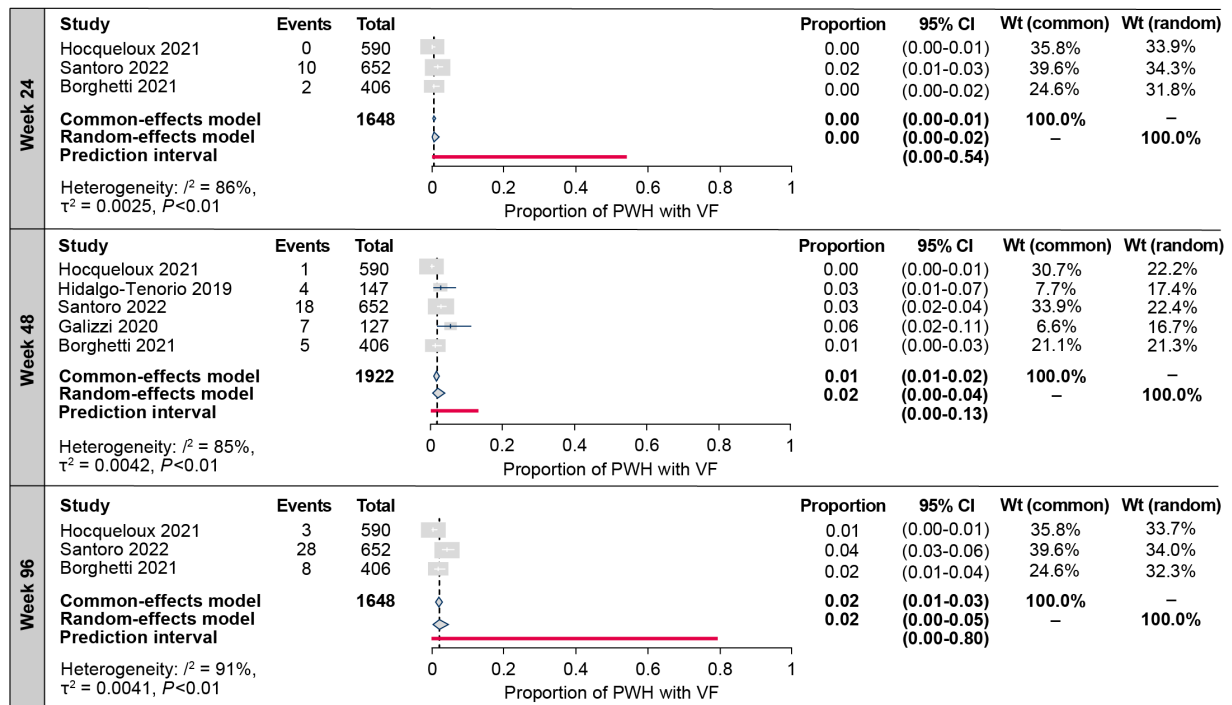


Supplementary Figure 3. Meta-analysis estimates of VF from sensitivity analysis RWE studies in PWH **(A)** with and **(B)** without historical M184V/I after switch to DTG + 3TC, using Freeman-Tukey double-arcsine-transformed proportions. All studies reporting outcomes were included regardless of VF definition. DTG, dolutegravir; PWH, people with HIV-1; RWE, real-world evidence; 3TC, lamivudine; VF, virologic failure; Wt, weight.

A PWH with M184VI before switch



B PWH without M184VI before switch



Supplementary Figure 4. Meta-analysis estimates of VF from base analysis interventional studies in PWH with historical M184V/I after switch to DTG + 3TC, using arcsine-transformed proportions. DTG, dolutegravir; PWH, people with HIV-1; 3TC, lamivudine; VF, virologic failure; Wt, weight. ^aThe 2 studies reporting VF at Week 96 had different VF definitions.

