

Table 2: Summary of the GRADE quality of evidence assessments for all outcomes for the DTG vs EFV comparison

Outcome	No of patients		Direct Effect	Risk of Bias	Inconsistency	Uncombined Estimates			Quality of direct evidence	Odds ratio (95% CrI)	Combined Estimates			Overall quality of evidence
	DTG	EFV ₆₀₀				Indirectness	Imprecision	Publication Bias			Absolute effects	Indirect evidence precision	Network Transitivity	
Viral supp. at 4 weeks	842/1175	190/823	7.90 (6.40, 9.75)	0	0	0	0	0	⊕⊕⊕⊕ High	9.81 (7.83, 12.25)	497 more per 1,000 (447 to 542)	0	0	⊕⊕⊕⊕ High
Viral supp. at 12 weeks	1016/1175	508/823	3.62 (2.90, 4.52)	0	-1	0	0	0	⊕⊕⊕ Moderate	4.14 (3.36, 5.11)	271 more per 1,000 (238 to 302)	0	0	⊕⊕⊕ Moderate
Viral supp. at 24 weeks	1053/1175	689/823	1.77 (1.35, 2.32)	0	0	0	0	0	⊕⊕⊕⊕ High	1.81 (1.44, 2.31)	79 more per 1,000 (51 to 105)	0	0	⊕⊕⊕⊕ High
Viral supp. at 48 weeks	1002/1167	654/820	1.60 (1.26, 2.04)	0	0	0	0	0	⊕⊕⊕⊕ High	1.64 (1.35, 1.96)	62 more per 1,000 (39 to 82)	0	0	⊕⊕⊕⊕ High
Viral supp. at 96 weeks	383/473	340/472	1.65 (1.21, 2.24)	0	-1	0	0	0	⊕⊕⊕ Moderate	1.94 (1.48, 2.56)	94 more per 1,000 (60 to 124)	0	0	⊕⊕⊕ Moderate
Viral supp. at 144 weeks	300/422	266/422	1.44 (1.08, 1.92)	-1	0	0	-1	0	⊕⊕ Low	1.44 (1.08, 1.95)	58 more per 1,000 (12 to 98)	0	0	⊕⊕ Low
VS at 48 weeks for >100,000	247/307	164/223	1.48 (0.96, 2.28)	0	0	0	-1	0	⊕⊕⊕ Moderate	1.64 (1.07, 2.53)	87 more per 1,000 (13 to 154)	0	0	⊕⊕⊕ Moderate
VS at 96 weeks for >100,000	95/134	94/131	0.96 (0.56, 1.63)	-1	0	0	-1	0	⊕⊕ Low	0.96 (0.56, 1.61)	7 fewer per 1,000 (-105 to 71)	0	0	⊕⊕ Low
Change in CD4 at 24	473	472	41.55 (17.63, 65.47)	0	-1	0	0	0	⊕⊕⊕ Moderate	--	28.3 cells/ml higher (15.24, 41)	0	0	⊕⊕⊕ Moderate
Change in CD4 at 48	473	472	57.28 (35.97, 78.60)	0	0	0	0	0	⊕⊕⊕⊕ High	--	32.95 cells/ml higher (20.43, 45.94)	0	0	⊕⊕⊕ Moderate
Change in CD4 at 96	473	472	40.73 (13.67, 67.78)	0	0	0	0	0	⊕⊕⊕⊕ High	--	24.03 cells/ml higher (4.45, 43.78)	-1	0	⊕⊕⊕ Moderate
Change in CD4 at 144	422	422	46.91 (17.24, 76.58)	-1	0	0	0	0	⊕⊕⊕ Moderate	--	49.08 cells/ml higher (20.22, 78.13)	0	0	⊕⊕⊕ Moderate
Change in body weight at 48 weeks	702	351	3.05 (1.94, 4.16)	0	-1	0	0	0	⊕⊕ Low	--	3.05 Kg higher (2.11, 3.97)	0	0	⊕⊕⊕ Moderate
Change in body weight at 96 weeks	702	351	5.63 (2.49, 8.76)	0	-1	0	0	0	⊕⊕ Low	--	5.15 Kg higher (2.43, 7.94)	0	0	⊕⊕⊕ Moderate
Mortality	2/1175	4/823	0.44 (0.10, 2.01)	0	0	0	-2	0	⊕⊕ Low	0.72 (0.29, 1.92)	2 fewer per 1,000 (-5 to 5)	0	0	⊕⊕ Low
Discontinuations	182/1167	206/820	0.63 (0.50, 0.79)	0	0	0	0	0	⊕⊕⊕⊕ High	0.58 (0.48, 0.70)	65 fewer per 1,000 (-84 to -44)	0	0	⊕⊕⊕⊕ High

Discontinuations due to AEs	18/465	63/469	0.26 (0.15, 0.45)	0	0	0	0	0	⊕⊕⊕⊕ High	0.30 (0.19, 0.46)	44 fewer per 1,000 (-56 to -31)	0	0	⊕⊕⊕⊕ High
Overall resistance	0/473	4/472	0.24 (0.02, 2.51)	0	0	0	-2	0	⊕ Very low	0.13 (0.03, 0.60)	12 fewer per 1,000 (-17 to -5)	2	0	⊕⊕⊕⊕ High
Resistance to anchor treatment	0/473	4/472	0.11 (0.01, 2.05)	0	0	0	-2	0	⊕ Very low	0.13 (0.04, 0.48)	13 fewer per 1,000 (-18 to -7)	2	0	⊕⊕⊕⊕ High
NRTI resistance	0/473	1/472	0.18 (0.04, 0.89)	0	0	0	-1	0	⊕⊕ Low	0.14 (0.04, 0.59)	7 fewer per 1,000 (-10 to -3)	1	0	⊕⊕⊕⊕ High
Neuropsychiatric AEs (any grade)	[35/248]	[517/2064]	--	-1	0	-1	0	0	⊕⊕ Low	0.40 (0.20, 0.82)	114 fewer per 1,000 (-169 to -30)	0	0	⊕⊕ Low
Depression (any grade)	35/414	44/419	0.79 (0.49, 1.25)	-1	0	0	-1	0	⊕⊕ Low	1.22 (0.65, 2.27)	11 more per 1,000 (-18 to 61)	0	0	⊕⊕ Low
Depression (Grade 3/4)	1/465	4/469	0.33 (0.05, 2.11)	-1	0	0	-1	0	⊕⊕ Low	0.16 (0.03, 0.87)	4 fewer per 1,000 (-7 to -1)	1	0	⊕⊕⊕ Moderate
Sleep Disorders (any grade)	74/465	56/469	1.40 (0.96, 2.04)	-1	0	0	-1	0	⊕⊕ Low	0.78 (0.35, 1.66)	13 fewer per 1,000 (-41 to 38)	0	-1	⊕ Very low
Dizziness (any grade)	32/465	148/469	0.16 (0.11, 0.24)	-1	0	0	0	0	⊕⊕⊕ Moderate	0.18 (0.10, 0.35)	137 fewer per 1,000 (-159 to -106)	0	0	⊕⊕⊕ Moderate
Suicidal Ideation	2/414	2/419	1.01 (0.14, 7.22)	-1	0	0	-2	0	⊕ Very low	0.26 (0.03, 1.99)	3 fewer per 1,000 (-6 to 4)	-1	0	⊕ Very low
Treatment emergent SAEs	108/1167	91/820	0.97 (0.72, 1.31)	0	0	0	-1	0	⊕⊕⊕ Moderate	0.79 (0.61, 1.03)	22 fewer per 1,000 (-44 to 3)	0	0	⊕⊕⊕ Moderate
Treatment emergent AEs	1019/1167	734/820	0.47 (0.35, 0.64)	0	0	0	0	0	⊕⊕⊕⊕ High	1.10 (0.58, 2.11)	7 more per 1,000 (-49 to 43)	-1	-1	⊕⊕ Low
Treatment-related SAEs	2/414	9/419	0.22 (0.05, 1.03)	0	0	0	-2	0	⊕⊕ Low	0.11 (0.02, 0.50)	18 fewer per 1,000 (-28 to -9)	1	0	⊕⊕⊕ Moderate
Treatment-related AEs	621/1167	566/820	0.47 (0.39, 0.57)	0	-1	0	0	0	⊕⊕⊕ Moderate	0.45 (0.37, 0.54)	185 fewer per 1,000 (-227 to -143)	0	0	⊕⊕⊕ Moderate

n/N in square brackets where no direct comparison between interventions of interest is available and reflects the number of patients in the network.

Legend: Uncombined estimates represent either direct estimates, if available, or indirect NMA estimates otherwise. Combined estimates are NMA estimates for comparisons where direct estimates were available. For uncombined estimates start with high quality evidence. -1 symbolizes a choice to rate down (e.g. high quality to moderate quality evidence); 0 symbolizes choice to not rate down; -- = not applicable because the NMA estimate is the only estimate.

The final quality of evidence updates that of the uncombined evidence. The quality can be moved up if the uncombined score was penalized for precision, which was overcome in network estimates. It can be moved down if the estimates are no longer precise or if there is evidence of inconsistency in loops containing the comparison (i.e. violation of transitivity).

Precision – We rated down for precision if the confidence interval crossed 1.1 or 0.9 and if there were less than 50 total events. **Consistency** – We assessed the consistency for direct treatment comparisons using I² estimates and visual inspection of point estimates. An I² of 75% or higher indicates considerable heterogeneity. This was conducted along the shortest indirect pathway with the largest number of trials for indirect estimates. **Risk of Bias** – For direct estimates we rated down for risk of bias if the majority of studies within a comparison were considered to be at high risk of bias and similarly along the principal indirect pathway for indirect estimates. **Indirectness** – Estimates obtained solely from indirect evidence were rated down for indirectness.

Table 3: Summary of the GRADE quality of evidence assessments for all outcomes for the EFV₄₀₀ vs EFV₆₀₀ comparison

Outcome	No of patients		Direct Effect	Risk of Bias	Inconsistency	Uncombined Estimates			Quality of direct evidence	Odds ratio (95% CrI)	Combined Estimates			Overall quality of evidence
	EFV ₄₀₀	EFV ₆₀₀				Indirectness	Imprecision	Publication Bias			Absolute effects	Indirect evidence precision	Network Transitivity	
Viral supp. at 4 weeks	[18/303]	[589/3714]	--	0	0	-1	-1	0	⊕⊕ Low	0.82 (0.45, 1.45)	26 fewer per 1,000 (-86 to 58)	0	0	⊕⊕ Low
Viral supp. at 12 weeks	[112/303]	[1913/3221]	--	0	0	-1	-1	0	⊕⊕ Low	1.25 (0.85, 1.88)	54 more per 1,000 (-40 to 143)	0	0	⊕⊕ Low
Viral supp. at 24 weeks	[210/303]	[3327/4079]	--	0	0	-1	-1	0	⊕⊕ Low	1.47 (0.95, 2.25)	54 more per 1,000 (-8 to 102)	0	0	⊕⊕ Low
Viral supp. at 48 weeks	276/321	260/309	1.16 (0.75, 1.79)	0	0	0	-1	0	⊕⊕⊕ Moderate	1.20 (0.90, 1.63)	26 more per 1,000 (-16 to 62)	0	0	⊕⊕⊕ Moderate
Viral supp. at 96 weeks	277/321	268/309	0.96 (0.61, 1.52)	0	0	0	-1	0	⊕⊕⊕ Moderate	0.95 (0.60, 1.54)	8 fewer per 1,000 (-98 to 66)	0	0	⊕⊕⊕ Moderate
Viral supp. at 144 weeks	--	--	--	--	--	--	--	--	--	--	--	--	--	--
VS at 48 weeks for >100,000	100/124	87/112	1.20 (0.64, 2.25)	0	0	0	-1	0	⊕⊕⊕ Moderate	1.30 (0.82, 2.10)	48 more per 1,000 (-41 to 128)	0	0	⊕⊕⊕ Moderate
VS at 96 weeks for >100,000	103/124	92/112	1.07 (0.54, 2.09)	-1	0	0	-1	0	⊕⊕ Low	1.06 (0.55, 2.09)	10 more per 1,000 (-106 to 104)	0	0	⊕⊕ Low
Change in CD4 at 24	321	309	14.00 (-2.09, 30.09)	0	0	0	-1	0	⊕⊕⊕ Moderate	--	7.77 cells/ml higher (-5.49, 21.8)	0	0	⊕⊕⊕ Moderate
Change in CD4 at 48	321	309	25.00 (6.57, 43.43)	0	0	0	-1	0	⊕⊕⊕ Moderate	--	17.3 cells/ml higher (2.00, 32.59)	0	0	⊕⊕⊕ Moderate
Change in CD4 at 96	321	309	26.00 (2.95, 49.05)	0	0	0	-1	0	⊕⊕⊕ Moderate	--	26.62 cells/ml higher (4.24, 50.34)	0	0	⊕⊕⊕ Moderate
Change in CD4 at 144	--	--	--	--	--	--	--	--	--	--	--	--	--	--
Change in body weight at 48 weeks	[278]	[351]	--	-1	0	-1	-1	0	⊕ Very low	--	1.06 Kg higher (-0.79, 2.83)	0	0	⊕ Very low
Change in body weight at 96 weeks	--	--	--	--	--	--	--	--	--	--	--	--	--	--
Mortality	5/321	5/309	0.96 (0.28, 3.36)	0	0	0	-2	0	⊕⊕ Low	0.91 (0.35, 2.49)	1 fewer per 1,000 (-4 to 9)	-1	0	⊕ Very low
Discontinuations	22/321	23/309	0.91 (0.50, 1.68)	0	0	0	-1	0	⊕⊕⊕ Moderate	0.91 (0.59, 1.45)	13 fewer per 1,000 (-65 to 61)	0	0	⊕⊕⊕ Moderate

Discontinuations due to AEs	16/321	34/309	0.42 (0.23, 0.79)	0	0	0	0	0	⊕⊕⊕⊕ High	0.42 (0.23, 0.77)	36 fewer per 1,000 (-51 to -14)	0	0	⊕⊕⊕⊕ High
Overall resistance	[8/302]	[127/3150]	--	-1	0	-1	-2	0	⊕ Very low	46.30 (0.59, 931.74)	385 more per 1,000 (-6 to 915)	0	0	⊕ Very low
Resistance to anchor treatment	2/321	3/309	0.64 (0.11, 3.85)	-1	0	0	-2	0	⊕ Very low	1.38 (0.31, 6.92)	5 more per 1,000 (-11 to 75)	0	0	⊕ Very low
NRTI resistance	[6/302]	[77/3769]	--	-1	0	-1	-2	0	⊕ Very low	40.41 (0.55, 920.27)	239 more per 1,000 (-4 to 875)	0	0	⊕ Very low
Neuropsychiatric AEs (any grade)	13/321	11/309	1.14 (0.50, 2.59)	-1	0	0	-1	0	⊕⊕ Low	1.14 (0.49, 2.71)	23 more per 1,000 (-101 to 200)	0	0	⊕⊕ Low
Depression (any grade)	[29/303]	[199/2819]	--	-1	0	-1	-1	0	⊕ Very low	1.48 (0.66, 3.54)	24 more per 1,000 (-18 to 113)	0	0	⊕ Very low
Depression (Grade 3/4)	--	--	--	--	--	--	--	--	--	--	--	--	--	--
Sleep Disorders (any grade)	--	--	--	--	--	--	--	--	--	--	--	--	--	--
Dizziness (any grade)	--	--	--	--	--	--	--	--	--	--	--	--	--	--
Suicidal Ideation	--	--	--	--	--	--	--	--	--	--	--	--	--	--
Treatment emergent SAEs	24/321	32/309	0.70 (0.40, 1.22)	0	0	0	-1	0	⊕⊕⊕ Moderate	0.70 (0.40, 1.20)	32 fewer per 1,000 (-69 to 20)	0	0	⊕⊕⊕ Moderate
Treatment emergent AEs	291/321	285/309	0.82 (0.47, 1.43)	0	0	0	-1	0	⊕⊕⊕ Moderate	0.81 (0.48, 1.36)	17 fewer per 1,000 (-75 to 21)	0	0	⊕⊕⊕ Moderate
Treatment-related SAEs	2/321	4/309	0.48 (0.09, 2.63)	0	0	0	-2	0	⊕⊕ Low	0.42 (0.05, 2.34)	12 fewer per 1,000 (-24 to 26)	0	0	⊕⊕ Low
Treatment-related AEs	126/321	148/309	0.70 (0.51, 0.96)	0	0	0	-1	0	⊕⊕⊕ Moderate	0.71 (0.52, 0.96)	85 fewer per 1,000 (-156 to -11)	0	0	⊕⊕⊕ Moderate

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