Primary investigators: Australia – MT Bloch, RJ Finlayson, J McMahon; Belgium – S De Wit, I Derdelinckx, E Florence, L Vandekerckhove, B Vandercam; Canada – J De Wet, RP LeBlanc, B Lebouche, D Longpre, B Trottier; Chile – C Beltran, CE Chahin, W Jensen, C Perez; Colombia – JMO Gutierrez, O Sussmann, JD Velez; Denmark – J Gerstoft, H Nielsen; Germany – K Arasteh, O Degen, S Esser, H-J Stellbrink, C Stephan, A Stoehr; Guatemala – EMR Alvarado, E Arathoon, RM Lopez, CR Mejia, LDG Patzan, R Pinzon; Honduras – C Parchment; Israel – M Chowers, I Levy, E Shahar, Z Sthoeger; Mexico – J Andrade, NPQ Perez, BEC Ramirez; Netherlands – JG den Hollander, B Rijnders; New Zealand – R Handy; Peru – N Bonifacio, P Campos, JA Hidalgo, RM Infante, ED Matos, Y Pinedo, ER Ticona; Portugal – JGS da Cunha, F Maltez, I Neves, P Pacheco, R Serrao; Puerto Rico – S Maldonado-Rivera, I Melendez-Rivera, RO Mendoza-Rodriguez, JO Morales-Ramirez, G Ortiz-Lasanta; Russia – S Kizhlo, VV Kulagin, VV Pokrovsky, TE Shimonova, AA Shuldyakov, OA Tsybakova, E Voronin, NG Zakharova; South Africa – E Baraldi, LF Fouche, F Hoosen, R Kaplan, JJ Lombaard, AA Mahomed, EA Mitha, L Mohapi, MS Rassool, N Siddique; Spain – J Berenguer, HK Freud, SM Guillen, FV Mendez, JS Moreno, DP Palter; Switzerland – A Calmy, M Cavassini, J Fehr; Taiwan – C-C Hung, W-C Ko, H-H Lin, Y-H Lin, H-C Tsai, W-W Wong; Thailand – A Avihingsanon, D Changpradub, P Chetchotisakd, S Kiertiburanakul, W Ratanasuwan, K Supparatpinyo; United Kingdom – A Clarke, A Fox, MA Johnson, MR Nelson, C Orkin, N Perry, A Ustianowski, IG Williams, A Winston; United States – DM Asmuth, NC Bellos, DS Berger, CJ Bettacchi, L Bhatti, T Campbell, RE Campo, KK Casey, JG Castro, GE Crofoot, D Cunningham, E DeJesus, J Feinberg, FA Felizarta, C Fichtenbaum, TT Jefferson, M Johnson, PN Kumar, ST Lewis, RA Loftus, AE Luque, CK McDonald, M Mogyoros, RM Novak, O Osiyemi, DM Parenti, DJ Prelutsky, DJ Riedel, WJ Robbins, PJ Ruane, M Scott, ASY Shon, J Sims, J Slim, L Sloan, DE Sweet, KT Tashima, P Tebas, MA Thompson, WJ Towner, KJ Vigil, BG Yangco, R Zane.

Key Exclusion Criteria

Documented or known resistance to any study drug. For the purpose of this study, resistance to doravirine or efavirenz includes the following NNRTI mutations: L100I, K101E, K101P, K103N, K103S, V106A, V106I, V106M, V108I, E138A, E138G, E138K, E138Q, E138R, V179L, Y181C, Y181I, Y181V, Y188C, Y188H, Y188L, G190A, G190S, H221Y, L234I, P225H, F227C, F227L, F227V, M230L, M230I. Resistance to emtricitabine, lamivudine, or tenofovir includes the following RT mutations: K65R, M41L, T69S (insertion complex), Q151M, M184I, M184V, L210W, T215F, T215Y, K219E, K219Q, D67N, K70R and K70E.

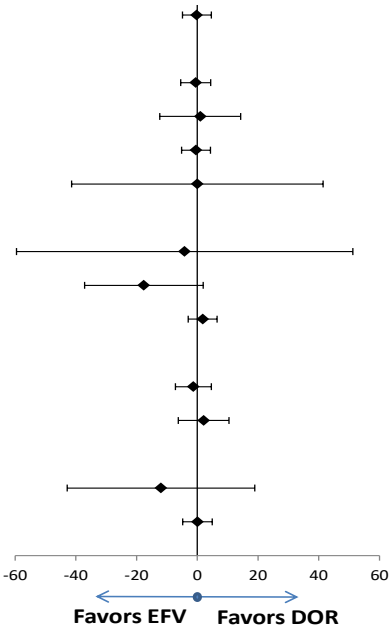
Treatment for a viral infection other than HIV-1 (such as hepatitis B) with an agent that is active against HIV-1, including, but not limited to, adefovir, tenofovir, entecavir, emtricitabine, or lamivudine (unless treatment occurred prior to the diagnosis of HIV). Significant hypersensitivity or other contraindication to any of the components of the study drugs.

Current (active) diagnosis of acute hepatitis due to any cause; evidence of decompensated liver disease; or liver cirrhosis and a Child-Pugh Class C score or Pugh-Turcotte (CPT) score >9. Pregnancy, breastfeeding, or expecting to conceive. Use of recreational or illicit drugs, or recent history of drug or alcohol abuse or dependence.

Virologic Response by Baseline Prognostic and Demographic Factors (Observed Failure)

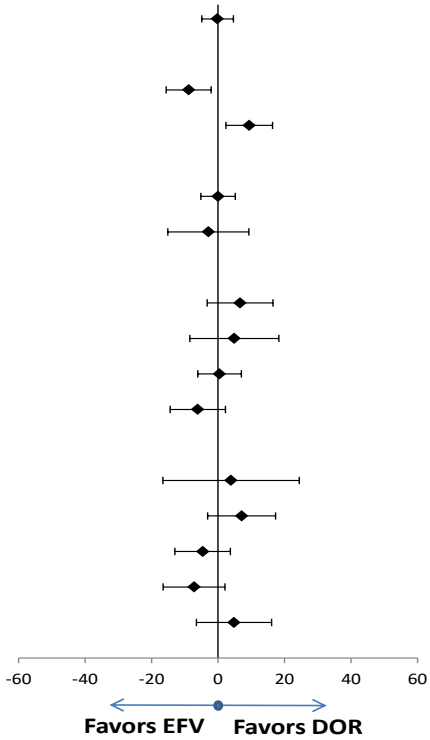
HIV-1 RNA <50 copies/mL

	% of Participants (N)		Difference (95% CI)
	DOR/3TC/TDF	EFV/FTC/TDF	
All participants	88.7 (346)	88.8 (331)	
Baseline HIV-1 RNA			
≤100,000 copies/mL	90.6 (277)	91.1 (258)	
>100,000 copies/mL	81.2 (69)	80.8 (73)	
≤500,000 copies/mL	89.3 (337)	89.9 (314)	
>500,000 copies/mL	66.7 (9)	70.6 (17)	
Baseline CD4+ T-cell Count			
≤50/mm^3	62.5 (8)	66.7 (9)	
>50 and ≤200/mm^3	70.6 (34)	88.2 (34)	
>200/mm^3	91.4 (304)	89.6 (288)	
Viral Subtype			
Subtype B	87.8 (222)	89.4 (226)	
Subtype Non-B	90.2 (122)	87.6 (105)	
HBV or HCV Co-infection			
Positive	88.9 (9)	100 (8)	
Negative	88.7 (337)	88.5 (323)	



HIV-1 RNA <50 copies/mL

	% of Participants (N)		Difference (95% CI)
	DOR/3TC/TDF	EFV/FTC/TDF	
All participants	88.7 (346)	88.8 (331)	
Age			
≤ Median (31y)	83.4 (175)	92.0 (187)	
> Median (31y)	94.2 (171)	84.7 (144)	
Gender			
Male	88.6 (290)	88.3 (283)	
Female	89.3 (56)	91.7 (48)	
Race/Ethnicity			
Asian	96.6 (58)	90.0 (60)	
Black	85.7 (63)	81.0 (63)	
White	89.8 (166)	89.6 (154)	
Hispanic/Latino	85.4 (123)	91.8 (110)	
Region			
Africa	85.3 (34)	81.5 (27)	
Asia/Pacific	96.6 (58)	89.5 (57)	
Europe	90.4 (83)	92.9 (85)	
Latin America	86.5 (89)	93.8 (80)	
North America	85.4 (82)	81.7 (82)	



Most Common† Laboratory Changes, DAIDS Grade 3 or 4

Criterion‡	DOR/3TC/TDF n/m	(%)	EFV/FTC/TDF n/m	(%)	Difference % (95% CI§)
Fasting LDL Cholesterol (mg/dL)					
Grade 3: ≥190	1/332	(0.3)	5/309	(1.6)	-1.3 (-3.5, 0.2)
Fasting Triglycerides (mg/dL)					
Grade 3: >500 to 1000	2/336	(0.6)	8/318	(2.5)	-1.9 (-4.4, -0.0)
Creatinine (mg/dL)					
Grade 3: >1.8 to <3.5 x ULN, or increase of 1.5 to <2.0 x above baseline	7/363	(1.9)	3/359	(0.8)	1.1 (-0.7, 3.2)
Aspartate Aminotransferase (IU/L)					
Grade 3: 5.0 to <10.0 x ULN	1/363	(0.3)	5/359	(1.4)	-1.1 (-3.0, 0.3)
Alanine Aminotransferase (IU/L)					
Grade 3: 5.0 to <10.0 x ULN	2/363	(0.6)	5/359	(1.4)	-0.8 (-2.7, 0.8)
Lipase (IU/L)					
Grade 3: 3.0 to <5.0 x ULN	3/363	(0.8)	5/359	(1.4)	-0.6 (-2.5, 1.2)
Creatine Kinase (IU/L)					
Grade 3: 10.0 to <20.0 x ULN	6/363	(1.7)	7/359	(1.9)	-0.3 (-2.5, 1.9)
Grade 4: ≥20.0 x ULN	2/363	(0.6)	4/359	(1.1)	-0.6 (-2.3, 1.0)

† Occurring in at least 4 participants in either treatment group.

‡ Participants are counted once per test in the highest grade reported. Only participants with a worsened grade from baseline were included.

§ The 95% CIs were calculated using Miettinen and Nurminen method.

n = Participants with results that met criterion; m = participants with at least one post-baseline test.

ULN = Upper limit of normal range.