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Question: Should TDF vs (d4T or ZDV) be used for initial ART?

Settings: Multiple locations

Bibliography: 1. Gallant JE, Staszewski S, Pozniak AL, DeJesus E, Suleiman JM, Miller MD, Coakley DF, Lu B, Toole JJ, Cheng AK; 903 Study Group. Efficacy and safety of tenofovir DF vs stavudine in combination therapy in antiretroviral-naive patients: a 3-year randomized trial. JAMA 2004; 292:191-201. 2. Gallant JE, DeJesus E, Arribas JR, Pozniak AL, Gazzard B, Campo RE, Lu B, McColl D, Chuck S, Enejesa J, Toole JJ, Cheng AK; Study 934 Group. Tenofovir DF, emtricitabine, and efavirenz vs. zidovudine, lamivudine, and efavirenz for HIV. N Engl J Med 2006; 354(3):251-60. 3. Rey D, Hoen B, Chavanet P, Schmitt MP, Hoizey G, Meyer P, Peytavin G, Spire B, Allavena C, Diemer M, May T, Schmit JL, Duong M, Calvez V, Lang JM. High rate of early virological failure with the once-daily tenofovir/lamivudine/nevirapine combination in naive HIV-1-infected patients. J Antimicrob Chemother 2009; 63:380-8.

Quality assessment							Summary of findings				Quality	Importance
No of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	TDF	(d4T or ZDV)	Relative (95% CI)	Absolute		
Mortality (follow-up mean 144 weeks)												
1	randomised trials	serious ^{1,2}	no serious inconsistency	no serious indirectness ³	serious ⁴	none	6/303 (2%)	5/299 (1.7%)	RR 1.18 (0.37 to 3.84)	3 more per 1000 (from 11 fewer to 47 more)	⊕⊕⊕⊕ LOW	CRITICAL
Clinical response - not reported												
0	-	-	-	-	-	none	0/0 (0%)	0/0 (0%)	-	-		
Severe adverse events (follow-up 1 study at 36 weeks, 1 study at 48 weeks, 1 study at 144 weeks)												
3	randomised trials	no serious limitations ⁵	no serious inconsistency	no serious indirectness ³	no serious imprecision	none ⁶	250/591 (42.3%)	247/595 (41.5%)	OR 1.04 (0.81 to 1.34)	10 more per 1000 (from 50 fewer to 72 more)	⊕⊕⊕⊕ HIGH	CRITICAL
Virologic response (follow-up 1 study at 36 weeks, 1 study at 48 weeks, 1 study at 144 weeks)												
3	randomised trials	no serious limitations ²	no serious inconsistency	no serious indirectness ³	no serious imprecision	none ⁶	384/595 (64.5%)	384/593 (64.8%)	RR 1 (0.76 to 1.3)	0 fewer per 1000 (from 155 fewer to 194 more)	⊕⊕⊕⊕ HIGH	CRITICAL
Adherence/tolerability/retention (follow-up 1 study at 36 weeks, 1 study at 48 weeks, 1 study at 144 weeks)												
3	randomised trials	serious ⁵	no serious inconsistency	no serious indirectness ³	no serious imprecision	none ⁶	445/591 (75.3%)	400/597 (67%)	RR 1.13 (1.05 to 1.21)	87 more per 1000 (from 34 more to 141 more)	⊕⊕⊕⊕ MODERATE	CRITICAL
Immunological response (follow-up 1 study at 48 weeks, 1 study at 144 weeks)												
2	randomised trials	no serious limitations ²	no serious inconsistency	no serious indirectness ³	serious ^{4,7}	none ⁶	559	558	-	MD 5.88 higher (45.08 lower to 56.84 higher)	⊕⊕⊕⊕ MODERATE	IMPORTANT
Drug resistance (follow-up 1 study at 36 weeks, 1 study at 144 weeks)												
2	randomised trials	no serious limitations ²	no serious inconsistency	no serious indirectness ³	serious ⁴	none ⁶	18/335 (5.4%)	2/338 (0.6%)	RR 6.12 (1.43 to 26.15)	30 more per 1000 (from 3 more to 149 more)	⊕⊕⊕⊕ MODERATE	IMPORTANT
Sexual transmission of HIV - not reported												
0	-	-	-	-	-	none	0/0 (0%)	0/0 (0%)	-	-		

¹ Only 1 out of 3 studies reported on mortality (Gallant), suggesting selective reporting.

² 2 studies out of 3 were open-label (Gallant and Rey), but studies were not downgraded based on these facts.

³ 1 study out of 3 was an indirect comparison of TDF/FTC/EFV vs. ZDV/3TC/EFV (Gallant) and 2 studies out of 3 (Gallant, Rey) were conducted only in developed country settings, but studies were not downgraded based on these facts.

⁴ Number of events <300 and/or confidence intervals include potential harm and benefit.

⁵ Assessment of adherence/retention/tolerability or assessment of adverse events may be subject to bias in an open-label study, so downgraded for this outcome.

⁶ All 3 studies were industry funded; not downgraded for this, however, as study drug did not show benefit so less concern for reporting bias.

⁷ None of the included studies provided standard deviations for the mean outcome so the same estimated SD value was used for all studies.