

GRADE table: Darunavir/ritonavir vs. Lopinavir/ritonavir

Question: Should Darunavir/ritonavir vs. Lopinavir/ritonavir be used for patients failing first line therapy?

Settings:

Bibliography: Mills AM, Nelson M, Jayaweera D, et al. Once daily darunavir/ritonavir vs. lopinavir/ritonavir in treatment-naive, HIV-1-infected patients: 96 week analysis. AIDS 2009;23:1679-1688.

Quality assessment							Summary of findings					Importance
No of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	No of patients		Effect		Quality	
							Darunavir/ritonavir	Lopinavir/ritonavir	Relative (95% CI)	Absolute		
Mortality (follow-up 96 weeks)												
1	randomised trials	no serious limitations ¹	no serious inconsistency	serious indirectness ³	serious ²	none	1/343 (0.3%)	5/346 (1.4%)	RR 0.2 (0.02 to 1.72)	12 fewer per 1000 (from 14 fewer to 10 more)	⊕⊕⊕ LOW	CRITICAL
Severe adverse events (follow-up 96 weeks)⁴												
1	randomised trials	serious ¹	no serious inconsistency	serious indirectness ³	no serious imprecision	none	34/343 (9.9%)	55/346 (15.9%)	RR 0.62 (0.42 to 0.93)	60 fewer per 1000 (from 11 fewer to 92 fewer)	⊕⊕⊕ LOW	CRITICAL
Clinical disease progression - not reported												
0	-	-	-	-	-	-	-	-	-	-	-	CRITICAL
Adherence/tolerability/retention (follow-up 96 weeks; reported as Retention, number still on randomised study drug⁵)												
1	randomised trials	no serious limitations ¹	no serious inconsistency	serious indirectness ³	no serious imprecision	none	284/343 (82.8%)	265/346 (76.6%)	RR 1.08 (1 to 1.17)	61 more per 1000 (from 0 more to 130 more)	⊕⊕⊕ MODERATE	IMPORTANT
Virologic response, proportion HIV-1 RNA <50 copies/ml (follow-up 96 weeks)												
1	randomised trials	no serious limitations ¹	no serious inconsistency	serious indirectness ³	no serious imprecision	none	271/343 (79%)	246/346 (71.1%)	RR 1.11 (1.02 to 1.21)	78 more per 1000 (from 14 more to 149 more)	⊕⊕⊕ MODERATE	IMPORTANT
Immunologic response (follow-up 96 weeks; Better indicated by higher values)												
1	randomised trials	no serious limitations ¹	no serious inconsistency	serious indirectness ³	no serious imprecision	none	343	346	-	not estimable ⁶	⊕⊕⊕ MODERATE	IMPORTANT
Drug resistance (follow-up 96 weeks), reported as acquired major PI mutation												
1	randomised trials	no serious limitations ¹	no serious inconsistency	serious indirectness ³	serious ²	none	0/343 (0%)	0/346 (0%)	-	not estimable ⁷	⊕⊕⊕ LOW	IMPORTANT

¹ Open-label, industry sponsored study. Down-graded for being open-label study for outcome of severe adverse events but not others.

² Low number of events <300 and CI indicates potential for benefit and harm.

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³ Evaluation in treatment naive patients is indirect measure of PI-naive patients who would use boosted PI in second line after failure of NNRTI based regimen.

⁴ Reported as "Any serious AE." For "Any AE leading to withdrawal," there were 19/343 in DRV/r arm and 35/346 in LPV/r arm.

⁵ In post hoc analysis by self reported adherence, those adherent (>95% adherence) had similar VL response (<50 copies/ml) rates in both arms (82 and 78% in DRV/r and LPV/r, respectively). For those sub-optimally adherent (<95%), VL response 76% in DRV/r arm compared to 53% in LPV/r arm (p<0.0001).

⁶ Median change from baseline in CD4 cell count was 188 cells/ul in LPV/r group and 171 cells/ul in DRV/r group .

⁷ No major PI mutations were found among those with VL >50 copies/ml who had baseline and endpoint genotypes.