

GRADE Table: Atazanavir/ritonavir vs. Lopinavir/ritonavir

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

Settings:

Bibliography: Molina JM, Andrade-Villanueva J, Echevarria J, et al. Once daily atazanavir/ritonavir versus twice daily lopinavir/ritonavir, each in combination with tenofovir and emtricitabine, for management of antiretroviral-naïve HIV-1-infected patients: 48 week efficacy and safety results of the CASTLE study. Lancet 2008;372:646-55. Molina JM, Andrade-Villanueva J, Echevarria J, et al. Atazanavir/ritonavir vs. Lopinavir/ritonavir in antiretroviral naïve HIV-1-infected patients: CASTLE 96 week Efficacy and Safety. 48th Annual ICAAC/IDSA Meeting, October 25-28, 2008, Washington DC. Abstract H-1250d.

Quality assessment							Summary of findings					Importance
No of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	No of patients		Effect		Quality	
							Atazanavir/ritonavir	Lopinavir/ritonavir	Relative (95% CI)	Absolute		
Mortality (follow-up 48 weeks)												
1	randomised trials	no serious limitations ¹	no serious inconsistency	serious indirectness ²	serious ³	none	6/440 (1.4%)	6/443 (1.4%)	RR 1.01 (0.33 to 3.1)	0 more per 1000 (from 9 fewer to 28 more)	⊕⊕⊕ LOW	CRITICAL
Severe adverse events (follow-up 96 weeks)⁴												
1	randomised trials	serious ¹	no serious inconsistency	serious indirectness ²	serious ³	none	63/441 (14.3%)	50/437 (11.4%)	RR 1.25 (0.88 to 1.77)	29 more per 1000 (from 14 fewer to 88 more)	⊕⊕⊕ VERY LOW	CRITICAL
Clinical disease progression - not reported												
0	-	-	-	-	-	-	-	-	-	-	-	CRITICAL
Adherence/Tolerability/Retention (follow-up 48 weeks; adherence questionnaire)												
1	randomised trials	serious ¹	no serious inconsistency	serious indirectness ²	no serious imprecision	none	330/440 (75%)	316/443 (71.3%)	RR 1.05 (0.97 to 1.14)	36 more per 1000 (from 21 fewer to 100 more)	⊕⊕⊕ LOW	CRITICAL
Virologic response, proportion <50 copies (follow-up 96 weeks)												
1	randomised trials	no serious limitations ¹	no serious inconsistency	serious indirectness ²	no serious imprecision	none	308/440 (70%)	279/443 (63%)	RR 1.08 (0.99 to 1.18) ⁵	54 more per 1000 (from 7 fewer to 121 more)	⊕⊕⊕ MODERATE	IMPORTANT
Immunologic response (follow-up mean 96 weeks; Better indicated by higher values)												
1	randomised trials	no serious limitations ¹	no serious inconsistency	serious indirectness ²	no serious imprecision	none	440	443	-	MD 21.2 lower (43.3 lower to 0.9 higher) ⁶	⊕⊕⊕ MODERATE	IMPORTANT
Drug resistance (follow-up 96 weeks) reported as major PI mutation												
1	randomised trials	no serious limitations ¹	no serious inconsistency	serious indirectness ²	serious ³	none	1/440 (2.3%)	0/443 (1.8%)	RR 1.26 (0.5 to 3.16)	5 more per 1000 (from 9 fewer to 39 more)	⊕⊕⊕ LOW	IMPORTANT

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¹ Open-label study, sponsored by industry. Not down-graded for being open-label unless outcome is "severe adverse events" or "adherence" where non-blinded treatment could bias outcome.

² Study evaluates ART-naive population, which is indirect population from PI-naive patients who would use PI in second line after failure on NNRTI based regimen.

³ Low number of events, <300 and CI indicates potential for appreciable benefit and harm.

⁴ Reported as, "Serious adverse events." Of note, even subjects discontinued due to diarrhoea in LPV/r arm and 3 subjects discontinued due to jaundice/hyperbilirubinemia in ATV/r arm.

⁵ ITT analysis where non-completer or rebound=failure (TLOVR). At 48 week outcomes, numbers for TLOVR and confirmed virologic response (CVR) were similar: for ATV/r 343/440 and LPV/r 338/443 (CVR) compared to ATV/r 343/440 and LPV/r 337/443 (TOLVR). CVR classifies rebounders who are re-suppressed as responders. TLOVR classifies response as 2 measurements < 50 copies/ml and maintained (without discontinuation or rebound).

⁶ Mean increase from baseline of CD4 cell count similar between groups: 268 cells/ul in ATV/r versus 290 cells/ul in LPV/r group at 96 weeks.