

## GRADE table: Fosamprenavir/ritonavir vs. Lopinavir/ritonavir

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

**Settings:**

**Bibliography:** Eron J, Yeni P, Gathe J et al. The KLEAN study of fosamprenavir-ritonavir versus lopinavir-ritonavir, each in combination with abacavir-lamivudine, for initial treatment of HIV infection over 48 weeks: a randomised non-inferiority trial. Lancet 2006;368:476-82.

Quality assessment							Summary of findings					Importance
No of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	No of patients		Effect		Quality	
							Fosamprenavir/ritonavir	Lopinavir/ritonavir	Relative (95% CI)	Absolute		
<b>Mortality (follow-up median 48 weeks)</b>												
1	randomised trials	no serious limitations <sup>1</sup>	no serious inconsistency	serious <sup>2</sup>	serious <sup>3</sup>	none	4/443 (0.9%)	1/444 (0.2%)	RR 4.01 (0.45 to 35.73)	7 more per 1000 (from 1 fewer to 78 more)	⊕⊕⊕ LOW	CRITICAL
<b>Severe adverse events (follow-up median 48 weeks; adverse events leading to discontinuation)</b>												
1	randomised trials	serious <sup>1</sup>	no serious inconsistency	serious <sup>2</sup>	serious <sup>3</sup>	none	53/436 (12.2%)	43/443 (9.7%)	RR 1.25 (0.86 to 1.83)	24 more per 1000 (from 14 fewer to 81 more)	⊕⊕⊕ VERY LOW	CRITICAL
<b>Clinical disease progression or death (follow-up median 48 weeks)</b>												
1	randomised trials	no serious limitations <sup>1</sup>	no serious inconsistency	serious <sup>2</sup>	serious <sup>3</sup>	none	11/443 (2.5%)	11/444 (2.5%)	RR 1 (0.44 to 2.29)	0 fewer per 1000 (from 14 fewer to 32 more)	⊕⊕⊕ LOW	CRITICAL
<b>Adherence/tolerability/retention (follow-up median 48 weeks; adherence by pill counts reported as median percentage)</b>												
1	randomised trials	serious <sup>1</sup>	no serious inconsistency	serious <sup>2</sup>	no serious imprecision	none	427/443 (96.4%)	435/444 (98%)	RR 0.98 (0.96 to 1.01)	20 fewer per 1000 (from 39 fewer to 10 more)	⊕⊕⊕ LOW	CRITICAL
<b>Immunologic response (follow-up median 48 weeks; measured with: median increase in CD4 count from baseline; Better indicated by higher values)</b>												
1	randomised trials	no serious limitations <sup>1</sup>	no serious inconsistency	serious <sup>2</sup>	no serious imprecision	none	443	444	-	Not estimable <sup>4</sup>	⊕⊕⊕ MODERATE	IMPORTANT
<b>Virologic response, proportion &lt;50 copies/ml (follow-up median 48 weeks)</b>												
1	randomised trials	no serious limitations <sup>1</sup>	no serious inconsistency	serious <sup>2</sup>	no serious imprecision	none	285/443 (64.3%)	288/444 (64.9%)	RR 0.99 (0.9 to 1.09)	6 fewer per 1000 (from 65 fewer to 58 more)	⊕⊕⊕ MODERATE	IMPORTANT
<b>Drug resistance (follow-up median 48 weeks), reported as acquired major PI mutations</b>												
1	randomised trials	no serious limitations <sup>1</sup>	no serious inconsistency	serious <sup>2</sup>	serious <sup>3</sup>	none	0/443 (0%)	0/444 (0%)	-	Not estimable <sup>5</sup>	⊕⊕⊕ LOW	IMPORTANT

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- <sup>1</sup> Open-label study; sponsored by industry. Not downgraded for this other than for severe adverse events and adherence, which may be subject to bias in open-label study.
- <sup>2</sup> Evaluates comparison in ART naive population, which is indirect to PI naive populations starting PI-based second line after NNRTI 1st line.
- <sup>3</sup> Low number of events <300 and CI indicates potential for appreciable benefit and harm.
- <sup>4</sup> Median increase in CD4 from baseline 176 cells/ul (IQR 106-281) in FPV/r group and 191 cells/ul (IQR 124-287) in LPV/r group
- <sup>5</sup> No major PI associated mutations in either arm among the 35 patients who had protocol-defined failure and baseline and endpoint genotypes available.