Lopinavir/ritonavir for COVID-19: A living systematic review

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Appendix 4: Evidence profile

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Question: Efficacy of lopinavir/ritonavir for the treatment of COVID-19 [a]
Setting:
Bibliography:

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Lopinavir/ritonavir + standard care	standard care	Relative (95% CI)	Absolute (95% CI)		
Mechanical ventilation or ECMO at day 7												
1	randomised trials	serious [b]	not serious	not serious	very serious [c]	none	6/94 (6.4%)	4/93 (4.3%)	**RR 1.48** (0.43 to 5.09)	**21 more per 1,000** (from 25 fewer to 176 more)	⨁◯◯◯ VERY LOW	
Respiratory failure												
1	randomised trials	serious [b]	not serious	not serious	serious [c]	none	None of the studies provided suitable data to estimate the effect on respiratory failure. One study reported that 27.3% of the patients assigned to the control group had respiratory failure or ARDS compared with 19.2% of patients assigned to lopinavir/ritonavir (RR 0.56; 95% CI, 0.32 to 0.99)				⨁⨁◯◯ LOW	
Mortality at day 7												
1	randomised trials	serious [b]	not serious	not serious	serious [c]	none	6/99 (6.1%)	7/100 (7.0%)	**RR 0.87** (0.30 to 2.49)	**9 fewer per 1,000** (from 49 fewer to 104 more)	⨁⨁◯◯ LOW	
Mortality at day 14												
1	randomised trials	serious [b]	not serious	not serious	serious [c]	none	15/99 (15.2%)	17/100 (17.0%)	**RR 0.89** (0.47 to 1.68)	**19 fewer per 1,000** (from 90 fewer to 116 more)	⨁⨁◯◯ LOW	
Mechanical ventilation or ECMO at day 14												
1	randomised trials	serious [b]	not serious	not serious	very serious [c]	none	3/84 (3.6%)	5/83 (6.0%)	**RR 0.59** (0.15 to 2.40)	**25 fewer per 1,000** (from 51 fewer to 84 more)	⨁◯◯◯ VERY LOW	
Mortality - Longer follow up												
2	randomised trials	serious [b]	not serious	not serious	serious [c]	none	19/133 (14.3%)	1.0%	**RR 0.77** (0.45 to 1.30)	**2 fewer per 1,000** (from 6 fewer to 3 more)	⨁⨁◯◯ LOW	

								9.0%		**21 fewer per 1,000** (from 50 fewer to 27 more)		
								30.0%		**69 fewer per 1,000** (from 165 fewer to 90 more)		
Serious adverse effects												
2	randomised trials	serious [b]	not serious	not serious	serious [c]	none	20/129 (15.5%)	32/116 (27.6%)	**RR 0.63** (0.39 to 1.03)	**102 fewer per 1,000** (from 168 fewer to 8 more)	⨁⨁◯◯ LOW	
Total adverse effects												
2	randomised trials	serious [b]	serious [a]	not serious	serious [c]	none	58/129 (45.0%)	49/116 (42.2%)	**RR 2.42** (0.22 to 26.91)	**600 more per 1,000** (from 329 fewer to 1,000 more)	⨁◯◯◯ VERY LOW	
Time to SARS-CoV-2 RT-PCR negativity												
1	randomised trials	serious [b]	not serious	not serious	very serious [c]	none	34	17	-	MD **0.3 lower** (3.29 lower to 2.69 higher)	⨁◯◯◯ VERY LOW	
IVM- Longer follow-up												
1	randomised trials	serious [b]	not serious	not serious	serious [c]	none	14/99 (14.1%)	18/100 (18.0%)	**RR 0.79** (0.41 to 1.49)	**38 fewer per 1,000** (from 106 fewer to 88 more)	⨁⨁◯◯ LOW	
ECMO- Longer follow-up												
1	randomised trials	serious [b]	not serious	not serious	serious [c]	none	2/99 (2.0%)	2/100 (2.0%)	**RR 1.01** (0.15 to 7.03)	**0 fewer per 1,000** (from 17 fewer to 121 more)	⨁⨁◯◯ LOW	

Total adverse events

	randomised trials	not serious	not serious	serious [d]	not serious	none	A systematic review reports the most common adverse effects were diarrhea and nausea. Adverse events possible relationship to lopinavir/ritonavir therapy were diarrhea, nausea, asthenia , abdominal pain, vomiting, headache, and rash.	⨁⨁⨁◯ MODERATE	

CI: Confidence interval; **RR:** Risk ratio; **MD:** Mean difference

Explanations

a. The certainty of evidence was downgraded for inconsistency, as the studies show contradictory results (I2=70).
b. The certainty of the evidence was downgraded in one level for risk of bias since the overall risk of bias for both studies was evaluated as 'some concerns' for all outcomes
c. The certainty of the evidence was downgraded in one level for imprecision, since each end of the confidence interval would lead to different conclusions. In the case of "Mechanical ventilation or ECMO at day 7 and day 14", it was decided to decrease an additional level due to this outcome few events were observed (n< 10). In the case of "Time to SARS-CoV-2 RT-PCR negativity", it was decided to decrease an additional level due to the small number of patients included in this study
d. The certainty of evidence was downgraded in one level for indirectness, since the evidence comes from studies of lopinavir/ritonavir in HIV-Infected adults.