

Peer Review File

Article information: <http://dx.doi.org/10.21037/jtd-20-1810>

Query NO.	Reviewer comments	Author's response	Location in revised manuscript
Reviewer 1			
1	Updating the data of confirmed cases and death.	As kindly suggested by reviewer 1, we have updated the data of confirmed cases and deaths.	Abstract part, Page 1, Lines 5, 6
2	The format of the second paragraph on page 9 is inconsistent with the preceding text. Why?	We apologize for this typo mistake. The format of this paragraph has been modified as the preceding text.	Interferons part, Page 10, Paragraph 2, Lines 1-9
3	The prospect of the future treatment of COVID-19, such as the combination of Chinese and western medicine, the new drugs or therapies based on the novel mechanism by which the	Thank you for pointed out this important issue. We have added a text that included the prospect of the future treatment of COVID-	Conclusion part Page 18, Lines 9-18

Query NO.	Reviewer comments	Author's response	Location in revised manuscript
	SARS-CoV-2 infects host cells, can be included in Conclusion part.	19 in the conclusion part.	
Reviewer 2			
Abstract and Conclusion		As kindly suggested by reviewer 2, we have updated the data of confirmed cases and deaths.	Abstract part, Page 1, Lines 5, 6
1	Line 5 – The authors should actualize the number of cases and deaths around the world.		
2	Line 7 – The authors should cite the WHO bulletin with this official declaration	We appreciate this note. Here we mentioned the name and the number of WHO report, and because we can't cite the text in the abstract part, so we have cited similar text of the WHO bulletin with this official declaration in the introduction section.	Page 2, paragraph 2, Lines 13-15
3	Line 18 – The expression	We have clarified this	Abstract part,

Query NO.	Reviewer comments	Author's response	Location in revised manuscript
	“relatively acceptable activity” is not good to explain this research in an abstract. Please clarify this sentence using precise expressions like "activity in vitro", "activity in clinical trials", "in vivo"	sentence as suggested by reviewer 2.	Page 1, Lines 17, 18
4	Line 19 – Substitute “novel coronavirus” for SARS-CoV-2	The novel coronavirus words have been replaced by SARS-CoV-2.	Abstract part, Page 1, Line 18
5	Line 20 (and at Conclusion) – The author should point the necessity of double-blind and randomized clinical trials, as recommended by FDA for example, to confirm the activity of these medicines.	As reviewer 2 suggested, we have pointed this sentence in the abstract and conclusion parts.	Abstract part, Page 1, Lines 19,20, and at Conclusion part, Page 19, Lines 5
INTRODUCTION			
6	Line 3-5: Please confirm if in these References 1 and 2, the text “ β CoVs chiefly infect mammals, while δ and γ CoVs	We appreciate this note. This text is cited from reference (3), not from References 1 and	Introduction part, Page 2, Paragraph 1, Lines 3, 4

Query NO.	Reviewer comments	Author's response	Location in revised manuscript
	predominantly infect poultry” really is written. I could not find it.	2. The “poultry” word has been replaced by “birds” word. You can check and see that in reference 3 (background section, paragraph 2 of ref. 3). We cited this text from ref 3.	
7	Line 5: Please check if the text “Human CoVs include α -CoVs, β -CoVs, MERS-CoV, SARS-CoV, and 2019 novel coronavirus” is in reference (3). I could not find these pieces of information in reference 3. Maybe ref 1.	Thank you for pointing out this issue. This text was cited from ref 1 and ref 3, we have checked this text in ref 3, and we have found it background section, paragraph 2 of ref 3. Also we have added the ref 1 as a citation too for this text.	Introduction part, Page 2, Paragraph 1, Line 5
8	Line 6: Word was in “SARS-CoV-2 was found” should be substituted for “...is....”	Thank you for pointed out this. The suggested correction has been made, and the sentence	Introduction part, Page 2, Paragraph 2, Line 1

Query NO.	Reviewer comments	Author's response	Location in revised manuscript
		now reads: SARS-CoV-2 is found.	
9	End of the second paragraph: It is needed to cite a reference, the WHO bulletin of this declaration	We agree with the reviewer 2. We have cited the reference for this declaration in introduction section.	Introduction part, Page 2, Paragraph 2, Line 13
10	3° paragraph: This whole paragraph is almost a copy from reference 2. Please rewrite it with your own words.	Thank you for pointed out this issue. We have modified the paragraph with our own words as the reviewer 2 suggested.	Introduction part, Page 2, Paragraph 3, Lines 1-5
11	End of 3° paragraph: This reference has no relation with SARS-CoV-2, only MERS-CoV and SARS-CoV. I don't believe this correlation with SARS-CoV-2 has a proper citation. Please, cite another reference with this suggestion.	We agree with the reviewer 2 in this suggestion. So we have added and cited another suitable reference in which SARS-CoV-2 is included.	Introduction part, Page 3, Paragraph 2, Lines 12, 13
12	Page 2 – 1° Paragraph (Lines 1-4): Please, use a citation to	We have use the citations that reveal all	Introduction part, Page 2,

Query NO.	Reviewer comments	Author's response	Location in revised manuscript
	<p>reveal all these pieces of information.</p> <p>Ref. 8 is from 2016 related to other coronaviruses, not SARS-CoV-2.</p>	<p>pieces of information in this paragraph.</p> <p>Regarding Ref 8, we have added a new citation related to SARS-CoV-2.</p>	<p>Paragraph 1, Lines 1-5</p> <p>Introduction part, Page 3, Paragraph 2, Lines 6</p>
Remdesivir			
13	<p>Page 4 – Line 5: In “It is presently used for Ebola virus infection treatment (16)” there is confusion. Remdesivir is not yet approved for EBOV infection by any Sanitary Agency. So, by using this same reference all you can say is that this drug has proved effective on EBOV infections in a human clinical trial.</p>	<p>Thank you for this suggestion. We have modified the sentence as suggested by reviewer 2.</p>	<p>Remdesivir part, Page 5, Paragraph 1, Lines 5, 6</p>
14	<p>Page 5 – Second paragraph: This reference 19 does not mention combinations of these 2 drugs in COVID-19 infection.</p>	<p>We appreciate this note. We have removed this paragraph as suggested</p>	<p>Remdesivir part, Page 6, Paragraph 2</p>

Query NO.	Reviewer comments	Author's response	Location in revised manuscript
	You should not write that.	by reviewer 2.	
Lopinavir/ritonavir (LPV/r)			
15	Page 5 (Lopinavir/ritonavir (LPV/r)), Line 2 – The word “mainly” means different possible uses for LPV/r. But there aren't second approved uses for this drug. You should exclude this word.	We have removed “mainly” word as suggested by reviewer 2	LPV/r part, Page 6, Paragraph 1, Lines 2
16	Line 2 – define AIDS	We agree with the reviewer 2 in this suggestion. We have defined AIDS as an acquired immunodeficiency syndrome.	LPV/r part, Page 6, Paragraph 1, Lines 2, 3
17	Lines 4-7: Should mention here that in SARS-CoV-2, there is a different mechanism inhibiting the 3CLprotease: J. Clin. Med. 2020, 9, 1131; DOI:10.3390/jcm9041131.	Thank you for this suggestion. We have added this mechanism of action as suggested and cited it.	LPV/r part, Page 6, Paragraph 1, Lines 6, 7
18	Page 6. The second paragraph lines 9-11: This is already being	We have added a part related to this new	LPV/r part, Page 7,

Query NO.	Reviewer comments	Author's response	Location in revised manuscript
	<p>done by SOLIDARITY and many other research groups. There are several negative results in trials that you should put in this part of the text for LPV/r combination to COVID-19. Examples:</p> <p>https://doi.org/10.1016/S0140-6736(20)31042-4 N Engl J Med 2020;382:1787-99.DOI: 10.1056/NEJMoa2001282.</p>	<p>research and cited it, as suggested by reviewer 2.</p>	<p>Paragraph 1, Lines 13-15</p>
Ribavirin			
19	<p>Page 6 (Ribavirin), Lines 9-11: Ref. 25 is not about SARS-CoV-2. Ref. 33 is a website citing an article. You should cite the original research (DOI: 10.1001/jama.2020.3204 The Singapore 2019 Novel Coronavirus Outbreak Research Team **** and JAMA. 2020;323(15):1488-1494. Epidemiologic Features and Clinical Course of Patients</p>	<p>Thank you for pointed out this important issue. We have modified the citation and references as the reviewer suggested. We removed the reference 25, and we have replaced the reference 33 (website) with suggested reference (original</p>	<p>Ribavirin part, Page 7, Paragraph 1, Lines 11</p>

Query NO.	Reviewer comments	Author's response	Location in revised manuscript
	Infected With SARS-CoV-2 in Singapore).	article).	
Favipiravir			
20	Page 7 (favipiravir). You could cite here that the Russian government approved this drug for COVID-19 treatment but did not show the clinical study and its results.	Thanks for this suggestion. We have added the sentence that refers to that and cited it.	Favipiravir part, Page 8, Paragraph 1, Lines 15, 16
Interferons			
21	Page 9 (last lines): There is an article citing the effects of Ribavirin/Interferon B-1/ LPV/r combination. You should find a space for this important study here.	As kindly suggested by reviewer 2, we have added that new study and cited it.	Interferon part, Page 10, Paragraph 2, Lines 10-13
Chloroquine and Hydroxychloroquine			
22	Page 11 (Chloroquine and Hydroxychloroquine): It is very important to cite these 3	Thank you so much for pointed out this important issue. As	Chloroquine and Hydroxychloroquine part,

Query NO.	Reviewer comments	Author's response	Location in revised manuscript
	<p>references pointing the other way around :</p> <p>JAMA. DOI:10.1001/jama.2020.8630, BMJ 2020;369:m1849, http://dx.doi.org/10.1136/bmj.m1849 DOI: 10.1056/NEJMoa2016638</p>	<p>suggested by reviewer 2, we have cited theses three references, and added cited text to this part.</p>	<p>Page 12, Paragraph 2, Lines 1-13</p>
Table 1			
23	<p>You should consider all articles that I mentioned in this column “Recommendation and evidence”. This recommendation should be done in a Systematic Review, not in a narrative review. I do not think this Recommendation should be done in this table.</p>	<p>We appreciate this note. We have removed the column of recommendation and evidence from table 1, as suggested by reviewer 2.</p>	
	<p>For Arbidol: You did not discuss combinations in the text. Why this here in Table 1?</p>	<p>We appreciate this note. But we have already discussed the combination of arbidol and LPV/r in the text, you can check again, you will see that in Arbidol part. So we didn't modify here.</p>	<p>Arbidol part, Page 8, Paragraph 1, Lines 3-6</p>

Query NO.	Reviewer comments	Author's response	Location in revised manuscript
	For Interferon: Please, put the other interferon on the table as well.	As suggested, we have added interferon beta-b1 to table 1.	Table 1, Row 7
	For Chloroquine phosphate: Shall cite longer and randomized studies telling just the opposite. ref. 48 is in vitro for SARS-CoV-1, not SARS-CoV-2.	Thank you for pointed out this issue. So we removed the Ref. 48 from table 1, as reviewer 2 suggested.	Table 1, Row 8
	Reference 49 is a Letter that cites clinical trials accessed on 18 February 2019? It does not look like this reference has pieces of evidence on chloroquine for COVID-19. Review this reference. Try to cite another.	We appreciate this note. We have found that the evidence in Ref. 49 is cited from Ref. 19. So we have removed ref. 49 from the table 1.	Table 1, Row 8
	For Hydroxychloroquine: If you consider the 3 articles with no good results for HCQ, it would change this recommendation? Please exclude this column.	As kindly suggested by reviewer 2, we considered and added to the table the 3 references with no good results for HCQ.	Table 1, Row 9

Query NO.	Reviewer comments	Author's response	Location in revised manuscript
		We have excluded the recommendation column.	
Reviewer 3			
1	Please indicate the search strategy in the Method part.	Thank you for this suggestion. We have added the search strategy in the method part.	Method part, Page 4, 5, Paragraph 2, Lines 1-22