

Response to Reviewer:

Thank you for your affirmation of this article and thank you for your valuable comments.

The drugs mentioned in our paper have certain theoretical basis, but the actual research results are not completely satisfactory. There is not enough sample size, scientific and objective clinical data to prove their effective.

As you mentioned, It is still need to explore what to use to treat patients with COVID-19 at different severity. Many issues need to be identified, including which drug is the first choice, how to use them in combination, and the dosage, delivery route and timing.

Based on your comments, we tried our best to add a table summarizing each drugs used in clinical practice. Unfortunately, the above-mentioned medication details can not be better summarized.

Table 1. Summarizing of each drugs used in clinical practice.^[1-6]

Antivirals	Notes	Usage and dosage (adults)
IFN	<ol style="list-style-type: none"> 1. Not recommended for the treatment of patients with severe or critical COVID-19, except in a clinical trial. 2. Patients with early (i.e., <7 days from symptom onset) mild and moderate may benefit. 3. IFN-α has primarily been used as nebulization and usually as part of a combination regimen. 	<ol style="list-style-type: none"> 1. Nebulized IFN-α: 5 million units, add 2ml of sterile water for injection, twice daily. Preferably less than 10 days. 2. Subcutaneous IFN-β: 8 million international units every other day. Preferably less than 10 days.
LPV/r	<ol style="list-style-type: none"> 1. Not recommended to treat Patients with COVID-19 at any severity. 2. Not recommended to use alone. 3. The plasma drug concentrations of typical doses are far below the levels that may be needed. 	<ol style="list-style-type: none"> Lopinavir 400 mg/ritonavir 100 mg orally twice daily. Preferably less than 10 days.
RBV	<ol style="list-style-type: none"> 1. There is not enough sample size, scientific and objective clinical data to prove effective. 2. Not recommended to use alone. Usually combination with IFN and/or LPV/r. 	<ol style="list-style-type: none"> 500mg per time, inject 2-3 times per day intravenously. Preferably less than 10 days.
CQ	<ol style="list-style-type: none"> 1. Not recommended to treat Patients with COVID-19 at any severity. 2. Recommendation against CQ with or without azithromycin. 	<ol style="list-style-type: none"> 1. CQ 600mg twice daily for 10 days (high dose, serious side effect). CQ 450mg twice daily for 1 day, then CQ 450 mg for 4 days (low dose, mild side effect). 2. HCQ 800 to 1600mg Oral On the

		first day, 1 to 3 divided doses. 200 to 800mg Oral Daily for 5 to 21 days, 1 to 2 divided doses. 3.CQP 500 mg twice daily for 10 days.
Arbidol	There is not enough sample size, scientific and objective clinical data to prove effective.	100 mg orally twice daily for 5 days. Preferably less than 10 days.
Favipiravir	There is not enough sample size, scientific and objective clinical data to prove effective.	1600mg for the first dose, then 600mg orally twice daily for 5 days.
Remdesivir	1.Remdesivir is the only Food and Drug Administration-approved drug for the treatment of COVID-19. 2.Consider remdesivir for hospitalized patients with COVID-19 who require supplemental oxygen but who do not require oxygen delivery through a high-flow device, noninvasive ventilation, invasive mechanical ventilation, or extracorporeal membrane oxygenation.	200mg on day 1, then 100 mg inject once daily intravenously for 5-7days.
Thymosin α 1	There is not enough sample size, scientific and objective clinical data to prove effective.	1.6mg subcutaneous injection, twice a week, each time 3-4 days apart. Preferably more than 4 weeks.

IFN: Interferon, LPV/r: Lopinavir / litonavir, RBV: Ribavirin, CQ:Chloroquine, HCQ: Hydroxychloroquine, CQP:Chloroquine phosphate.

References:

1. General Office of the national health and Health Commission. Novel coronavirus pneumonia diagnosis and treatment plan (trial version 8)[EB/OL]. (2020-08-18)[2020-08-18]. http://www.gov.cn/zhengce/zhengceku/2020-08/19/content_5535757.htm.
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3. NIH: Coronavirus Disease 2019 (COVID-19) Treatment Guideline. <https://www.covid19treatmentguidelines.nih.gov/>.
4. NHC of the PRC, NATCM of the PRC. Guidance for Corona Virus Disease 2019:Prevention, Control, Diagnosis and Management. 2020 Feb.
5. National Institute for Health and Care Excellence (UK):COVID-19 rapid guideline: managing COVID-19.2020 Dec 18.
6. Lamontagne F, et al. A living WHO guideline on drugs for covid-19.BMJ. 2021 Mar 1;372:n526.

The above is a reply to your review comments. If there is any wrong answer or understanding, please point out. Thank you.