

# Remdesivir and Lopinavir/Ritonavir as Potential Drugs to Treat Corona Virus Disease 2019

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## ABSTRACT

Drugs that are efficacious against SARS-CoV-2 have yet to be established. Remdesivir and Lopinavir/ritonavir have garnered considerable attention for their potential to treat coronavirus disease 2019 (COVID-19). Remdesivir not only *in vivo* but also *in vitro* testing shows the inhibition of human coronavirus replication, including SARS-CoV as well as Lopinavir/ritonavir that shows promising antiviral drug against SARS-CoV-2.

**Keywords:** Remdesivir; Lopinavir; Ritonavir; COVID-19; SARS-CoV-2

## INTRODUCTION

Drugs that are efficacious against SARS-CoV-2 have yet to be established. Remdesivir and Lopinavir/ritonavir have garnered considerable attention for their potential to treat coronavirus disease 2019 (COVID-19).

## REMDESIVIR

Remdesivir is a 1 cyano substituted adenosine analogue prodrug with broad antiviral activity, initially used against Ebola and it has been shown to inhibit SARS-CoV-2 [1,2]. Its antiviral mechanism is due its incorporation into viral RNA chains resulting premature termination, Remdesivir has been recently recognized as a promising antiviral drug against RNA viruses, especially 2019-nCoV as it been showed by preliminary data in various studies [3,4].

Remdesivir, as a prodrug with a broad-spectrum antiviral activity against coronaviruses, was recently confirmed to inhibit 2019-nCoV *in vitro* [5-8]. Not only *in vivo* but also *in vitro* testing this drug shows the inhibition of human coronavirus replication, including SARS-CoV [5,7,8]. Therefore, Remdesivir was initially only available for compassionate use but received orphan drug status from the US Food and Drug Administration on March 23, 2020.

Thus, Remdesivir is currently evaluated in phase 4 clinical trials for SARS-CoV-2, in the United States, South Korea, China, and Europe. Two of on-going multicentre ones are evaluating this drug in hospitalized patients with moderate or severe symptoms .and it showed reduction of pneumonia associated symptoms of some COVID-19 patients [9,10]. Remdesivir is generally well tolerated but hepatotoxicity and nephrotoxicity has been observed as it

showing in a recent study that promises its antiviral activity against SARS-CoV-2.

## LOPINAVIR/RITONAVIR

Besides Remdesivir, Lopinavir/ritonavir showed promising antiviral drug against SARS-CoV-2 [11,12]. Lopinavir/ritonavir is generally used in the treatment for HIV infection by suppressing the replication of HIV-1 [13]. *In vitro* Lopinavir/ritonavir demonstrated activity against coronaviruses *via* inhibition of 3-chy-motrypsin-like protease, this drug was found to inhibit SARS-CoV-2 replication *in vitro* [13,14]. Some clinical studies in SARS were associated with reduced mortality and intubation rates [11,12]. Lopinavir/ritonavir can also reduce pneumonia-associated symptoms of some COVID-19 patients [15,16]. That is proven in other study that it can significantly lead to the reduction of acute respiratory distress syndrome caused by SARS infection [17].

In a clinical study, the therapeutic effect of Lopinavir/ritonavir combined therapy was better than that of the therapy without Lopinavir/ritonavir, no adverse effects in liver toxic and side effects compared with the control group after the combination treatment with Lopinavir/ritonavir and adjuvant drugs. However, some data suggest that Arbidol monotherapy is more effective than Lopinavir/ritonavir in treating COVID-19, and indicate that Arbidol monotherapy may be superior to Lopinavir/ritonavir in treating COVID-19. The most commonly used and studied Lopinavir/ritonavir dosing regimen for COVID-19 treatment is 400 mg/100 mg twice daily for up to 14 days with or without ribavirin as it recommended by China National Health Commission, 2020

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[18,19].

Combinational therapy of Lopinavir with the other effective compounds against SARS-CoV-2 virus may rise synergy and reduce adverse effects of Lopinavir/ritonavir that include gastrointestinal distress and hepatotoxicity [20]. Another study proved that the combination treatment of Lopinavir/ritonavir and routine adjuvant medicine against pneumonia could produce much better efficacy on patients with COVID-19 infection compared to treatment with adjuvant medicine alone [21].

The 7<sup>th</sup> edition of the novel coronavirus diagnosis and treatment plan published by the National Health Commission of the People's Republic of China, options for antiviral therapy include aerosolized  $\alpha$  interferon, Lopinavir/ritonavir, ribavirin in combination with Lopinavir/ritonavir, chloroquine phosphate, or Arbidol [22].

## CONCLUSION

Remdesivir and Lopinavir/Ritonavir are highly effective in the control of 2019-nCoV infection *in vitro* as *in vivo*. Since these compounds have been used in human patients with a safety track record, we suggest that they should be used in human patients suffering from the novel coronavirus disease.

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