

Opinion



# Uncertainty about the Efficacy of Remdesivir on COVID-19

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The coronavirus disease 2019 (COVID-19) pandemic is betraying what we hoped for and going into a boring and exhausting war. To break this everlasting vicious cycle, vaccines and special antiviral drugs must be developed.<sup>1</sup>

Agents to treat COVID-19 can be broadly classified into two categories. One is an agent that directly attacks the virus, and the other that interferes with the virus' life cycle. The ideal agent, of course, is to attack or kill the virus directly.

However, to date, a means that can directly attack viruses is disinfectants or antibodies, while none of the antiviral agents directly attacks the virus' body itself yet. Neutralizing antibody should be obtained by convalescent plasma from recovered patients and the amount of supply is limited. Monoclonal antibodies are still under clinical trial. Disinfectants cannot be used directly on humans. Antivirals used to date interfere with the life cycle of viruses, and are classified into three types.

First, there is an antiviral agent that prevents viruses from entering the host cell. Umifenovir is a good example.

Next, there is an antiviral that prevents the virus from activation. Protease inhibitors such as ritonavir-boosted lopinavir belong to this category.

And perhaps the most preferred antiviral agent is the drug that inhibits the viral replication.

Remdesivir is currently the most attracting attention as a drug that ultimately interferes with the activity of RNA-dependent RNA polymerase (RdRp) by inhibiting replication. The basic structure of remdesivir is the nucleoside (nucleotide). Since this structure serves as a nucleoside analogue, RNA chain elongation of corona virus cannot proceed any more. As a result, RdRp is inhibited by preventing replication of the virus.

Currently, indications for administering remdesivir in COVID-19 are mainly patients with severe lower respiratory disease. Although the formal standard for severe COVID-19 has not yet been established, it is generally agreed that high requirement for oxygen on room air or under the mechanical ventilation or extracorporeal membrane oxygenation.

Is the remdesivir a definitive treatment regimen for COVID-19?

Regrettably, the current assessment of remdesivir does not seem to be entirely positive.

The first full-scale clinical trial of remdesivir was conducted in China from February to March 2020, and the results were very disappointing. It did not significantly reduce COVID-19 disease duration and mortality. Moreover, a number of serious side effects occurred quite a bit, and the clinical trial had to be terminated early.<sup>2</sup>

On the other hand, a clinical trial conducted in the United States produced relatively favorable result.<sup>3</sup> In remdesivir group, time to recovery was shortened compared with that of the placebo group. However, the mortality was not significantly different between the two groups.

Taken together, the results suggest that remdesivir shortens the duration of the disease, but does not affect prognosis significantly.

Then, is the remdesivir less valuable as a COVID-19 treatment?

I cannot conclude that it is.

From a practical standpoint, COVID-19 pandemic is still not suppressed, so it is inevitable to try drugs that could work.

Several drugs have been suggested, but at this point remdesivir is worth trying as a solution.

Remdesivir is undergoing clinical trials in a few medical institutions in Korea, and recently received emergency approval by the Korean Ministry of Food and Drug Safety.

Unlike the precedent of oseltamivir used during the swine flu pandemic in 2009, however, remdesivir is not expected to have the effect of lowering the rate of propagation and reducing the incidence by administering to all patients in the early stage of COVID-19 pandemic.

It should not be forgotten that remdesivir was not originally designed to target COVID-19. It is an antiviral drug originally designed to treat hepatitis C, Ebola, and Marburg virus.

Since there is no specific targeting drug to use right now, it is only a repurposed drug used on the basis of the mechanism of action. Therefore, don't expect miracles about remdesivir's performance and lower expectations.

In a word, at least now remdesivir is not a magic panacea. Even if remdesivir has a strong effect, we will need to find a partner or partners with something synergistic. Eventually, a definite antiviral treatment strategy for COVID-19 should be an appropriate and effective combination regimen.

Until the regimen is established, optimism for remdesivir should be avoided for the time being.

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