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# Remdesivir to Treat COVID-19: Current Evidence

**Open Access** **Short Communication**

**Nijhawan R[1], Verma V[1], Gupta A, Mahajan k*[2]**

[1]DM Fellow, Department of cardiology, Indira Gandhi Government Medical College, Shimla, India
[2]Assistant Professor, Department of cardiology, Indira Gandhi Government Medical College, Shimla, India

***Address for Correspondence**

Kunal Mahajan, Assistant Professor, Department of Cardiology, Indira Gandhi Government Medical College, Shimla, India

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## Introduction

Since its inception in Wuhan, Hubei province, China in December 2019, coronavirus disease 2019 (COVID-19),a lethal disease caused by SARS-CoV-2 (Severe acute respiratory syndrome-Coronavirus-2) has caused havoc around the globe.1 So far as on 25th April 2020, it has infected more than 2.9 million people worldwide and has claimed more than 2,00,000 deaths worldwide. Despite desperate efforts by the researchers worldwide, no anti-viral drug or vaccine with proven efficacy against COVID-19 is yet available.1This has led the researchers to explore various investigational anti-viral drugs to combat this virus. The main rationale behind trying these investigational drugs is their proven/probable efficacy against either the other RNA viruses or the previous coronaviruses like SARS-CoV (Severe acute respiratory syndrome-Coronavirus), and MERS-CoV (Middle East respiratory syndrome-Coronavirus), which caused epidemics in 2002, and 2012 respectively *[1]*. One such drug is remdesivir (introduced by Gilead Sciences in 2017), which possesses broad-spectrum antiviral activity and has shown efficacy in nonclinical models against filoviruses (e.g., Ebola) and past coronaviruses *[2,3,4]*. Remdesivir is an adenosine nucleotide analog prodrug that gets metabolized to its active form GS-5734 inside the respiratory epithelial cells. The active compound inhibits the action of viral RNA-dependent RNA polymerase (RdRp) and incorporates into the growing viral RNA chains, resulting in premature termination of viral RNA replication4. Thus, with this mechanism, Remdesivir has the potential to reduce lung viral load and improve clinical signs of disease.

**Keywords:** Remdesivir; New drug; Coronavirus; COVID-19

As aforementioned, remdesivir has shown good in-vitro activity against Ebola and coronaviruses *[2,3]*. Phase 1 clinical trials done in patients infected with the Ebola virus have established the safety of intravenous infusions of remdesivir without any evidence of liver or kidney toxicity.5The first evidence of the effectiveness of remdesivir in COVID-19 came from in-vitro studies, which revealed promising results with potent blockage of virus infection at low-micromolar concentration and a high selectivity index *[6]*. In another study by Beck et al. *[7]*, Using a pre-trained deep learning-based drug-target interaction model called Molecule Transformer-Drug Target Interaction (MT-DTI), remdesivir showed a good inhibitory potency against the viral proteins of SARS-CoV-2 *[7]*. Remdesivir has an intracellular half-life of greater than 35 hours *[1]*. Importantly, remdesivir is yet to be approved by United States food and drug administration, and is reserved only for compassionate use or enrollment in a clinical trial. The current recommended dose of remdesivir is a single 200-mg loading dose, followed by 100-mg daily infusion.1 No hepatic or renaldose adjustments are required; however, the initiation is not recommended in patients with an estimated glomerular filtration rate less than 30 mL/min. The initial reports concerning compassionate use of remdesivir in severe COVID-19 patients have been promising (See details in Table 1); however, conclusions regarding remdesivir based on these initial reports might be premature. Nonetheless, if results are anything to go by, it is a great boon for COVID-19 patients, more so for critically ill patients. COVID-19 is a public health emergency, and we desperately need an effective treatment. With vaccine availability still far away, remdesivir is an excellent start in our fight against COVID-19. The need of the hour is adequately powered, and blinded placebo-controlled randomized trials of remdesivir with clinically valid and quantifiable endpoints. The world will be eagerly waiting for future results of such trials with remdesivir.

| S.no | Type of study and Author | Description | Result with Remdesivir | Caveats |
|---|---|---|---|---|
| 1 | Case Report by Michelle L. Holshue, et al.[8] | A 35-years-old male patient who was admitted on 4thday of coronavirus disease 2019 (COVID-19) illness, developed pneumonia and respiratory distress on 9thday of illness, which was progressively worsening. There was a drop in oxygen saturation to below 90% | 1. He was started on intravenous remdesivir (compassionate use) on 11th day of illness while supportive management continued and the patient's condition improved within next 1 day and supplemental oxygen was discontinued.<br>2. He subsequently maintained an oxygen saturation of 94-96% while breathing ambient air. Most of his symptoms recovered in a week's time. | 1.Interestingly the viral load of the patient had decreased before starting remdesivir injection. There is a high possibility that this immediate recovery after initiating remdesivir was because of self-defense mechanisms and other supportive treatment, instead of the drug.<br>2.The beneficial role of remdesivir in immediate recovery of the patient is difficult to ascertain with surety and needs further consideration and validation. |
| 2 | Case Report by Emily Hillaker, et al.[9] | A previously healthy 40 year-old male was admitted to the hospital three days after the onset of COVID-19 symptoms, including dry cough, fever, and shortness of breath progressing to intubation and mechanical ventilator support. | 1.Despite submitting an early request for compassionate use of remdesivir, it could be made available only on the 9th day of hospitalization.<br>2.Supportive measures, in addition to a 5-day course of hydroxychloroquine, were maintained until then.<br>3. But despite all measures, throughout this time, patient required aggressive mechanical ventilatory support.<br>4. However, within 60 hours after initiating remdesivir, the patient was successfully extubated and was maintaining saturation at room air within 24 hours of extubation. | 1. Viral load levels were not done.<br>2. Patient was already on an improving trend when remdesivir was initiated as his oxygen requirement was on a downward trend.<br>3. He was afebrile by the 9th and his sputum cultures were reported to be negative.<br>4. He had already taken 5-days course of hydroxychloroquine and azithromycin before remdesivir, which might have an impact on recovery. |

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| 3 | Observational study by J. Grein, et al.[10] | Remdesivir administered on a compassionate-use basis to 61 confirmed COVID-19 patients, who either had an oxygen saturation of 94% or less on ambient air or who were receiving oxygen support. | 1. Overall improvement in oxygen support class was recorded in 68% of patients.<br>2. Among 30 patients on mechanical ventilation, 17 (57%) were successfully extubated<br>3. Overall mortality was only 13%, which is noteworthy, and very less in comparison to other reports showing high mortality in severe COVID-19 patients.10,11<br>4. 23% of patients had serious adverse events (including multi-organ failure, septic shock, acute kidney injury, and hypotension). | 1. Small sized study.<br>2. Absence of a randomized control group.<br>3. In absence of control group, it is difficult to ascertain whether the serious adverse events that occurred in 23% of patients were because of remdesivir or as a result of COVID-19.<br>4. Lack of information about disease biomarkers and viral loads was noteworthy.<br>5. Heavy involvement of "Gilead Sciences", the company that manufactured remdesivir in selecting the patients for study and in preparation of manuscript. Both are potential sources of favourable bias towards the drug. |

**Table 1:** Clinical experience with remdesivir in patients with COVID-19.

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## Conflicts of Interest

The authors have no conflict of interest to declare.

## Author's Contribution

All the authors made substantial contributions to the conception/design of the work, acquisition, analysis, or interpretation of data, drafting the work or revising it critically for important intellectual content. All the authors have read and approved the final version of the manuscript and agreed to be accountable for all aspects of the work.

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