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THE PRACTICE OF REMDESIVIR FOR TREATING COVID-19 DURING PANDEMIC

K.M. Saravanan*
Department of Biotechnology, Bharath Institute of Higher Education and Research, Chennai - 600 073, India

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ABSTRACT

A RNA-dependent RNA polymerase (RdRP) inhibitor, Remdesivir, is estimated to be a current treatment for Coronavirus infectious Disease 2019 (COVID-19). The United States Food and Drug Administration (FDA) issued remdesivir an Emergency Use Authorization (EUA) to cure COVID-19 sufferers. This mini-review discusses some key clinical studies and their outcomes on administering remdesivir to treat COVID-19 in light of the COVID-19 pandemic. The studies reveal that remdesivir inhibits viral RdRP and is effective against many coronaviruses. However, the safety profiles of the drug have to be studied in detail and further, the published research and official documentation on remdesivir treatment provide evidence for clinical practices.

Corresponding Author:

Dr. K.M. Saravanan,
Bharath Institute of Higher Education & Research,
Chennai - 600 073, India.
Email:
saravananbioinform@bharathuniv.ac.in

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1. INTRODUCTION

Although various drugs have been explored, none have been authorized for COVID-19. While administering drugs that are not authorized, several precautions should be taken, including frequent monitoring of haematological parameters, serum electrolytes, blood glucose and renal and hepatic functions [1]. Remdesivir (an adenosine analogue of monophosphoramidate prodrug), a viral RdRP inhibitor active against other coronaviral infections, has been recognized as a prospective COVID-19 treatment option [2,3]. Remdesivir has been found in many clinical cohort reports to significantly decrease recovery duration in persons infected with Covid-19 and had indications of a respiratory tract infection [4] because there is currently no proof that Remdesivir progresses survival or other outcomes in hospitalized patients, the WHO has issued a conditional recommendation against taking it, regardless of disease severity [5].

Interestingly, Remdesivir's Phase III clinical trial for the treatment of COVID-19 began in early 2020 and has so far generated positive findings. Taiwan provisionally authorized the use of remdesivir in cases with severe COVID-19 in late May 2020 [6]. An influx of conditional licences followed in various nations and regions, including the European Union and Canada [7]. Before these conditional permissions, remdesivir had received extraordinary approval for emergency use in Japan and the United States, respectively (on 7 May 2020) [8]. Remdesivir has been used in several clinical studies to treat COVID-19 and suggested that the drug should be directed in a hospital providing comparable care to an inpatient hospital [9].

2. HISTORY OF REMDESIVIR DISCOVERY

Gilead Sciences manufactured Remdesivir (GS-5734), which was produced by the US Centers for Disease Control and Prevention (CDC) and the US Army Medical Research Institute of Infectious Diseases

(USAMRIID) (https://www.gilead.com). The beginning point of Remdesivir discovery started based on the previous understanding of effective antiviral chemicals targeting RNA viruses. A library of 1000 small molecular chemicals centred on nucleoside analogues was assembled [10]. Since nucleosides are weakly cell-permeable, modified nucleoside derivatives, including monophosphate, ester, and phosphoramidate prodrugs, make up a small molecular chemical library [11]. These prodrugs are typically very permeable and are converted into nucleosides or phosphorylated nucleosides inside of cells. Adenosine C-nucleoside "GS-441524" with a 1′-CN modification and its prodrug form of the monophosphate were both shown to be especially efficient (GS-5734, later renamed as remdesivir) [10]. Multiple groups examined antiviral efficacy in vitro and in vivo after demonstrating that remdesivir has wide activity against RNA viruses [12]. Eastman et al. discuss the discovery and development of remdesivir, which led to multiple emergency use permission, including the COVID-19 pandemic. Remdesivir should have a favourable safety profile in humans due to its low affinity for mitochondria [10]. Remdesivir 150 mg was administered numerous doses for 7 or 14 days, and reversible grades 1 and 2 alanine aminotransferase (ALT) and aspartate transaminase (AST) increases were seen. However, the medication has no harmful effects on reproduction or development [13].

3. COVID AND REMDESIVIR

Remdesivir has recently received much attention due to its potential for treating coronavirus infection that causes the severe acute respiratory syndrome. Remdesivir medicine is introduced into key nations worldwide through the Patent Cooperation Agreement (PCT) process during the pandemic. Remdesivir has been used under compassionate use because there are no viable therapeutic choices for COVID-19. The European Medicines Agency (EMA) gave remdesivir conditional authorization on 3 July 2020, making it the first antiviral medication licenced for COVID-19.

4. SOME IMPORTANT COHORT STUDIES

Remdesivir administration was not linked with survival in this cohort analysis of US veterans hospitalized with COVID-19. However, it was associated with longer hospitalization [14]. A systematic cohort study demonstrates that regular use of remdesivir is linked to increased hospital bed utilization but not improved patient survival. The biological consequences of remdesivir have been well studied [15]. Another notable study examined 312 remdesivir- and 818 non-remdesivir-cohorts [16]. Treatment with remdesivir was associated with significantly better recovery and a 62% lower risk of death compared to the current standard of care for patients with severe COVID-19. The Solidarity Trial of the WHO was the largest clinical trial to demonstrate the best potential COVID-19 treatments. Although their findings showed no statistically significant changes in mortality rates between the remdesivir and control groups, the FDA approved the antiviral medicine. According to FDA recommendations, adults and paediatric patients can receive this medicine in hospitals [17]. In another interesting trial, patients with moderate COVID-19 who were randomized to a 10-day course of remdesivir had no statistically significant difference in clinical state at 11 days after starting therapy compared to those who received conventional care. The difference in clinical status between patients who received a 5-day course of remdesivir and those who received conventional care was statistically significant, but the difference was of questionable clinical significance [17]. Another systematic trial suggests early remdesivir therapy, within a week of symptom onset, is linked to a lower need for mechanical ventilation and a lower 28-day mortality rate [18].

Researchers found no statistically significant mortality per month benefit with hydroxychloroquine or high-dose corticosteroids or in combination in a large observational study assessing the possible relevance of COVID-19 therapies in cancer patients; however, remdesivir showed promise. Discrepancies in access to medicines are often evident in treatment receipts which reflect clinical decision-making [19]. The medicine was well tolerated and safe in renal and hepatic toxicities in a multicenter cohort analysis of 51 COVID-19 kidney transplant recipients treated with remdesivir. Still, randomized trials are needed to establish its efficiency [20]. As with influenza A/H1N1, SARS, and MERS, pregnancy-related immunological changes could make pregnant women more vulnerable to severe COVID-19 (MERS). Evidence from a cohort study in the United States (US) reveals that severe COVID-19 during pregnancy (mostly in the third trimester) is linked to iatrogenic premature birth. Overall, the limited data suggest that remdesivir is well tolerated in the later phases of pregnancy (2nd/3rd trimesters), with minimal risk of significant side effects [21]. A 28-year-old woman in Japan was diagnosed with COVID-19 two days after delivery and treated with remdesivir. Remdesivir concentrations in maternal serum and human milk were investigated. Given the low concentration of Remdesivir in the participant's milk, the presence of antibodies to SARS-CoV-2 should protect the infant from infection, and a variety of other advantages of human milk, breastfeeding appears to be safe during Remdesivir treatment [22].

Researchers from Italy studied the safety and variations in heart beat rate in COVID-19 patients administered with Remdesivir. Despite a considerable drop in heartbeat rate after Remdesivir treatment, no severe cardiovascular toxicity was found in COVID-19 patients, even in cardiovascular comorbidities,

according to their findings [23]. An interesting study was undertaken to determine the clinical benefit of combining remdesivir with dexamethasone to treat COVID-19 patients who needed oxygen [24]. Including remdesivir with dexamethasone did not result in a shorter hospital stay or lower in-hospital mortality. Nonetheless, it appeared to reduce the combined outcome of death and critical care unit admission. Patients with COVID-19 treated with high-flow oxygen or noninvasive ventilation experienced a shorter recovery time and faster clinical improvement when baricitinib + remdesivir was added to their treatment regimen. Significant adverse effects were reduced when the two were used together [25]. PubMed, Embase, Cochrane, CNKI, and Wanfang were scoured for case study data on COVID-clinical TB characteristics [26]. Clinical characteristics and differences between living and dying COVID-TB patients were analyzed, and case reports and case series were analyzed. The most commonly prescribed medications included lopivir/ritonavir (11.48%), umifenovir hydrochloride (9.84%), tenofovir (6.56%), remdesivir (1.64%), and lamivudine (1.64%). There was little difference in care given to those who did and did not survive.

5. CONCLUSION

The first coronavirus treatment advised in 2019 is remdesivir. It is a novel nucleoside analogue with broad antiviral activity against respiratory infections caused by MERS-CoV, SARS-CoV, and SARS-CoV-2, as well as RNA viruses like ebolavirus (EBOV). The medication was created using a library of small antiviral compounds that target newly emerging pathogenic RNA viruses. According to the majority of clinical case studies that have been published, remdesivir may reduce mortality rates in hospitalized patients who need supplemental oxygen while maintaining a high safety level. Although the approval of this treatment represents a significant advancement in the fight against COVID-19, it will not be sufficient to address the problems with public health caused by the virus. Many therapeutic strategies have been offered, and over 25 vaccines are in various stages of research; nonetheless, infection peaks oscillate regularly, raising concerns about the efficiency of prophylactic efforts and the disease's permanence. This paper examines the most current findings from published case studies in the treatment and potential mitigation of one of the century's most dangerous pandemics.

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COMPETING INTEREST

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