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Pharmacology of Remdesivir – Short Review

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Abstract

Remdesivir is a broad-spectrum antiviral medication which appears to inhibit SARS-CoV-2, in vivo and in vitro. Remdesivir is a RNA polymerase inhibitor. Our goal was to systematically research the literature to understand the pharmacology, clinical effects and outcome of remdesivir in patients with COVID-19.

Keywords

Remdesivir, COVID-19, SARS -CO-V-2, Chronic kidney disease, Corticosteroid etc

Introduction

Remdesivir appears to be a mixed result in persistent COVID-19 with a prominent side effect. COVID-19-related mortality is elevated among persistent patients with co-existing diseases, including hypertension, diabetes and cardiovascular disease.[1] Approximately 50 million patients worldwide have been affected by COVID-19, with an estimated 1. 2 million patients being affected by the virus [2]. Older population with obesity, hypertension, diabetes and chronic kidney diseases has lower chances of recovery when infected [3]. Corticosteroid therapy is the only drug that can effectively treat COVID-19, but no other drug has shown the same efficacy and safety profile. [4-5] Remdesivir inhibits RNA polymerase limiting viral replication. [6,7] Originally developed for Ebola treatment, Remdesivir has also been used to treat coronavirus in-vitro and has been used to treat pulmonary damage in monkeys infected with COVID-19 [6,8] Remdesivir approved on October22, 2020[9]. We evaluate the safety and efficacy of remdesivir in humans for the treatment of COVID-19. Adenosine analogue Remdesivir (GS-5734) exhibits broad-spectrum antiviral activity against a number of viruses, including the Middle East respiratory syndrome virus (MERS-CoV), Nipah virus, Ebola virus (EBOV), and respiratory syncytial virus. [10,11,12] The nucleoside triphosphate GS-443902 works as an analogue of adenosine triphosphate (ATP) and competes with the natural substrate of ATP to selectively inhibit viral RNA-dependent polymerase (RdRp). The primary mechanism of inhibition is the inclusion of the nucleoside triphosphate GS-443902 into nascent RNA chains by viral RdRp, resulting in delayed termination of RNA chains during viral replication.[13] REMDESIVIR is a prodrug and inhibits viral RNA polymerase, when intracellularly metabolized to an ATP analogue. In vivo efficacy against EBOV in non-human primates led to its inclusion in clinical studies for the treatment of acute Ebola virus disease (EVD). It should be noted however, that the efficacy in-vitro or in animal studies does not inevitably predict outcomes in humans. [14] Regarding coronviruses, remdesivir has been shown to inhibit all animal and human coronaviruses in vitro, including MERS-CoV and SARS-CoV-1. [12,15,16]. Remdesivir was found to be superior to combined interferon beta plus lopinavir-ritonavir regime in the urine model of MERS-CoV infection [17]. Administration of remdesivir showed a significant reduction in viral load in bronchoalveolar lavage compared to the vehicle and also decreased the pulmonary infiltrates in SARS-CoV-2 infection of rhesus macaque model. Thus, it demonstrated both antiviral as well as the clinical effects [18]. In the absence of an effective treatment, Remdesivir has been shown to be effective in inhibiting the replication of the virus in human nasal epithelial cells (HNECs) and in human bronchial epithelial cells (BECs). These results supported the use of Remdesivir in patients with COVID-19 SARS infection.[19]

Safety of Remdesivir in COVID-19 studies:

Renal Safety:

Healthy individuals had no signs of Nephrotoxic No dose changes are currently recommended in patients with mild to moderate renal impairment; however, they are contraindicated in patients with severe renal impairment. [20]

Hepatic Safet

Remdesivir was associated with moderate to severe renal and liver dysfunction. Since remdesivir undergoes rapid hydrolase cleavage, the impact of liver failure on remdesivir plasma levels is minimal. [20]

Pregnancy,Lactation and pediatric population

SARS-CoV-2 can affect a woman's pregnancy in many ways. SARS-CoV-2 infection can result in an increase in preterm delivery rates, which can lead to the need for intensive care associated with severe disease. Shortly it is called mortibirth. This leads to a higher likelihood of pre-eclampsia associated with SARS-CoV-2 infection during pregnancy. Although not common, SARS-CoV-2 can also transfer infection to the fetus. SARS-CoV-2 in pregnancy can lead to direct and indirect infection. [21]

Drug Interaction

Remdesivir has already shown that sub-micromolar concentration can effectively inhibit human and Zoonotic CoV in tissue culture experiments.[22] The effect of the inhibitor/inducer on the IV pharmacokinetics of remdesivir will be significantly reduced due to the high to moderate extraction ratio (0.6 to 0.8). [23,24] The risk of drug interaction increases when multiple drugs are taken together, but COVID-19 is expected to have a more complex disease-drug-drug interaction. Infection with SARS-CoV-2 showed a growing frequency of hospitalization and hospitalization in an intensive care unit (ICU).[25] In the novel coronavirus disease (COVID-19) disease, the inflammatory response plays an important role in disease-drug or drug-drug interactions. Changes in transporters and DMEs can lead to changes in the pharmacokinetic parameters of the drugs used. Therefore, inflammation may play an important role in drug efficacy and toxicity.[26]

Adverse effect:

Decreased glomerular filtration rate.
Decrease hemoglobin level.
Decreased lymphocyte count.
Respiratory failure.
Anemia.
Pyrexia.
Hyperglycemia.
Increased blood creatinine level.
Increased blood glucose level.
Constipation.
Elevated alanine aminotraferase level. [27]

Dose of Remdesivir:

The dose of Remdesivir is 200 mg IV loading dose on day 1 and 100 mg daily IV maintenance doses for 5-9 days.[28]

Discussion:

Remdesivir is an antiviral drug that exhibits significant inhibitory activity against SARS-CoV-2 in vitro and in vivo studies and is being repurposed for other treatments for COVID-19 It seems to be ahead of drugs. Animal studies clearly show that early administration of remdesivir is more effective than other acute viral diseases. From this perspective, treatment patients with pre-existing respiratory failure may not be the best candidates for remdesivir. Special consideration should be given to the disproportionate increase or decrease in ALT or GFR during remdesivir treatment. Currently, in primary care, concomitant use of remdesivir and a vasopressor is contraindicated in patients with end organ failure. Once a patient starts remdesivir treatment, vasopressers are not a reason to stop treatment. Vasopressors at low/medium dose for inotrope support are allowed, as long as sedation and/or paralytics are administered while ventilators are in use. Remdesivir does have some adverse reactions, but it is a life-saving drug during COVID

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