Remdesivir- A Potential drug for COVID-19

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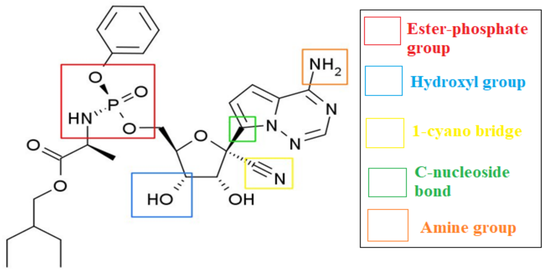
Introduction

Remdesivir (GS-5734) is a nucleotide analog, specifically an adenosine analog, evidenced to have broad-spectrum activity against the single-stranded RNA viruses. In 2009, Gilead Sciences developed the antiviral drug Remdesivir for treatment for Hepatitis C and then in 2014 used for treating Ebola but in both cases it was found to be ineffective.

Remdesivir and its SAR

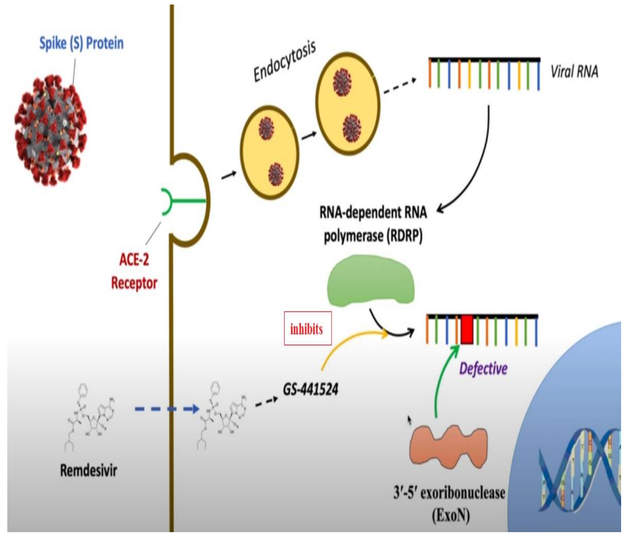
Remdesivir is basically an altered version of the natural building block adenosine – which is essential for DNA and RNA.



Each of the color coded boxes are vital chemical molecules that are important for its activity.

Mechanism of action alone of its and against COVID-19

Mechanism against Ebola Virus was known by inhibiting RdRp.
COVID-19 is an RNA virus. When the novel coronavirus SARS-CoV2 enters a human cell, an enzyme called RdRP helps the virus replicate. Remdesivir is a prodrug that undergoes metabolic conversion to active nucleoside triphosphate metabolite which then works by inhibiting the viral enzyme RNA-dependent RNA polymerase.



New hope for COVID-19

Remdesivir resembles an RNA subunits, incorporation of this drug into the viral RNA halts replication.
COVID-19 susceptibility to antiviral Remdesivir (GS-5734) is mediated by the viral polymerase and the proofreading exoribonuclease. It has reported to have high potent EC50 values for comparable viruses (MERS and SARS) of approximately 0.07μm. Hence it is being used against coronavirus and some patients have recovered during clinical trials in US.

Clinical trials

Trials conducted in US of more than 1000 patients evaluated 5 day and 10 day dosing durations of the drug in coronavirus patients. Nearly 50% of patients in the 5 days treatment showed clinical improvement in 10 days, whereas in 10 days treatment group showed improvement in 11days.

Ref: Clinical trial of Gilead sciences drug Remdesivir in COVID-19 treatment shows positive results Apr 30, 2020

Lancet China study done on more than 200 patients mentioned that the drug remdesivir did not result in significant reductions of SARS-COV-2 RNA loads.

What does FDA says?

Remdesivir is not FDA approved. On May 1 2020, the FDA granted emergency use authorization of remdesivir for its use in patients in critical state. The decision was made from a trial that showed the drug improved time to recovery compared with those placebo.

Ref: Emergency Use Authorization of remdesivir by the US Food and Drug Administration May 6, 2020

Dosage regime

It is administered intravenously by injection. An initial one-time dose of 200mg. Followed by 100mg per day for 10 days. A treatment course of 10 days is recommended for adults and pediatric patients requiring invasive mechanical ventilation or ECMO and 5 days for patients not requiring invasive mechanical ventilation or ECMO.

Side effects

Increased liver transaminases may indicate possible liver damage.

Facts for COVID-19 treatment in India

Currently it is not available in India. Glenmark, Cipla and Dr Reddy's are working on developing Remdesivir.