

Combination of anti-asthmatics with remdesivir may reduce the necessity for the usage of ventilators in severe COVID-19 cases including the elderly.

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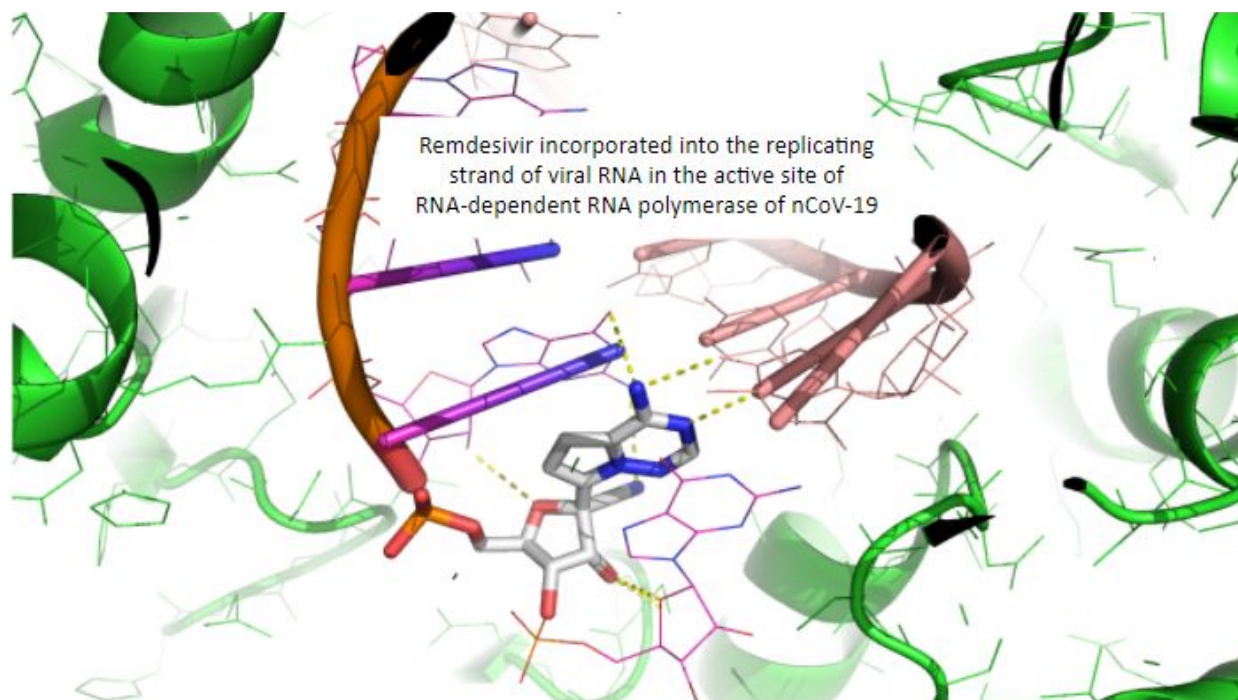


Figure 1. Structure of remdesivir (white color) incorporated into the replicating strand of nCoV-19 RNA in the active site of the viral RNA-dependent RNA polymerase (green color) halting the viral replication. PDB ID: 7C2K.

Coronavirus disease-2019 (COVID-19) is a pandemic. The novel coronavirus - 2019 (nCoV-19) is the causative virus that primarily spreads through aerosolized droplets from an infected person's sneeze, cough or even talking in the public without wearing a facial mask (1)! Healthy humans within the range of these aerosols are highly prone to the viral exposure. Nasal cavity, throat and airway passages are the primary areas where the nCoV-19 can be easily detected using a simple swab (2). The virus specifically targets the lung epithelial cells

containing ACE2 receptor owing to which, the immune system responds sometimes with severe cytokine storms (3, 4). In such cases, the alveoli and airway passages are filled up with fluid rich in proteases and other proteins such as mucin including reactive oxygen species (5). Usually it takes time for this fluid to clear from the airway passages due to which the patient suffers severe breathing problems (5). Another side effect is inflammation which constricts the airway passages thus adding to the breathing problems. In some cases, ventilators must be employed to ease the breathing for patients.

However, ventilator usage could be limited in supply (6) at the hospitals thus causing fatalities. Bronchodilators in combination with the anti-inflammatory drugs may help ease the respiratory issues. Fluid clearance from the alveoli and airway passages may take time but meanwhile if one can relax the airway passages by using anti-asthmatics in combination with anti-inflammatory drugs, then the necessity for using ventilators can possibly be decreased. Although this may not only help the healthcare providers to overcome the limited supply of ventilators but also, can prevent any potential fatalities associated with breathlessness.

Additionally, if this combination therapy is used along with the antiviral agents like remdesivir, a possible synergy can be expected. Remdesivir (7) is a nucleotide prodrug that intervenes directly with viral replication. As shown in Figure 1, it gets incorporated into the newly synthesized strand of viral RNA in the active site of the viral RNA-dependent RNA polymerase (RdRp). By incorporating remdesivir into the viral RNA, the

replication process comes to a halt due to certain structural changes that cause unfavorable RNA synthesis reaction in the active site of RdRp (8). Thus, the combination of remdesivir with anti-asthmatics (bronchodilators) and/or anti-inflammatory drugs may help ease the symptoms of breathlessness that could potentially avoid fatalities especially owing to the limited supply of ventilators at hospitals in developing countries and villages. However, this administration of various combinations must be performed by or under the supervision of a qualified medical professional. Any adverse effects caused due to drug-drug interactions in the liver may possibly result in liver damage and ultimately death. Further research is needed to test this hypothesis not only on large cohorts but also on different age groups because the elderly population are most likely not able to clear the fluid from alveoli and airway passages as effectively as younger people. Smoking makes this worse!

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