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COVID-19 Treatment: The Race Against Time

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ABSTRACT

The new outbreak of the novel coronavirus infection emerged in Wuhan- China in late 2019, by the end of Mar 2020, it has spread in more than 178 countries and territories. There is no vaccine or antiviral treatment for COVID-19. Currently, there are several drugs and vaccines being tested for their potential activity against the disease. In this review, we briefly discuss some of the investigational drugs and vaccines being tested against COVID-19 as well as their potential drawbacks.

Keywords: COVID-19, treatment, clinical trials, Chloroquine, Lopinavir-ritonavir, Remdesivir, Tocilizumab, Camostat mesilate

INTRODUCTION

The world is carrying two concurrent wars against the newly emerged coronavirus disease (COVID-19), which was first reported in the Chinese city of Wuhan late last year. On the one hand, the world is trying to slow down or stop the spread of the disease, and on the other hand, desperately trying to find effective treatments. There is an increasing number of clinical trials for testing potential treatment or vaccine for COVID-19. Currently, there are 60 active and recruiting clinical trials (as of 31st of Mar 2020; refer to ClinicalTrials.org). The majority of the trials aim to repurpose commonly used medications including, antimalaria, anti-influenza, and anti-HIV combinations as well as other commonly available drugs. In this review we briefly discuss some of the investigational compounds that showed promising results based on their compassionate use and are currently in clinical trials as potential antivirals against COVID-19.

Chloroquine / Hydroxychloroquine

Chloroquine/hydroxychloroquine is one of the most promising compounds that has gained international attention for its potential activity against COVID-19 (1). Despite the lack of conclusive evidence of their effectiveness against COVID-19, the FDA issued an emergency authorisation for their use against COVID-19. While the drug was shown to inhibit the virus in vitro, the required dose in human is thought to be quite high and could lead to severe toxicity. Also, the use of hydroxychloroquine is associated with various side effects and could, although rarely, cause cardiomyopathy, that can only be reversed by immediate discontinuation, thus reduces its potential usefulness in some patients (2).

Lopinavir-Ritonavir

Lopinavir-ritonavir is a combination of fixed doses of protease inhibitors used for the treatment of HIV (3). The use of this combination was shown to have potent antiviral activity against the severe acute respiratory syndrome (SARS) virus (4). The treatment was also shown to be effective as a post exposure prophylaxis against other viral diseases including middle east respiratory syndrome (MERS) (5). However, the results of a recent trail of the combination (lopinavir-ritonavir) in 199 adults with laboratory confirmed COVID-19 reported no benefits observed with the combination compared to standard care (5).

Remdesivir

Remdesivir is a monophosphoramidate prodrug of an adenosine analogue (6). It is an investigational broad-spectrum antiviral drug with in vitro activity against multiple RNA viruses, including Ebola and CoV (7). Results from animal testing reported promising results in inhibiting other coronavirus infections including severe acute respiratory syndrome (SARS) and middle east respiratory syndrome (MERS) (8). Despite the lack of solid clinical trials, the drug was administered to several patients with COVID-19 infections (9). Currently, there are several ongoing clinical trials to investigate the potential antiviral efficacy remdesivir against COVID-19 in China and the US (10). However, the drug failed its previous attempt in prolonging Ebola patients in the recent African outbreak of Ebola virus (11).

Tocilizumab

Tocilizumab is a humanized antibody of the IgG1 subclass that inhibits the inflammatory cytokine, interlukine-6 (IL-6) receptor, leading to an immunosuppression (12). The drug is approved for the treatment of mild to severe adult rheumatoid

arthritis, giant cell arteritis, and juvenile idiopathic arthritis (13). The drug is being tested in patients with potential risk of cytokine storm driven hyperinflammation (also known as cytokine release syndrome) a systemic inflammatory response that can be trigged by infections including COVID-19 (14). Recent findings from China suggested that COVID-19 mortality might be due to virally driven hyperinflammation. Although, immunosuppressants are not recommended in viral infections and their use may exacerbate COVID-19, in the case of cytokine storm, the drug is likely to be beneficial (15). Currently, the drug has been approved in China for COVID-19 patients with pneumonia and elevated IL-6 (16). Therefore, it is recommended that severe COVID-19 patients should be screened for potential hyperinflammation and to identify those patients that may benefit from the use of such medications.

Camostat Mesilate

Camostat mesilate is a protease inhibitor that is approved for the treatment of pancreatic inflammation in Japan (17). COVID-19 entry into the cell depends on binding of the viral spike proteins (S) to cellular receptors, angiotensin converting enzyme 2 (ACE2) and on S protein priming by host proteases (TMPRSS2) (18). Camostat mesilate has recently been shown to block COVID-19 entry into the cell by inhibiting the cellular host TMPRSS2 (19). While this explains the potential mechanism of viral entry, however, more testing is required before it can possible be labelled as an effective therapy for the treatment of COVI-19.

There are no effective treatment or vaccine for the newly emerged COVID-19 virus. Hence, there is an urgent need for safe and effective treatment for this devastating virus. While most of these drugs are presently used for other viral infections, and some were shown to be effective in a small number of patients with COVID-19 (based on the results of small trials and compassionate use), we believe it is still premature to assume the efficacy of any of these drugs against COVID-19. The current brief review summarises some of the potential therapeutics currently being investigated in human trials. It will serve as a basis for future antiviral research for the treatment of COVID-19 as well as other related viruses.

LIMITATIONS

The current manuscript is a brief review of the therapeutics being tested in clinical trials based on the details provided by ClinicalTrials.org. Therefore, it cannot be viewed as a comprehensive review of the literature for these drugs. Also, the drugs discussed in the manuscript still under investigation, and thus the manuscript should not be used as a basis for therapeutic uses for the treatment of COVID-19.

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