

# Covid 19 medicines: Drugs which entered clinical trial

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## Abstract.

Coronavirus disease 2019(COVID 19) is an illness caused by novel corona virus which is now known as SARS-CoV-2. This disease has become a global pandemic as a large population worldwide is suffering from it. Due to this reason, researchers have conducted clinical trials for some potential drugs like hydroxychloroquine, favipiravir, remdesivir, lopinavir-ritonavir, Dexamethasone and Tocilizumab. Hydroxychloroquine which was previously used to treat rheumatoid arthritis, when taken in combination with azithromycin has shown to prevent SARS-CoV-2 in some cases. Faviravir which was previously used to treat influenza and ebola virus has shown promising results. Remdesivir is a broad spectrum antiviral drug has also emerged as a potential drug but further information is required to verify its effects. Lopinavir-ritonavir is an anti-HIV drug. Both of them are protease inhibitor, as a result this drug is

beneficial for treating COVID 19. Dexamethasone is a corticosteroid drug previously used to treat rheumatic conditions, has shown to prevent SARS-CoV2. Tocilizumab is a immunosuppressant drug which blocks IL6 and used to prevent COVID 19. Itolizumab was previously used for treating psoriasis, has showed positive results in treating SARS-CoV-2. This article shows a comparative study of the different drugs which has entered the clinical trials.

## Keywords:

Covid19, Corona virus, SARS-CoV-2 , Drugs , Pandemic , Remedy.

## 1. Introduction:

The entire world is facing severe predicament due to Corona Virus Disease 2019 (COVID-19). Coronavirus or COVID-19 is an infectious disease which is

considered globally pandemic and many countries, humans are suffering due to this. Most of the people suffering with this will experience mild or moderate symptoms (asymptomatic in many cases) and in many cases patients are having cough and throat discomfort. Coronavirus disease 2019 (COVID-19) is defined as illness caused by novel corona virus now called as severe acute respiratory syndrome coronavirus 2 (SARS CoV-2). It was first located amid an outbreak of respiratory issue in Wuhan City, Hubei Province, China. It was initially reported to the WHO on December 31, 2019. On January 30, 2020 the World health organization (WHO) declared that COVID - 19 is a globally pandemic issue and an emergency situation for people.

Corona viruses cause a large variety of diseases in mammals, including livestock, domesticated animals like dogs, cats, etc., as well as primates including human. Human coronaviruses are commonly associated with mild respiratory and enteric diseases, although they are also known to cause more critical lower respiratory tract illnesses [1]. Infection with these highly pathogenic coronaviruses can result in Acute Respiratory Distress Syndrome (ARDS), which may lead to long-term reduction in lung function, arrhythmia, and even death.

Although the mortality rate is minuscule compared to other pathogenic threats, the viral disease is life threatening predominantly in ageing individuals and people with a weak immune system. Compared to MERS or SARS, SARS-CoV-2 appears to spread more efficiently, making it difficult to contain and therefore withholds an increasing pandemic potential.

There has been a number of coronavirus outbreaks noted till date, such as the severe acute respiratory syndrome coronavirus (SARS-CoV) epidemic that occurred in 2003 with 8,000 cases worldwide and a death rate of ~10%, which cost the global economy with an estimated \$30 to \$100 billion [2]; MERS-CoV in 2012, which caused 2,500 confirmed cases and a fatality rate of 36%, with a total of 2494 diagnosed cases causing 858 deaths, the majority in Saudi Arabia [3]. In December 2019, the third pathogenic HCoV, named 2019 novel coronavirus (2019-nCoV/SARS-CoV2) shuddered the whole world. It is very much important to promote an idea which can pave a way to discover the vaccine to cure the affected patients and moreover to save our Mankind. Researchers are working to find a remedy to these pandemic. Studies and numerous clinical trials are conducted

whose results provided some potential drugs for SARS-CoV-2.

## **2. Potential drugs for the treatment of Covid 19**

### **2.1 Role of hydroxychloroquine in Covid 19 treatment**

Hydroxychloroquine has shown mixed results in clinical trials for treatment of SARS-CoV-2 in combination with azithromycin. In some clinical trials hydroxychloroquine was found to be safe with mild adverse conditions like nausea, vomiting and abnormal liver functioning, whereas in some other clinical trials the result showed severe adverse conditions like first degree atrioventricular blockage, blurred vision and even death. HCQ was also used as a prophylactic drug by healthcare workers and specific high risk populations [4]. HCQ has been previously used to treat auto immune diseases like rheumatoid arthritis and lupus as well as for treatment of malaria [5]. At molecular level, HCQ affects the activity of lysosomes by increasing their pH and disrupting the lysosomal membrane stability. HCQ inhibits the viral particle glycosylation of the Spike protein(S) and Membrane proteins (M) thus preventing viral infection. It also reduces production of cytokine and TLR signaling

pathways thus suppressing our immune system [6]. But due to severe side effects, WHO announced to stop use of HCQ in the Solidarity Trial.

### **2.2 Role of favipiravir in Covid 19 treatment**

Favipiravir is a drug which consists of favipiravir triphosphate which is a purine nucleoside analogue that acts as a competitive inhibitor of RNA Dependent RNA Polymerase. It was previously used to treat Influenza and Ebola virus. It has shown promising results for short term treatment for SARS-CoV-2. But as FPV is associated with hyperuricemia and QT prolongation, further evidence is required for long term effects of the treatment [7].

### **2.3 Role of remdesivir in Covid 19 treatment**

Remdesivir is a broad spectrum antiviral drug used to treat SARS-CoV-2. It was previously used for treatment of Middle East Respiratory syndrome (MERS), Severe Acute Respiratory Syndrome 1(SARS-CoV-1) and Ebola virus. It inhibits RNA Dependent RNA polymerase thus inhibiting viral RNA synthesis. It emerged as a promising drug for its in-vitro activity against SARS-CoV-2 till now, but further

information is required to verify its effects [8].

#### **2.4 Role of Lopinavir–ritonavirin Covid 19 treatment.**

This drug is sold under the brand name Kaletra among others, is a fixed dose combination medication for the treatment and prevention of HIV/AIDS. It is actually a combination of lopinavir with a lower dose of ritonavir. Treatment with lopinavir–ritonavir was not very different from standard care. After the administration mortality at 28 days was found similar in the lopinavir–ritonavir group with the standard-care group. The percentages of patients with detectable viral RNA at various point of time were similar in both cases. In hospitalized adult patients with severe Covid-19, no benefit was observed with lopinavir–ritonavir treatment beyond merely standard care. Future trials in patients with severe illness helped to exclude the possibility of a treatment with this drug [9].

#### **2.5 Role of dexamethasonein Covid 19 treatment**

Dexamethasone is a steroid drug sometimes used for asthma, cancer, and rheumatoid arthritis came to the spotlight because it could reduce deaths in hospitalized coronavirus patients with severe

complications by about a third, according to a new study .According to the UK RECOVERY trial low-dose of dexamethasone (6 mg PO or IV daily for 10 days) reduced deaths by 35% in ventilated patients and by 20% in other patients receiving oxygen only in comparison to patients who received standard of care. No such benefit was seen in patients who did not require respiratory intervention [10].

Corticosteroids are not usually prescribed for treatment of COVID-19 or any viral pneumonia. It is more likely to produce cardiogenic shock from increased work of the heart need to distribute oxygenated blood supply and thoracic pressure from ventilation. Dexamethasone is generally safe. It presents a favourable benefit-risk profile, particularly in patients with severe forms of pneumonia, while the benefit is less prominent in patients with non-severe forms of pneumonia. As the treatment is short, even at high doses, corticosteroids are not associated with serious side effects. Potentially higher blood glucose levels (hyperglycaemia) are temporary. Prolonged use (i.e., used for more than two weeks) may be associated with adverse effects such as glaucoma, cataract, fluid retention, hypertension, psychological effects (e.g., mood swings, memory issues, confusion or

irritation), weight gain, or increased risk of infections and osteoporosis. All these adverse effects are not associated with short term use (with the exception of hyperglycaemia that can worsen diabetes) and it is unsafe for pregnant women [10].

## **2.6 Role of tocilizumabin Covid 19 treatment**

Tocilizumab also known as Atlizumab is an immunosuppressive drug. About 25% of COVID 19 patients experienced severe complications including acute respiratory distress syndrome (ARDS), and even progressed into an intensive care unit (ICU) admission and died. The exploration for the mortality causes and advancing novel therapeutic development of severe COVID-19 was crucial at the moment. The biopsy samples analysis at autopsy suggested that increased alveolar exudate caused by aberrant host immune response and inflammatory cytokine storm probably impedes alveolar gas exchange and contributes to the high mortality of severe COVID-19 patients. The researches have identified that pathogenic T cells and inflammatory monocytes incite inflammatory storm with large amount of interleukin 6, therefore monoclonal antibody that targets the IL-6 pathways may

potentially curb inflammatory storm. Moreover, Tocilizumab treatment that blocks IL-6 receptors showed inspiring clinical results like quick return of normal temperature and improved respiratory function. Hence Tocilizumab is suggested as an effective treatment in severe patients of COVID-19 to calm the inflammatory storm and reduce mortality. But it is suggested that these drugs be used indiscriminately since these drugs cause more harm than good [11][12].

## **2.7 Role of itolizumab in Covid 19 treatment.**

Itolizumab sold under the trade name Alzumab can be used for preliminary treatment of Covid 19 is a 'first in class' humanized IgG1 monoclonal antibody developed by Biocon and the Center of Molecular Immunology (CIM), Havana. It selectively targets CD6, a pan T cell marker involved in co-stimulation, adhesion and maturation of T cells. Itolizumab, by binding to CD6, down regulates T cell activation, causes reduction in synthesis of pro-inflammatory cytokines and possibly plays an important role by reducing T cell infiltration at sites of inflammation. According to some studies this drug helps

inemergency treatment of acute respiratory distress syndrome (ARDS) in patients with coronavirus disease 2019 (COVID-19). Biocon said in a statement that Itolizumab (Alzumab), long used for treatment of acute psoriasis, was approved in injectable form, 25 mg/5 mL, for use in India for the treatment of cytokine release syndrome in patients with moderate-to-severe ARDS. The repurposed drug was originally launched in India in 2013 for treating chronic plaque psoriasis. Itolizumab has proven to be an efficacious intervention in treating the serious hyper-immune response seen with COVID-19, the results came from a randomized controlled study of Itolizumab that was focused on safety and efficacy in preventing CRS in patients with ARDS due to COVID-19. It is the world's first anti-CD6 novel biologic therapy to be approved for treating patients with moderate-to-severe COVID-19, as stated by Biocon. COVID-19 has been observed to stimulate a strong immune response leading to CRS, which is a "storm" of cytokines that can damage the lungs and other organs. In worst-case scenarios, the outcomes can be multiple organ failure and death. In the trial, all patients treated with itolizumab responded positively and recovered.

## **Conclusion**

Several studies show severity of symptoms in Covid 19 can be categorised into mild, moderate, severe. In moderate and severe cases, availability of adequate oxygen support, appropriate and timely administration of anti-coagulants and widely available and inexpensive corticosteroids in accordance with the protocol can be considered as the backbone of COVID-19 therapy, the ministry stated. For mild cases, which are nearly 80 percent of the total cases, Hydroxychloroquine (HCQ) has been recommended. The standard of care treatment strategies have shown to yield positive results, its added. Hence after intensive studies we may conclude that among these drugs the most potent one is the broad spectrum antiviral medication Remdesivir, Favipiravir is considered effective too rest are mildly effective or ineffective for serious Covid 19 treatment. Our World is now counting every hour to get the specialized drug or vaccine to fight against the pandemic situation. Till the time we are able to have a particular targeted drug against COVID 19 we have to rely on the available drugs and use different combinations of those drugs to treat the affected individuals depending on the severity and manifestation of infection.

Hence this review article will provide us a wholesome understanding of the different drugs which doctors are using to treat COVID 19 infected patients worldwide.

### **Acknowledgment**

The authors sincerely acknowledge University of Engineering and Management, Kolkata.

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