

# COVID-19: Review of the Proposed Pharmacological Treatments 2

Dr. Aviv Ouanounou

Dental Pharmacologist and corresponding author of *COVID-19: A Review of the Proposed Pharmacological Treatments*

Co-authors: Sarah Lam  
Andrew Lombardi

## INTRODUCTION

- Coronavirus belongs to a large family of viruses called the coronaviridae.
- Several coronaviridae viruses circulate within the human population and commonly target the upper respiratory system, usually resulting in a mild infection such as the common cold.
- Others, such as SARS-CoV-2, can cause more severe illness which may result in death.
- Understanding the mechanism of transmissibility and pathogenesis of SARS-CoV-2 will allow researchers to identify specific therapeutic agents to prevent or treat COVID-19.

## THE MECHANISM OF COVID-19 SYNDROME

- SARS-CoV-2 is a single strand RNA envelope virus which depends on its structural spike to bind with and enter the host cell.
- This binding is dependent on enzymes that help the virus enter the cell.
- Once inside the cell, the virus hijacks the host machinery to undergo viral replication.
- Viral infection of the body can then bring about what is known as a Cytokine Storm - a host immune response characterized by high concentrations of pro-inflammatory cytokines. This creates an excess of inflammation that contributes to the severity and pathogenesis of COVID-19.

## POTENTIAL THERAPIES

- Currently there is no vaccine or specific therapeutic drug to treat COVID-19, other than supportive treatment.
- However, existing drugs used to combat other viral infections are being repurposed in an attempt to find an effective therapy.
- Many clinical trials are ongoing to check the efficacy of these drugs.
- There are 3 main categories of drugs:
  - Antiviral Drugs – drugs that target the mechanism of the virus itself
  - Immunomodulators – agents that alter and suppress the immune system response
  - Other agents, such as cortical steroids

## ANTIVIRAL DRUGS

- Remdesivir – a broad spectrum antiviral drug developed five or six years ago at the time of the Ebola outbreak. Causes inhibition of RNA polymerase, an important enzyme in viral replication. Research results are conflicting. Despite this, the US FDA have approved Remdesivir as an emergency therapy for hospitalized patients.
- Ribavirin – an RNA polymerase inhibitor. Studies are conflicting. There is a suggestion that combining Ribavirin with Interferon may be beneficial.
- Kaletra – a combination antiviral containing lopinavir and Ritonavir that is used to manage HIV positive patients. Lopinavir inhibits HIV proteases, an enzyme required for viral assembly. Due to its poor bioavailability and extensive biotransformation, it is administered with ritonavir. In a randomized control trial in January, no benefit was observed in COVID-19 patients receiving this combination therapy vs standard care. However, other studies are showing some improvement in symptoms when taking this combination with Interferon.
- Favipiravir – an RNA polymerase inhibitor developed in Japan six or seven years ago. Approved in some countries for the treatment of Ebola, Influenza and Norovirus. Preliminary clinical results show significant improvement in chest imaging in COVID-19 patients compared with the lopinavir/Ritonavir combination. Studies also show a reduction in respiratory symptoms, faster viral clearance and fewer adverse events. Not very effective in critically ill COVID-19 patients.
- Chloroquine and Hydroxychloroquine – indicated for treatment of inflammatory disease such as rheumatoid arthritis, lupus, and in the treatment of malaria. Despite positive claims of the effectiveness of chloroquine and

hydroxychloroquine, most clinical trials have shown that they are not effective in the treatment of COVID-19. Due to the risk of cardiac complications, the FDA have issued a safety warning in relation to the use of chloroquine and hydroxychloroquine in the treatment of COVID-19.

- Arbidol – approved for prophylaxis and treatment of influenza A and Influenza B in Russia and China. Has been demonstrating very good results in vitro. Study shows that SARS-Cov-2 virus was undetectable in 95% of patients taking Arbidol for 14 days as compared with 50% of patients in the control group.

## IMMUNOMODULATORS

- Actemra – a monoclonal antibody. Though there is no data to recommend it, some have suggested it may be helpful.
- Interferon
- Azithromycin – Some studies are inconclusive. Other studies show that azithromycin combined with hydroxychloroquine may be of some benefit.

## CORTICAL STEROIDS

- Widely used to treat severe pneumonia and prevent lung damage.
- Can suppress systemic inflammation.
- Suggested they may be of benefit as an adjunct to COVID-19 treatment.
- There is evidence to suggest that a specific subset of COVID-19 patients may benefit from cortical steroids.
- Low-dose cortical steroids may be therapeutic in patients with severe symptoms.