Favipiravir and Umifenovir – A Promising Drug Combination

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Covid-19 infection caused by SARS-CoV-2 has infected about 8 million people across the globe affecting over 150 countries, the United States being the most affected one. This is one of the worst ever pandemic with over 450 thousand deaths so far and the virus is still spreading. The major problem with this infection is breathing difficulties, which results in death. There is currently no drug available which is known to treat this disease effectively.

The drug discovery teams at the pharmaceutical industry and institutes have been working on the strategy to repurpose and try the drugs already been in use. Amongst the drug which have been tried or were supposed to be helpful in this infection include Macrolide Antibiotic-Azithromycin, Antimalarial drugs – Chloroquine/ Hydroxychloroquine, Immune system-modulating drugs – Tocilizumab, Broad-spectrum antiviral drug – Ribavirin, HIV & SARS drugs – Lopinavir/Ritonavir/ Nelfinavir and other Flu drugs like Arbidol/Favipiravir /Baloxavir. Cocktail or combination of these drugs is also thought to be effective for the treatment of Covid-19 infection.

One such promising combination is that of two antiviral drugs Favipiravir and Umifenovir. A Pharmaceutical company has recently started a new randomized, open-label study to test the combined efficacy of two antiviral drugs as a potential Covid-19 treatment strategy. This combination is proposed to be effective because these two drugs have different mechanisms of antiviral action and therefore proposed to be effective in prophylaxis and treatment of the disease.

Favipiravir is a prodrug which after getting converted to Favipiravir-RTP binds to and inhibits RNA dependent RNA polymerase (RdRp), which ultimately prevents viral transcription and replication and therefore effective against RNA viruses like Covid-19. (Fig 1) Favipiravir was originally developed as a drug for influenza and primarily acts by preventing the entry and exit of the virus from the cell[1]. This drug is still undergoing Clinical Trials for several viral infections. It is also being tested to be used alone or in combination with other drugs for the treatment of Covid-19.

Umifenovir is an indole-based, dual-acting direct antiviral/ host-targeting agent used for the treatment and prophylaxis of hepatitis, influenza, and other respiratory infections in some countries. It is also being tested to be used alone or in combination with other drugs for the treatment of Covid-19[2]. Umifenovir inhibits membrane fusion of the influenza virus. Umifenovir acts by preventing contact between the virus and target host cells by inhibiting the fusion between the viral envelope and the host cell membrane thereby preventing viral entry to the host cells. This can help prevent new infections as well as prevent the spread of infection to new organs once a human is exposed to the virus.

This drug has shown antiviral activity against both influenza A and influenza B viruses. Umifenovir is also known to exhibit modulatory effects on the immune system and also induces interferon-production and stimulates the phagocytic function of macrophages. All these effects make it a

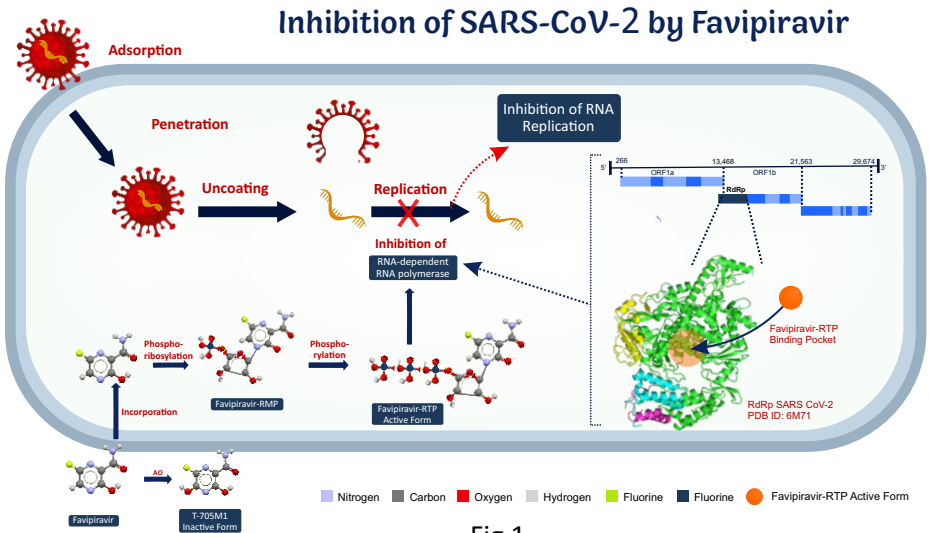

Fig 1

promising candidate for Covid-19 treatment[3].

The SARS-CoV-2 virus like other influenza viruses is transmitted mainly by droplets and enters the human host through mouth, nose, or eyes. Although it affects almost all the organs but initially affects the lungs and lower respiratory tract. Once inside the body, it enters the cells and start replicating fast and therefore the symptoms start getting worse as the disease progresses.

These two drugs, when used in combination, are thought to have a synergistic effect because, on one hand, Umifenovir can prevent the entry of the virus into the cell while Favipiravir can prevent the replication of the virus inside the cell. Therefore, this combination is expected to be effective in the cases where a subject is in close proximity of an infected patient like health workers as well as if one has already been exposed to the virus i.e. symptomatic or asymptomatic Covid-19 positive cases.

Apart from there are many other clinical trials currently in progress to find out a potential drug or drug combination for the treatment of Covid-19 infection and the time will tell which turns out to be a boon for the ailing humans.

References

1 https://pubchem.ncbi.nlm.nih.gov
2 drugbank.ca
3 https://en.wikipedia.org/wiki/Umifenovir