



Review Article

Can favipiravir help in coronavirus treatment?

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ABSTRACT

COVID-19 is the ailment realized by an illness of the SARS-CoV-2 contamination, first perceived in the city of Wuhan, in China's Hubei region in December 2019. COVID-19 was as of late known as 2019 Novel Coronavirus (2019-nCoV) respiratory disease before the World Health Organization (WHO) articulated the official name as COVID-19 in February 2020. Many drugs are being tried for coronavirus, but the favipiravir which was accepted for Chinese flu. The dynamic favipiravir restrains RNA polymerase and forestalls replication of the viral genome, this is main work done by the favipiravir. In this review we will learn about how favipiravir can be used and its mechanism its mechanism of action and various trials that support that favipiravir can be medication for treatment of coronavirus.

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1. Introduction

COVID-19 is the ailment realized by an ailment of the SARS-CoV-2 contamination, first perceived in the city of Wuhan, in China's Hubei region in December 2019.¹ COVID-19 was as of late known as the 2019 Novel Coronavirus (2019-nCoV) respiratory infirmity before the World Health Organization (WHO) articulated the official name as COVID-19 in February 2020.² The SARS-CoV-2 contamination has a spot with the gathering of contaminations called coronaviruses, which furthermore joins the diseases that cause the ordinary cold, and the diseases that cause progressively certified infections, for instance, genuine exceptional respiratory issue (SARS), which was achieved by SARS-CoV in 2002, and Middle East respiratory condition (MERS), which was realized by MERS-CoV in 2012.³ Like the distinctive coronaviruses, the SARS-CoV-2 disease on a very basic level causes respiratory tract pollutions, and the reality of the COVID-19 ailment can go from chronic form to deadly.⁴ Globally there are 4,801,202 confirmed cases and deaths are 318895

which is growing very rapidly in a heavy pace.⁵

The most widely used way to control the spread of coronavirus. Wearing a face shield will help to reduce the spread of the infection. After 2-14 days there have been cases in spite of the fact of using various protective measures there have been separated cases which recommend this might be longer. In the event that you create manifestations, you should remain at home to forestall the spread of the sickness into the network. Wearing a face cover will help forestall the spread of the infection to other people.⁶

Novel coronavirus has an incubation period of 5 to 7 days, but most of the symptoms appear on 14th day.⁷ It has a unique pathogenesis by using spike protein. causes both upper respiratory tract disease and lower respiratory tract contamination. or on the other hand wheezes in the room) - contact transmission (infection from the infected surface by touching nose, eye. The most accepted approach is to manage is by washing the hands. Wash your hands normally and absolutely with soap and water (foam for 20 seconds) OR utilize a sanitizer hand sanitizer. Different activities that help to reduce the spread of COVID-19: - keep 2 feet distance from contact with other people who are infected- do

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not touch your mouth, nose, eyes or face without washing - clean and disinfect surfaces (liquor or obscure based cleaning plans work best for coronaviruses) - face cover won't shield you from COVID-19 direct, yet can help in reminding you to abstain from contacting your face, and will help forestall the spread of the ill. The spread is through droplets during sneezing and coughing and through surface (tables, paper, desks).⁸

The SARS-CoV-2 infection is thought to spread from individual to-individual by means of-

1. Drop transmission (enormous respiratory drops that individuals wheeze, hack or trickle)
2. Vaporized transmission (when somebody hacks or wheezes in the room)
3. Contact transmission (contacting a tainted surface at that point contacting your mouth, nose or eyes).
4. Direct transmission (kissing, shaking hands).

The most significant approach to forestall COVID-19 is to WASH YOUR HANDS. Wash your hands normally and completely with cleanser and water (foam for 20 seconds) OR utilize a liquor based (in any event 60%) hand sanitizer. Different activities that help to forestall the spread of COVID-19:

1. Maintain social distancing by having a space of 6 metre between 2 persons.
2. Do not touch nose, eyes, mouth frequently.
3. Clean and sanitize surfaces (liquor or fade based cleaning arrangements work best for coronaviruses)
4. Face veils won't shield you from COVID-19 straightforwardly, yet can help in reminding you to abstain from contacting your face, and will help forestall the spread of the illness to other people.
5. Social removing
6. Self isolation if have a travel history from abroad.^{9,10}
7. Old, and individuals experiencing previous ailments have a large chances of getting infected. There is investigate that proposes that smokers might be increasingly frail to the SARS-CoV-2 tainting. There is comparably confirmation to propose that individuals who use e-cigarettes at a lot higher danger of creating genuine respiratory contaminations have high risk for covid 19 infections.

1.1. Treatment of coronavirus with various drugs

There were many drugs which were used to treat coronavirus.¹¹

-Baricitinib Clinical examinations are in readiness to decide the sensibility of a Janus kinase (JAK) inhibitor called baricitinib (appeared under the brand name Olumiant for the treatment of rheumatoid joint torment) in the treatment of COVID-19 patients.

- Bevacizumab A VEGF inhibitor called bevacizumab (uncovered under the brand name Avastin for express sorts of trading off new development) being inspected as a

treatment for certifiable lung injury (ALI) and remarkable respiratory bitterness condition (ARDS) in on an amazingly key level got out patients with COVID-19 pneumonia at the Qilu Hospital of Shandong University in Jinan, China.

Chloroquine phosphate – most commonly used for wild fever. Chloroquine has been seemed to have a wide level of antiviral effects, including threatening to coronavirus. Studies in Guangdong Province in China recommend that chloroquine may help improve understanding outcomes in people with novel coronavirus pneumonia.

Colchicine -A progressively settled alleviating drug called colchicine is being concentrated to - thwart troubles of COVID-19 in high peril patients. Colchicine has for quite a while been used in the treatment of gout.

EIDD-2801- A gathering of authorities at UNC-Chapel Hill is certain that a broad range oral antiviral called EIDD-2801 could be used as a potential prophylactic or treatment for COVID-19 and distinctive coronaviruses. Ridgeback Biotherapeutics has approved EIDD-2801 and has gotten assent from the FDA to start tolerant preliminaries.

Favipiravir- An antiviral medicine called favipiravir which was addressed February 17, it has gathered support in China for the treatment of influenza, was other than ensured for use in clinical starters as a treatment for novel coronavirus pneumonia. Fujifilm revealed the start of a Phase 3 clinical starter of Avigan (favipiravir) on COVID-19 patients in Japan. Avigan is gotten a handle on in Japan for use as an antiviral in the treatment of influenza. Fujifilm point by point the start of a Phase 2 clinical foundation of favipiravir in around 50 COVID-19 patients in the U.S. Fingolimod A got a handle on quiet called fingolimod (showed under the brand name Gilenya for the treatment of falling constantly from the certainty sorts of various sclerosis) is being examined as a treatment for COVID-19 at the First Affiliated Hospital of Fujian Medical University in Fuzhou, China.

Hydroxychloroquine and azithromycin- In a little report charged by the French government, 20 patients with COVID-19 were treated with a mix of the counter wild fever calm hydroxychloroquine and the macrolide antibacterial medication azithromycin (Zithromax). Results showed that all patients taking the mix were virologically reduced inside 6 days of treatment

Hydroxychloroquine sulfate It was accounted for in the diary Clinical Infectious Diseases on March 9 that the jungle fever sedate hydroxychloroquine was successful in executing the coronavirus in research facility tests. Hydroxychloroquine was first avowed by the FDA in 1995 under the brand name Plaquenil, and it is moreover in Bangkok's Rajvithi Hospital, had made utilized in the treatment of patients with lupus and joint pain.

Ivermectin an adversary of parasitic medication called ivermectin has been demonstrated to be unimaginable against the SARS-CoV-2 tainting in an in-vitro lab gather

by masters at Monash University in Melbourne, Australia. Further clinical basics should be done to affirm the sensibility of the medication in people with COVID-19.

Leronlimab -CCR5 rival called leronlimab has indicated guarantee in quieting the 'cytokine storm' in hardly any from a general perspective cleared out COVID-19 patients hospitalized in the New York area.

Lopinavir and ritonavir- A medication blend called lopinavir/ritonavir upheld to treat HIV under the brand name Kaletra is being amassed in mix in with this flow season's flu disease steady oseltamivir (Tamiflu) in Thailand. It was spoken to on February 18, 2020 that an old Chinese lady, the key patient to get the "Thai mixed refreshment that preliminaries for patients with COVID-19 had made a flat out recuperation following to experiencing veritable COVID-19-related pneumonia.

1.2. Favipiravir

Favipiravir is a changed pyrazine simple that was at first affirmed for helpful use in safe instances of influenza.^{12,13} The antiviral targets RNA-subordinate RNA polymerase (RdRp) proteins, which are essential for the interpretation and replication of viral genomes.^{14–16} Not exclusively does favipiravir repress replication of flu A and B, however the medication has indicated guarantee in the treatment of avian flu, and might be an elective alternative for flu strains that are impervious to neuramidase inhibitors.¹⁷ Favipiravir has been explored for the treatment of dangerous pathogens, for example, Ebola infection, Lassa infection, and now COVID-19.^{18–20}

1.3. Indication

In 2014, favipiravir was affirmed in Japan to treat instances of flu that were inert to ordinary treatment. Given its adequacy at targetting a few strains of flu, it has been explored in different nations to treat novel infections including Ebola and most as of late, COVID-19.²¹

1.4. Mechanism of action

The system of activity of favipiravir is novel contrasted with existing flu antivirals that principally forestall section and exit of the infection from cells.²² The dynamic favipiravir-RTP specifically restrains RNA polymerase and forestalls replication of the viral genome.¹⁸ There are a few theories regarding how favipiravir-RTP communicates with RNA subordinate RNA polymerase (RdRp).²² Some investigations have demonstrated that when favipiravir-RTP is joined into a beginning RNA strand, it forestalls RNA strand stretching and viral proliferation. Studies have additionally discovered that the nearness of purine analogs can decrease favipiravir's antiviral movement, recommending rivalry between favipiravir-RTP and purine nucleosides for RdRp binding.²³ In spite of the fact that

favipiravir was initially evolved to treat flu, the RdRp reactant area (favipiravir's essential objective), is relied upon to be comparative for other RNA viruses. This rationed RdRp synergist space adds to favipiravir's wide range coverage.

1.5. There are two distributed preliminaries for favipiravir for the treatment of COVID-19:

An open-mark, non-randomized preliminary in Shenzhen (N=80)²⁴ analyzed the adequacy of favipiravir (n=35) versus lopinavir/ritonavir (n=45) for treating COVID-19. Essentially shorter viral freedom time (essential end-point) was found for favipiravir versus lopinavir/ritonavir (middle 4 days versus 11 days; $p < 0.001$). Patients accepting favipiravir additionally demonstrated critical improvement in chest imaging contrasted and those getting lopinavir/ritonavir, with an improvement pace of 91.43% versus 62.22% ($p = 0.004$). Less unfavorable responses were revealed for favipiravir (11.43%) contrasted with lopinavir/ritonavir (55.56%) ($p < 0.01$).

An open-name, randomized preliminary in Wuhan (N=240)²⁵ inspected the adequacy of favipiravir (n=120) versus arbidol (n=120) for treating COVID-19. There was no distinction in the 7-day clinical recuperation rate (essential endpoint) for favipiravir versus arbidol in the general populace (61.21% versus 51.67%; $p = 0.14$). Be that as it may, for a sub-populace of non-basic patients without hypertension or diabetes, the 7-day clinical recuperation rate was essentially better with favipiravir (71.43%; 70/98) versus arbidol (55.86%; 62/111) ($p = 0.02$).

No FDA-affirmed drugs have shown wellbeing and viability in randomized controlled primers for patients with COVID-19 (26,27). World Health Organization (WHO), UK National Health Service (NHS) and Australian wellbeing specialists have not given any exhortation on the utilization of favipiravir. It is likewise not included in the seventh version of Chinese Guidelines for the Prevention, Diagnosis, and Treatment of Coronavirus-initiated Pneumonia for initial to treat COVID-19.^{26–28}

2. Conclusion

Given that the distributed proof for favipiravir is constrained, further examination is expected to close its viability and wellbeing for treating patients with COVID-19. Nine clinical preliminaries are arranged and are probably going to report brings about the months ahead. These discoveries will decide if favipiravir ought to be used more broadly in this setting. No worldwide expert bodies suggest the utilization of the drug for the treatment of COVID-19.

3. Source of Funding

None.

4. Conflict of Interest

None.

References

- Zhong N, Zheng B, Li Y, Poon L, Xie Z, Chan K, et al. Epidemiology and cause of severe acute respiratory syndrome (SARS) in Guangdong; 2003.
- Organization WH. Laboratory testing for coronavirus disease 2019 (COVID-19) in suspected human cases: interim guidance; 2020.
- Wang X, Shi L, Jiang S, Zhang D, Wang P, Tong, et al. Structure of MERS-CoV spike receptor-binding domain complexed with human receptor. *Cell*. 2013;p. 986.
- WHO; 2020. Available from: <https://www.who.int/emergencies/diseases/novel-coronavirus-2019>. Lastupdate.
- Times of India coronavirus case . Available from: <https://timesofindia.indiatimes.com/coronavirus>.
- Lai CC, Shih TP, Ko WC, Tang HJ. HsuehSevere acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and corona virus disease-2019 (COVID-19); 2020.
- Backer JA, Klinkenberg D, Wallinga J. Incubation period of 2019 novel coronavirus; 2020.
- World health organisation coronavirus disease 2019. Available from: <https://www.who.int/emergencies/diseases/novel-coronavirus-2019/advice-for-public>.
- Wang C, F PWGH, Hayden GF. GaoA novel coronavirus outbreak of global health concern The Lancet. 2020;.
- Riou J, Althaus CL. Pattern of early human-to-human transmission of Wuhan 2019 novel coronavirus (2019-nCoV), December 2019 to January 2020. *Euro Surveill*. 2020;25(4).
- COVID-19: Prevention & Investigational Treatments. Available from: <https://www.drugs.com/condition/covid-19.html>.
- FURUTA Y, KOMENO T, NAKAMURA T. Favipiravir (T-705), a broad spectrum inhibitor of viral RNA polymerase. *Proc Jpn Acad Ser B Phys Biol Sci*. 2017;93(7):449–63.
- Madelain V, Nguyen THT, Olivo A, de Lamballerie X, Guedj J, Taburet AM, et al. Ebola Virus Infection: Review of the Pharmacokinetic and Pharmacodynamic Properties of Drugs Considered for Testing in Human Efficacy Trials. *Clin Pharmacokinet*. 2016;55(8):907–23.
- de Farias ST, dos Santos Junior AP, Rêgo TG, José MV. Origin and Evolution of RNA-Dependent RNA Polymerase. *Front Genet*. 2017;8:125.
- Shu B, Gong P. Structural basis of viral RNA-dependent RNA polymerase catalysis and translocation. *Proc Natl Acad Sci U S A*. 2016;113(28):E4005–14.
- Hayden FG, Shindo N. Influenza virus polymerase inhibitors in clinical development. *Curr Opin Infect Dis*. 2019;32(2):176–86.
- World Health Organization: Influenza (Avian and other zoonotic).
- Madelain V, Nguyen THT, Olivo A, de Lamballerie X, Guedj J, Taburet AM, et al. Ebola Virus Infection: Review of the Pharmacokinetic and Pharmacodynamic Properties of Drugs Considered for Testing in Human Efficacy Trials. *Clin Pharmacokinet*. 2016;55(8):907–23.
- Nagata T, Lefor AK, Hasegawa M, Ishii M. Favipiravir: A New Medication for the Ebola Virus Disease Pandemic. *Disaster Med Public Health Prep*. 2015;9:79–81.
- Rosenke K, Feldmann H, Westover JB, Hanley PW, Martellaro C, Feldmann F, et al. Use of Favipiravir to Treat Lassa Virus Infection in Macaques. *Emerg Infect Dis*. 2018;24(9):1696–9.
- Coronavirus puts drug repurposing on the fast track;.
- Pharmaceuticals and Medical Devices Agency: Avigan (favipiravir) Review Report;.
- Venkataraman S, Prasad B, Selvarajan R. RNA Dependent RNA Polymerases: Insights from Structure, Function and Evolution. . *Viruses*. 2018;10(2).
- Cai Q, Yang M, Liu D, Chen J, Shu D, Xia J, et al. Experimental Treatment with Favipiravir for COVID-19: An Open-Label Control Study. *Eng*. 2020;.
- Chen C, Huang J, Cheng Z, Wu J, Chen S, Zhang Y. Favipiravir versus Arbidol for COVID-19: A Randomized Clinical Trial. *medRxiv*. 20037432;.
- The Guardian. Japanese flu drug 'clearly effective' in treating coronavirus, says China; 2020. Available from: <https://www.acc.org/latest-incardiology/articles/2020/03/17/11/22/chinese-clinical-guidance-for-covid-19-pneumonia-diagnosis-and-treatment>.
- National Centre for Infectious Diseases (NCID) Singapore. Interim treatment guidelines for COVID-19 (v1.0) 2. 2020; Available from: <https://www.bioworld.com/articles/433290-fujifilm-stock-rises-as-japan-considers-avigan-for-covid-19-treatment>.
- National Health Commission (NHC) of the People's Republic of China. Guidelines for the Prevention, Diagnosis, and Treatment of Novel Coronavirus-induced Pneumonia; 2019. Available from: <https://www.fda.gov/emergency-preparednessand-response/counterterrorism-and-emerging-threats/coronavirus-disease-2019-covid-19>.

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