Favipiravir (AVIGAN®) to Treat Coronavirus Disease 2019 (COVID-19)

INTRODUCTION

Favipiravir is a new type of RNA-dependent RNA polymerase (RdRp) inhibitor. Favipiravir is converted to the ribofuranosyl triphosphate derivative by host enzymes and is a promising antiviral drug targeting the influenza viral RNA-dependent RNA polymerase (RdRP).

Favipiravir has been approved for treatment of novel influenza on February 15, 2020 in China. This drug is currently undergoing clinical trials in treating COVID-19.

EVIDENCE on EFFECTIVENESS and SAFETY

Based on the systematic search conducted from scientific databases, we identified two studies on the efficacy and safety of Favipiravir for COVID-19 treatment. Currently, China is conducting six clinical trials that involve investigating favipiravir's safety and efficacy for COVID-19, with some comparing favipiravir to lopinavir/ritonavir or baloxavir marboxil.[1]

Chen C (2020) conducted a prospective, multicenter, open-label, randomised superiority trial at three hospitals. They included 240 patients with COVID-19 pneumonia from Zhongnan Hospital of Wuhan University (n= 120), Leishenshan Hospital (n= 88) and The Third People's Hospital of Hubei Province (n=32) from Feb 20, 2020 to Mar 12, 2020. The study compared the efficacy and safety of favipiravir and arbidol to treat COVID-19 patients on seven day's clinical recovery rate. The patients with chest CT imaging and laboratory-confirmed COVID-19 infection, aged 18 years or older were randomly assigned to receive favipiravir or arbidol. Of 116 cases in the favipiravir group, 98 were classified as ordinary COVID-19 patients, 18 were critical COVID-19 patients, and 42 COVID-19 patients were with hypertension and/or diabetes. Of 120 cases in the arbidol group, the ordinary and critical COVID-19 patients were 111 and nine respectively; 35 were with hypertension and/or diabetes.

The clinical recovery rate was 51.67% (62/120) in the arbidol group and 61.21% (71/116) in the favipiravir group after a 7 day's antiviral treatment (p = 0.1396), with the difference of recovery rate between two groups was 0.0954 (95% CI: -0.0305, 0.2213). Concretely, for ordinary patients with COVID-19, seven day's clinical recovery rate was 55.86% (62/111) in the arbidol group and 71.43% (70/98) in the favipiravir group (p = 0.0199), with the difference of recovery rate between two groups of 0.1557 (95% CI: 0.0271, 0.2843); for critical patients with COVID-19, clinical recovery rate was 0 (0/9) in the arbidol group and 5.56% (1/18) in the favipiravir group (P = 0.4712), with the difference of recovery rate between two groups of 0.0556 (95% CI: -0.0503, 0.1614); for COVID-19 patients with hypertension and/or diabetes, clinical recovery rate was 51.43% (18/35) in the arbidol group and 54.76% (23/42) in the favipiravir group (p = 0.7704), with the difference of recovery rate between two groups of 0.0333 (95% CI: -0.1904, 0.2571).

There was no significant difference between the two groups in terms of adverse effects i.e. liver function test (LFT) abnormality, psychiatric symptom reactions and digestive tract reactions. However, those in the favipiravir group had significantly higher serum uric acid compared with arbidol group (p=0.0014).

The authors concluded that in ordinary COVID-19 patients untreated with antiviral previously, favipiravir can be considered as a preferred treatment because of the higher seven day's clinical recovery rate and more effectively reduced incidence of fever, cough except some antiviral-associated adverse effects.[2]

Cai Q et al. (2020) conducted an open-label non-randomised control study in the isolation ward of the national clinical research center for infectious diseases (The Third People's Hospital of Shenzhen), Shenzhen, China from 30 January to 14 February 2020, for patients with laboratory-confirmed patients with COVID-19. The study aimed to compare the clinical effect of favipiravir and lopinavir/ritonavir on COVID-19 patients. From 30 January, 56 patients with laboratory-confirmed COVID- 19 were screened, of which 35 were eligible for the favipiravir arm of the study. A total of 91 laboratory confirmed COVID-19 patients who had started treatment with LPV/RTV between 24 January and 30 January 2020 were screened, of which 45 were eligible for the control arm of this study.

It was found that favipiravir was independently associated with faster viral clearance and a higher improvement rate in chest imaging.

In terms of safety, those in the favipiravir group experienced significantly lower adverse reactions (diarrhoea, vomiting, nausea, rash, liver and kidney injury and others) compared with the other group ($p<0.001$).

In this pilot study of a non-randomised control trial, they found that favipiravir showed significantly better treatment effects on COVID-19 in terms of disease progression and viral clearance. Therefore, if causal, these results should be important information for establishing standard treatment guidelines to combat the SARS-CoV-2 infection/ COVID-19.[3]

CONCLUSION

1. There are two open label clinical trials (non-randomised and randomised superiority trial) conducted in China during the COVID-19 outbreak. Chen C et al. conducted a trial of favipiravir compared with arbidol while Cai Q conducted a trial of favipiravir versus lopinavir/ritonavir.
2. Both studies showed that favipiravir can be considered as one of the potential treatments for COVID-19 as it showed significantly better treatment effects on COVID-19 in terms of higher seven day's clinical recovery rate, disease progression and viral clearance.

REFERENCE

1. Mak E. Sihuan starts clinical trial of Ebola drug favipiravir for COVID-19. Accessed on 26 March 2020. Link: https://www.bioworld.com/articles/433502-sihuan-starts-clinical-trial-of-ebola-drug-favipiravir-for-covid-19 on 26 March 2020)

2. Chang Chen, Jianying Huang, Zhenshun Cheng, et al,. Favipiravir versus Arbidol for COVID-19: A Randomized Clinical Trial, medRxiv preprint. doi: https://doi.org/10.1101/2020.03.17.20037432

3. Q. Cai, M. Yang, D. Liu et al., Experimental Treatment with Favipiravir for COVID-19: An Open-Label Control Study, Engineering. doi: https://doi.org/10.1016/j.eng.2020.03.007

Based on available evidence up to 26 March 2020

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