

Should favipiravir be used for COVID-19?

This write-up summarises a rapid evidence review of favipiravir for treating COVID-19. The information may be revised as new evidence emerges.

Background

A news article titled “Japanese flu drug ‘clearly effective’ in treating coronavirus, say China” was published in the Guardian on 18 Mar 2020.¹ Favipiravir (brand name Avigan), an antiviral drug, is a new type of RNA-dependent RNA polymerase (RdRp) inhibitor which can block the replication of RNA viruses and may have antiviral action against SARS-CoV-2.²

It was approved in Japan in 2014 for the treatment of novel or re-emerging pandemic influenza virus infections. Use is limited to cases in which other influenza antiviral drugs are not sufficiently effective because favipiravir was only investigated in non-clinical studies in avian influenza A (H5N1 and H7N9), and efficacy against seasonal influenza A or B has not been sufficiently demonstrated.³

Favipiravir was also trialed for treating Ebola; however, there was no evidence that favipiravir monotherapy was effective.⁴

Clinical evidence

There are two published trials for favipiravir for the treatment of COVID-19:

- An open-label, non-randomised trial in Shenzhen (N=80)⁵ examined the efficacy of favipiravir (n=35) versus lopinavir/ritonavir (n=45) for treating COVID-19. Significantly shorter viral clearance time (primary endpoint) was found for favipiravir versus lopinavir/ritonavir (median 4 days versus 11 days; $p < 0.001$). Patients receiving favipiravir also showed significant improvement in chest imaging compared with those receiving lopinavir/ritonavir, with an improvement rate of 91.43% versus 62.22% ($p = 0.004$). Fewer adverse reactions were reported for favipiravir (11.43%) compared to lopinavir/ritonavir (55.56%) ($p < 0.01$).
- An open-label, randomised trial in Wuhan (N=240)⁶ examined the efficacy of favipiravir (n=120) versus arbidol (n=120) for treating COVID-19. There was no difference in the 7-day clinical recovery rate (primary endpoint) for favipiravir versus arbidol in the overall population (61.21% versus 51.67%; $p = 0.14$). However, for a sub-population of non-critical patients without hypertension or diabetes, the 7-day clinical recovery rate was significantly better with favipiravir (71.43%; 70/98) versus arbidol (55.86%; 62/111) ($p = 0.02$).

According to other news reports:

- A Japanese health ministry source suggested that favipiravir was not as effective in patients with more severe symptoms, from their clinical studies of 70 to 80 participants.¹
- One medical center in South Korea started administration of favipiravir on 22 February and, while the drug has not been approved for treating COVID-19, the Ministry of Food and Drug Safety (MFDS) in South Korea is considering a fast-track approval to import favipiravir.⁷

Three registered clinical trials are planned or ongoing (Table 1).

Table 1: Ongoing or planned studies for favipiravir in patients with COVID-19

Study identifier	Study Design (Location)	Intervention	Comparator	Date of primary completion
NCT04303299 ⁸	OL, R, (Thailand)	lopinavir/darunavir + ritonavir + favipiravir +/- chloroquine	placebo	October 2020
NCT04310228 ⁹	OL, R, MC (China)	favipiravir +/- tocilizumab	tocilizumab	May 2020
Sihuan Pharmaceutical ¹⁰	R, MC (China)	favipiravir (high, middle and low dosage)	–	Not reported

Abbreviations: MC, multicenter; OL, open label; R, randomised.

Recommendations from professional bodies

The US Food and Drug Administration (FDA)¹¹ has not specifically approved any medication for treating COVID-19. World Health Organization (WHO), UK National Health Service (NHS) and Australian health authorities have not provided any advice on the use of favipiravir. It is also not included in the 7th edition of Chinese Guidelines for the Prevention, Diagnosis, and Treatment of Novel Coronavirus-induced Pneumonia for tentative treatment of COVID-19.^{2, 12}

Conclusion

Given that the published evidence for favipiravir is limited to two open-label trials, further investigation is needed to conclude its efficacy and safety for treating patients with COVID-19. Three clinical trials are planned and are likely to report results in the months ahead. These findings will determine whether favipiravir should be used more widely in this setting. Currently, no international professional bodies recommend the use of favipiravir for the treatment of COVID-19.

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