Tittle	Summary of Evidence: Use of Favipiravir in Patients with COVID-19
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Requesting Area	COVID-19. Keralty Public Health Crisis Committe
Name	COVID-19. Keralty Public Health Crisis Committe
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Question:

Is the administration of Favipiravir effective and safe in the management of patients with COVID-19?

Methodology: A Rapid Systematic Review was carried out (Manual of Rapid Systematic Reviews. Global Institute of Clinical Excellence. 2019).

Search Terms: COVID 19, 2019 Cov, SARS-Cov2, Favipiravir.

Types of studies: Clinical practice guidelines (CPG), systematic literature reviews (SLR), meta-analysis, clinical trials, and other primary studies

Information sources: Pubmed, Science Direct, Cochrane Library, Clinical Trials.

Background:

Favipiravir, a purine nucleic acid analogue and a potent RNA polymerase inhibitor dependent on RNA (Rdrp) indicated in the management of Influenza and Ebola, is considered for compassionate use in COVID-19. The National Medical Products Administration (NMDA) of China gave emergency approval for this medicine (1).

Favipiravir, traded under the Avigan brand, is an antiviral medicine used to treat influenza in Japan (1). It is also being studied to treat other viral infections. It is a derivative of pirazinacarboxamide. It is manufactured by Toyama Chemical (Fujifilm Group) and was approved for medical use in Japan in 2014 (10).

The drug has been approved for use in clinical trials for coronavirus disease 2019 in China. In March 2020, Italy approved the drug for experimental use against COVID-19 and has started testing in three of the most affected regions by the disease. However, the Italian Pharmaceutical Agency has reminded the public that existing evidence in support to this drug is scarce and preliminary (9).

Occupational Therapy:

Currently, four clinical trials are ongoing to evaluate the safety and efficacy of Favipiravir in monotherapy or combined and compared with placebo (2, 3), standard care (4) or tocilizumab (5); two of which are in the recruitment phase and two are in the pre-prerecruiting one.

There was no difference between the treatment groups for the clinical recovery rate in seven days corresponding to the main outcome. A shorter time of symptoms such as fever and cough were reported in secondary outcomes.

In post-hoc analysis of the main outcome due to disease stage, it was found that for patients with moderate disease the clinical recovery rate at day 7 was 55.9% in the comparison group and 71.4% in the Favipiravir group (P=0.0199). While for critically ill patients, the clinical recovery rate at day 7 was nil in the comparison group and 5.6% in the Favipiravir group (P = 0.47).

Regarding to safety, non-serious adverse events were reported in both groups. Abnormal liver function tests (ALT, AST), serum uric acid elevation, psychiatric symptoms reactions, digestive tract reactions.

Analysis of evidence: The risk of bias of the clinical trial was evaluated with the Cochrane Bias Risk Tool (8), finding:

- The method of generating the assignment sequence is not reported, nor the strategies for concealing it, which leads to selection bias, the lack of homogeneous distribution of the characteristics of the participants between the comparison groups
- There is no blinding of the intervention at any level.
- Although there was loss of participants (wear bias), It was reported with the reason

Other Findings:

The frequency of adverse events reported in the intervention group does not represent the totality of reported events (according to table 4).

On the other hand, researchers are considered to make a strong assumption to explain the characteristics of the PCR test, since only 46.5% of the participants in the intervention group were positive to the PCR test on enrollment day and 38.3% of the group that compares. In addition, five patients had no chest CT report

Conclusions:

- Current evidence, given from a single trial, suggests a potential benefit in decreasing fever and cough. Patients with moderate disease may have benefits in the clinical recovery rate. In addition, it suggests being a safe intervention. However, the methodological limitations of the study do not allow recommending the use of Favipiravir in the management of COVID-19, at least until new evidence becomes available.

- It is necessary to note that the available evidence around COVID-19 occurs rapidly and it is, therefore, subject to change. This recommendation will therefore be updated.

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