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A mini-review on clinical studies of Molnupiravir for COVID-19 conducted in selected Asian countries

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Abstract

The key goal of this mini review article is to provide enough data and info on the several clinical trials conducted in some number of countries in the Asia on the use of the drug Molnupiravir for Coronavirus disease 2019 (COVID-19). It is caused by severe acute respiratory syndrome coronavirus 2 has extended across the globe in the previous years. Vaccines and antiviral agents were being tested for their efficacies in order to prevent the occurrence of the disease. An antiviral agent, Molnupiravir which is ribonucleoside analog which is a prodrug that can be converted to its active form intracellularly. There were countries like USA and United Kingdom conducted the preliminary clinical trials for the efficacy of this drug. In the Asian region, countries like Japan, Israel, Philippines, Russia, South Korea and Taiwan participated in the clinical studies for Molnupiravir which is under Phase 3 clinical trial. Doses from 200 – 800 mg/kg were utilized in the studies. These certain doses are well tolerated and there were no severe adverse effects that were noted. Thus, Molnupiravir is a potential antiviral agent that can be utilized to treat and prevent COVID-19 infections and endeavored to be fully established.

Keywords: Molnupiravir; COVID-19; Antiviral; Clinical studies; Asian Region

1. Introduction

COVID-19 or Coronavirus disease in 2019 is a worldwide health problem which occurred in the last quarter of the year 2019. Its causative agent is SARS-COV-2 or known as Severe/Acute Respiratory Syndrome Coronavirus 2. Primary symptoms of this disease include fever, dry cough, diarrhea, and throat soreness. It spread across the globe in the early months of 2020 which affected all sectors of different countries [1,2].

There were vaccines and antiviral agents that were developed for COVID-19. Most of them undergone clinical studies. An example of an antiviral agent for COVID-19 is Remdesivir, which was proven to be efficacious [3]. Other agents such as Baricitinib and Tocilizumab are also effective to treat infections caused by COVID-19 [4]. All of these mentioned medicinal agents undergone clinical trials for the said disease.

One of the current antiviral agents that is indicated for COVID-19 is Molnupiravir. This drug molecule is a small ribonucleoside prodrug of N-hydroxycytidine. It is the first orally administered drug for COVID-19, directing-acting antiviral which is effective at reducing nasopharyngeal SARS-COV-2 viral RNA and it is safe and tolerable [5]. It was recently approved by US Food and Drug Administration and a number of countries in Europe and Asia permitted already its emergency use authority for COVID-19 treatment [6].

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Molnupiravir is already on the late phase clinical trials in United States of America and United Kingdom. There were also Asian countries such as Japan, Israel and South Korea who are active country participants in the clinical studies for this antiviral drug against COVID-19 [7]. This review study summarizes the results and findings through a mini literature review of the different clinical studies in selected areas of the Asian region in the usage of Molnupiravir for COVID-19 infections as an oral antiviral agent.

2. Methods

This review was conducted using journal databases such as BMJ, Directory of Open Access, Elsevier, Google Scholar, The Lancet Journals and Wiley online library. Search approach was established for articles on each database without impairments on language and duration of the undertaking of the study. The search started in December 3, 2021. The search keywords utilized include Molnupiravir, EIDD-2801, EIDD-1931, COVID-19, Molnupiravir clinical trials, or a combination of these keywords. Appropriate studies or articles were classified using specific criteria as follows: articles focused on clinical trials on Molnupiravir, articles related to reports of different trials done or participated by a specific country in Asia and research studies related to clinical outcomes of Molnupiravir for COVID-19 infections. Other parameters considered were the study design, intervention, population size, and if any adverse or side effects of the antiviral drug. The clinical studies mentioned were verified in the clinicaltrials.gov as reference. There was no online review undertaking for this study that occurred [8-11].

3. Results and discussion

Molnupiravir is also known as EIDD-2801 or MK-4482. It is a ribonucleoside prodrug of N-hydroxycytidine (NHC). Once administered orally, the compound circulates systemically and undergoes phosphorylation process. The phosphorylated compound incorporates into the viral RNA catalyzed by viral RNA polymerase and misallocates the viral polymerase to integrate guanosine or adenosine during replication process. This leads to an accumulation of errors throughout the viral gene characteristics that render the virus nonvirulent and unable to undergo replication process. This mechanism institutes its antiviral activity against SARS-COV-2 and other RNA viruses [12,13].

Molnupiravir is the first oral direct acting antiviral agent to be efficacious against nasopharyngeal SARS-COV-2 infectious virus and its RNA. Both USA and UK pioneered the early stages of clinical trial (Phase I and II) of the drug utilizing two doses, 400 and 800 mg. After the 5-day treatment, the higher dose, 800 mg demonstrated significant viral clearance in patients or participants in the preliminary clinical trials. Mild adverse effects such as dizziness and insomnia were noted in average of 1% of the total number of participants in phase II clinical trial. However, it was proven that the antiviral drug was safe and tolerable [14,15].

Table 1 Phase III clinical studies in utilization of Molnupiravir for COVID-19 partaken by Asian countries

Participating countries under Asian region	Clinicaltrials.gov identifier	Year started	Dose of Molnupiravir	Primary outcomes
Japan Israel Philippines Russia Taiwan	NCT04575597	2020	200, 400 and 800 mg (Every 12 hours for 5 days)	Significant viral clearance, sustained recovery up to 29 days and reduced hospitalization
Israel Philippines Russia South Korea	NCT04575584	2020	200, 400 and 800 mg (Every 12 hours for 5 days)	Sustained recovery up to 29 days [16]

There are on-going Phase III clinical trials in which different countries across the globe participated. There are a number of countries in the Asian region partake in the clinical studies such as Japan, Israel, Philippines, Russia, South Korea and Taiwan [16].

In October 2020, a double-blind randomized and multicenter clinical trial with a registration number of NCT04575597. Asian countries that participated in this clinical study are Japan, Israel, Philippines, Russia and Taiwan. There are 1850 adult non-hospitalized having mild to moderate COVID-19 as participants in the trial. Initial results showed that patients who received Molnupiravir with doses of 200-800 mg for a total of 10 doses, had expressively decreased rates of hospitalization or mortality as compared to placebo-treated patients within 29 days. A very few numbers of patients discontinue the treatment due to adverse effects [17,18].

Another Phase III clinical trial conducted in October 2020 and completed by August 2021 with a registration number of NCT04575584. Countries belonging to the Asian region that joined were Israel, Philippines, Russia and South Korea. This was a double-blind randomized and multicenter clinical study bearing 304 hospitalized adults having mild, moderate to severe COVID-19 infections. Doses of 200-800 mg of Molnupiravir (with a total of 10 doses) was given to the participant under the treatment group. Time to sustained recovery were observed after 5-7 days of treatment [19].

In the last quarter of 2021, the US Food and Drug Administration approved the emergency use authorization of Molnupiravir as an oral antiviral for treatment of COVID-19 in certain adults. Currently, there are a number of countries worldwide especially in the Asian region such as Japan, Philippines, South Korea and Taiwan signaled the approval of its emergency use for COVID-19 infections [20,21].

4. Conclusion

Molnupiravir is an oral antiviral agent that is considerably effective in decreasing viral load in COVID-19 infected patients in a 5-day regimen. Results of the clinical trials under Phase III participated by countries in the Asian region proved sustained recovery among patients having mild to moderate COVID-19 infections and given with the antiviral agent dosed at 200-800 mg. Henceforth, this drug could probably be an efficacious and safe antiviral agent against COVID-19.

Compliance with ethical standards

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Disclosure of conflict of interest

The authors declare that they have no conflict of interest.

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