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COMMENTARY

What will be the role of molnupiravir in the treatment of COVID-19 infection?

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The global COVID-19 pandemic is currently underway. To date, there are approximately 4.55 million deaths and 219 million people infected [1]. The massive vaccination campaign is continuing, representing an important weapon to stop the COVID-19 pandemic. Since the pandemic began, in addition to COVID-19 vaccine development, several pharmacological treatments have been studied [2–4]. One antiviral treatment that has shown good results is remdesivir [5–7]. However, some clinical trials have failed to fully confirm its beneficial effects against Sars-CoV-2, and, in addition, the drug is expensive and must be administered intravenously in a hospital setting. Recently, other antiviral alternatives are demonstrating effective results in preregistration studies. Among them, molnupiravir, an oral antiviral agent, has emerged as a promising new drug that molecularly targets the RNA polymerase of Sars-CoV-2. The RNA polymerase are key enzymes in the viral replication cycle. Molnupiravir is the isopropyl prodrug of the ribonucleoside analogue β-D-N4-hydroxycytidine (NHC) [8]. In vitro evidence shows that molnupiravir was found to be a potent inhibitor of SARS-CoV-2 replication, with an EC_{50} in the submicromolar range [9]; this viral injection effect was also observed in animal models [10]. In addition, molnupiravir in phase I/II/III clinical trials has demonstrated good efficacy and safety. Data indicate that molnupiravir reduced the risk of hospitalization or death by approximately 50% in non-hospitalized adults who had mild to moderate COVID-19 and were at risk for a serious disease outcome [11]. In addition, molnupiravir has shown to reduce the risk of hospitalization or death in all subgroups, with efficacy unaffected by the timing of symptom onset, underlying risk factors, or type of Sars-CoV-2 variant (gamma, delta, and mu). Another positive aspect is that the data demonstrate a generally good safety profile. The clinical study showed that the incidence of any adverse event was comparable in the molnupiravir and placebo groups (35% and 40%, respectively), and that the incidence of drug-related adverse events was also comparable (12% and 11%, respectively). In addition, fewer subjects discontinued study therapy because of an adverse event in the molnupiravir group compared with the placebo group (1.3% vs 3.4%) [11].

Several additional aspects have to be defined for molnupiravir, such as the optimal dose to be administered, the timing of administration and any interactions with other drugs used to manage the COVID-19 infection. The safety profile of molnupiravir also has to be better defined by large-scale epidemiological data from the post-marketing phase. Molnupiravir is the first oral, direct-acting antiviral shown to be highly effective at reducing nasopharyngeal SARS-CoV-2 infectious virus and viral RNA and has a favorable safety and tolerability profile. Oral administration of molnupiravir is a big advantage over antiviral injections that work against COVID-19, such as remdesivir. With preliminary analysis showing promising results against COVID-19 infection, future clinical trials are awaited with interest.

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