Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

The emergence of powerful oral anti-COVID-19 drugs in the post-vaccine era

The quest for effective drugs to treat COVID-19 has been a priority since the outbreak of the disease. The clinical application of remdesivir has been greatly restricted by the need for intravenous administration, as well as unstable concentrations in plasma and variable antiviral activity in different organelles.[1] Four neutralising antibodies (bamlanivimab, etesevimab, casirivimab, and imdevimab) have been approved by the United States Food and Drug Administration; however, their high cost and need for intravenous administration render them inaccessible to the public. Therefore, effective and economical oral drugs are the priority for the prevention and control of COVID-19, because they can be used after exposure to SARS-CoV-2 or at the first sign of COVID-19.

Molnupiravir is an oral antiviral drug with β-D-N^4-hydroxycytidine (NHC) as the active ingredient, and has been jointly developed by Merck (Kenilworth, NJ, USA) and Ridgeback (Miami, FL, USA). NHC monophosphate can pair with adenine or guanine and induce lethal mutations during subsequent RNA synthesis; however, NHC does not terminate strand synthesis and is therefore resistant to the proofreading function of SARS-CoV-2 nsp14.[2] Data from the phase 3 MOVe-OUT trial[3] showed that treatment with molnupiravir reduced hospitalisation or mortality by approximately 50% compared with placebo in patients with mild or moderate COVID-19—a very promising finding given that more than 4·7 million deaths worldwide have been attributed to COVID-19 to date. Molnupiravir showed a stronger antiviral effect than remdesivir (50% inhibitory concentration [IC_{50}]: 0·3 μmol/L *vs* 0·77 μmol/L) and ideal toxicity (50% cytotoxic concentration [CC_{50}]>10 μmol/L) in vitro.[4] The phase 2 clinical trial also showed a promising result: no live virus could be isolated from patients who received 400 mg (n=42) or 800 mg (n=53) molnupiravir for 5 days, whereas live virus was isolated from 11·1% of patients in the placebo group (n=54; p=0·03). Moreover, molnupiravir has a favourable safety and tolerability profile.[5]

However, given that 7·3% of participants treated with molnupiravir were still hospitalised during a 29-day observation period—and the potential for molnupiravir, a mutagenic ribonucleoside, to be carcinogenic[6]—the development of oral antiviral treatment for COVID-19 still needs further study. In addition to molnupiravir, four more oral anti-COVID-19 drugs are in phase 3 clinical trials: the 3CL protease inhibitors PF-07321332 (developed by Pfizer [New York, NY, USA]) and s217622 (developed by Shionogi [Osaka, Japan]), the RdRp inhibitor AT-527 (jointly developed by Roche [Basel, Switzerland] and Atea [Boston, MA, USA]), and the SARS-CoV-2 ACE2 and TMPRSS2 antagonist proxalutamide (initiated by Kintor Pharma [Suzhou, China]). While COVID-19 is prevalent, the combined use of immunomodulatory or anti-inflammatory agents, antivirals, and host-factor antagonists might be the optimal therapy for the disease. The emergence of affordable and powerful oral anti-COVID-19 drugs and the increased uptake of vaccination will bring hope for the end of the COVID-19 pandemic.

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