RECOVERY
Randomised Evaluation of COVID-19 Therapy

Intervention

Molnupiravir 800 mg twice daily for 5 days

Summary of information on molnupiravir in COVID-19

Molnupiravir is a prodrug of the ribonucloside analogue N-hydroxycytidine (NHC), being rapidly converted into this form in plasma after absorption. NHC is then converted into the active triphosphate form in host cells by endogenous kinases. The SARS-CoV-2 viral RNA polymerase incorporates this into nascent viral RNA, resulting in copying errors that accumulate every replication cycle, ultimately preventing replication by a mechanism known as error catastrophe. This molecular target is conserved between Coronaviruses, and appears to have a high genetic barrier to resistance.[1] Molnupiravir is given orally and has been well tolerated in clinical studies so far, with infrequent reports of gastrointestinal and allergic reactions.

Molnupiravir is licensed in the United Kingdom for the treatment of mild-moderate COVID-19 within 5 days of symptom onset. In the MOVe-OUT trial of 1433 such patients it reduced the risk of hospitalisation or death by 30%, from 9.7% in the placebo group to 6.8% in molnupiravir group.[2] Evidence in hospitalised patients is limited, and the MOVe-IN trial randomised patients 1:1:1:1 to placebo vs. molnupiravir at 3 different doses (200mg, 400mg, 800mg). This study was abandoned after recruiting 304 inpatients as the manufacturer decided it was unlikely to demonstrate clinical benefit, although no safety concerns were raised.[3] However, the study was underpowered to identify moderate but important benefits in hospitalised patients, so a larger trial is needed.

Potential harm

The summary of product characteristics lists the following adverse reactions:

- headache, dizziness
- diarrhoea, nausea, vomiting
- rash, urticarial

Anaemia has also been reported in some trials.

Frequently asked questions

1. What are the contraindications to molnupiravir?

- Known hypersensitivity to molnupiravir or its excipients
- Age <18 years old
- Pregnancy or breast-feeding. Women of child-bearing potential should not get pregnant while taking molnupiravir or for 4 days afterwards
- Prior treatment with molnupiravir during the index illness

2. Can it be given to pregnant or breast-feeding women?

No.

3. ***Can patients who have already received molnupiravir be recruited into the molnupiravir comparison in RECOVERY?***

No. If they received any doses of molnupiravir prior to admission they should not be included in this comparison.

4. ***Can patients who have received monoclonal antibodies (eg, sotrovimab, Ronapreve, tocilizumab) be recruited into the molnupiravir comparison in RECOVERY?***

Yes.

5. ***Can molnupiravir be given to patients with kidney or liver disease?***

Yes, there are no eligibility criteria based on kidney or liver function.

6. ***Can molnupiravir be given via an enteral feeding tube?***

No. The capsules should not be opened and must be swallowed whole.

7. ***If participants are discharged before completing the course, should they complete it at home?***

Yes. They should be provided with the remainder of their course to complete at home.

References

1. Agostini ML, Pruijssers AJ, Chappell JD, et al. Small-Molecule Antiviral beta-d-N (4)-Hydroxycytidine Inhibits a Proofreading-Intact Coronavirus with a High Genetic Barrier to Resistance. *J Virol* 2019; **93**(24).
2. Merck. Merck announces results from MOVe-OUT Study. 2021. https://www.merck.com/news/merck-and-ridgeback-biotherapeutics-provide-update-on-results-from-move-out-study-of-molnupiravir-an-investigational-oral-antiviral-medicine-in-at-risk-adults-with-mild-to-moderate-covid-19/.
3. Merck. Merck progress update. 2021. https://www.merck.com/news/merck-and-ridgeback-biotherapeutics-provide-update-on-progress-of-clinical-development-program-for-molnupiravir-an-investigational-oral-therapeutic-for-the-treatment-of-mild-to-moderate-covid-19/.