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BRIEF EDITORIAL REPORT

Clinical and animal evidence for efficacy of molnupiravir in the treatment of infection with SARS-CoV-2 (COVID-19)

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The media has rightly and widely reported the effectiveness of a new orally-active antiviral drug named molnupiravir (MK-4482, EIDD-2801) against SARS-CoV-2 (COVID-19). The clinical evidence has been sufficiently strong to prompt the suspension of a phase III randomised trial (the MOVe-OUT trial), and the manufacturers (MSD and Ridgeback Biotherapeutics) are making an application for Emergency Use Authorisation to the US Food and Drug Administration. Recognising the potential of the drug, the Australian government has purchased 300,000 doses. This brief report of the evidence is presented for the benefit of TMJ readers.

The MOVe-OUT trial was in at-risk, non-hospitalized adult patients with mild-to-moderate COVID-19. In the light of these results, recruitment to the study has been stopped after enrollment of approximately 1400 patients, so a further analysis will doubtless appear in due course. I note that the reference below is a sponsor publication and that the trial does not appear to have been published in a peer-reviewed journal. In the present form several explicit risks and uncertainties are acknowledged, including the possibility that future results will not support this interim analysis.

The manufacturer's report[1] presents the results shown in the table below.

These are highly encouraging results, giving strong clinical support to detailed positive results in mice with transplanted COVID-infected human lung tissue.[2] In that work, Dr Angela Wahl and colleagues at the University of North Carolina at Chapel Hill, NC, USA describe the effect of giving molnupiravir (EIDD-2801) to the mice to come to a detailed understanding of the pathogenesis of the coronavirus infection (including SARS-Cov-2 infection) and the efficacy of the drug in treating COVID-19 infection in that model. They observed expression of viral genes peaking 2 days after infection, and stimulation of native genes also. Molnupiravir or placebo was administered to the mice either 2 days after infection, whence viral titres were reduced by 95%, or 12 hours before and 12-hourly thereafter, with a 100,000-fold reduction in viral titres. In contrast, animals not given molnupiravir displayed marked lung destruction when inoculated. These results can be seen graphically in Fig. 4 of the paper.[2]

These human and animal results show dramatically the efficacy of molnupiravir against SARS-CoV-2 infection.

As a point of interest relating to the controversy over the emergence of SARS-CoV-2, the Chapel Hill investigators found in the course of their work evidence consistent with direct human COVID-19 infection from bats.

Treatment	Hospitalised	Not hospitalised	% requiring to be hospitalised	Deaths by day 29
Molnupiravir	28	385	7.3	0
Placebo	53	377	14.1	8

Number and proportion of COVID-19 patients needing to be admitted to hospital after treatment with either molnupiravir or placebo in the MOVe-OUT Clinical Trial, and the number of deaths with each treatment up to 29 days. Differences are statistically significant.

References

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