Therapeutics Technical Advisory Group | Te Rōpū Haumanu Kowheori-19
Update for health professionals: Evusheld cannot neutralise current circulating variants

Date: 27 February 2023

The Therapeutics Technical Advisory Group (Therapeutics TAG) was established by the Ministry of Health in August 2021 to provide expert advice on existing and emerging medicines for use in the management of COVID-19.

Changes to circulating variants and immune escape from Evusheld

Evusheld has been available in Aotearoa since 25 August 2022 for pre-exposure prophylaxis or treatment for SARS-CoV-2 infection in severely immunocompromised people. It is a combination of two long-acting antibodies: tixagevimab and cilgavimab. These have been derived from donated B-cells of patients who have recovered from SARS-CoV-2 infection (Wuhan variant). Tixagevimab and cilgavimab each target distinct and non-overlapping epitopes of the SARS-CoV-2 spike protein located in the receptor binding domain. The antibodies neutralise SAR-CoV-2 infection by binding to the spike protein and blocking interactions between the virus and the host's cellular receptors.

As new variants have emerged, the utility of Evusheld has decreased due to variants with increased immune escape and mutations in the target regions of the epitopes. Evusheld has been identified as unlikely to neutralise BA.4/5 and ineffective against variants BA.2.75, BA.4.6, BF7, BQ.1, and BQ.1.1. [1, 2] **Evusheld is currently predicted to have neutralising activity against fewer than 10% of circulating SARS-CoV-2 variants in Aotearoa.[3]**

Evusheld was initially used to provide enhanced protection in some severely immunocompromised people who remain vulnerable to COVID-19 despite vaccination. However, these targeted against the SARS-CoV-2 spike protein from an earlier variant and now has little-to no neutralising activity for currently circulating variants. **Therefore, Evusheld should no longer be used as pre-exposure prophylaxis for SARS-CoV-2 infection.**

Evusheld has also been used as treatment in specific patients including severely immunocompromised people with persistent COVID-19 infections. Due to the small numbers expected to gain benefit from Evusheld, urgent WGS with the purpose of identifying people for Evusheld treatment will no longer be available. For some patients, convalescent plasma from the New Zealand Blood Service may be an appropriate alternative treatment but should only be considered in discussion with an Infectious Diseases physician or Clinical Microbiologist.

Therapeutics TAG advises that Paxlovid™ (or remdesivir) are preferable treatments to Evusheld.

Updates to the COVID-19 clinical guidelines

The COVID-19 Therapeutics Technical Advisory group has clinical guidelines (link) that are updated at regular intervals and when new evidence emerges. On 9 January 2023, the guidelines were updated to note the increasing prevalence of variants against which Evusheld has no neutralising activity. **On 24 February 2023, the guidelines were further updated to reflect that Therapeutics TAG do not recommend the use of Evusheld.**

References

1. Planas D, Bruel T, Staropoli I, Guivel-Benhassine F, Porrot F, Maes P, et al. Resistance of Omicron subvariants BA.2.75.2, BA.4.6, and BQ.1.1 to neutralizing antibodies 2023 [updated 2023/02/14. 824]. Available from: https://doi.org/10.1038/s41467-023-36561-6.
2. Cao Y, Jian F, Wang J, Yu Y, Song W, Yisimayi A, et al. Imprinted SARS-CoV-2 humoral immunity induces converging Omicron RBD evolution 2022 [2022.09.15.507787]. Available from: https://www.biorxiv.org/content/biorxiv/early/2022/09/23/2022.09.15.507787.full.pdf.
3. de Ligt J, Geoghegan J, Douglas J, Hadfield J, Winter D, Jefferies S, et al. COVID-19 Genomics Insight (CGI) Report. No.33, 16th February 2023, Unpublished ESR report.