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Covid-19: Evusheld protects the most vulnerable patients, analysis shows

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The antibody drug Evusheld is effective for protecting clinically extremely vulnerable people from covid-19, including its omicron variants, a preprint study has reported.¹

The prophylactic treatment, manufactured by AstraZeneca, is a combination of two long acting antibodies (tixagevimab and cilgavimab). It is given as two separate, sequential intramuscular injections in the same session and can be administered in the community.

A research team, led by the University of Birmingham alongside academics from King's College London and the UK Health Security Agency, carried out a systematic review and meta-analysis to examine its effectiveness in immunocompromised patients.

The paper, published as a preprint ahead of peer review, examined the outcomes among 24 773 immunocompromised participants across 17 international studies, 10 775 of whom received Evusheld.

Overall, it reported that the treatment was 86% (95% confidence interval 6.2% to 99.7%; $P=0.04$) effective for preventing covid specific death, 88% (47.1% to 98.7%; $P<0.001$) effective in preventing intensive care admission, 69% (50.8% to 81.6%; $P<0.001$) effective in preventing hospital admission, and 40% (29.8% to 49.7%; $P<0.001$) effective in preventing SARS-CoV-2 infection.

The study's senior investigator, Lennard Lee, senior research fellow at the University of Birmingham and academic medical oncologist at the University of Oxford, said, "There is strong evidence emerging across the world that this approach of using prophylactic antibody therapies in combination with vaccination is a revolutionary approach to safeguard the most vulnerable patients this winter. The science and data suggest that it would be a successful approach for many cancer and immunocompromised patients at the highest level of risk."

Evusheld is already being given to immunocompromised patients in countries including the United States, France, and Israel, but the UK government is waiting for more data on the duration of protection it provides against omicron and its subvariants before deciding whether it should be used.²

For the meta-analysis, reviewers included six studies that compared a tixagevimab and cilgavimab intervention group with a control group. They all reported on the primary outcome of breakthrough SARS-CoV-2 infections after tixagevimab/cilgavimab administration, with covid related hospital

admissions, intensive treatment admissions, and mortality assessed as secondary outcomes.

The authors acknowledged limitations of the analysis, including that the real world studies differed in quality, did not have perfect controls, and comprised different groups of patient. And while most studies reported clinical outcomes during the omicron wave, the authors noted that the original Provent licensing study—the only one they scrutinised that included a randomised controlled trial—was performed before the recent waves driven by the omicron variants.

They concluded, "This systematic review has illustrated that there is now a growing body of real-world evidence validating the original phase 3 study as to the clinical effectiveness of tixagevimab/cilgavimab and demonstrating effectiveness in the omicron era. It is critically important that larger-scale and better-controlled pilots and evaluations are performed to highlight the significant clinical benefit of prophylactic antibody treatment in immunocompromised groups."

Commenting on the findings, Kovilen Sawmynaden, senior principal scientist at the medical research charity LifeArc, said that the analysis indicated that Evusheld could offer "real benefits" to the UK's half a million immunocompromised people.

"As the authors allude to, larger and better controlled studies are needed to keep adding to this body of data and perhaps would go some way to mitigating some of the concerns (around both efficacy and supply) raised by the Medicines and Healthcare Products Regulatory Agency (MHRA)," she said.

A spokesperson for the Department of Health and Social Care for England said that the government would not be procuring any doses "at this time." They said that the UK National Institute of Health and Care Excellence had begun its appraisal of Evusheld and that should the treatment prove to be clinically and cost effective "it will be made available on the NHS in the usual way."

1 Suribhatla R, Starkey T, Ionescu M, Pagliuca A, Richter A, Lee L. Systematic review of the clinical effectiveness of tixagevimab/cilgavimab for prophylaxis of covid-19 in immunocompromised patients. *MedRxiv* [preprint]. 2022:11.07.22281786 doi: 10.1101/2022.11.07.22281786

2 Iacobucci G. Evusheld: Government is urged to expedite covid antibody treatment for vulnerable patients. *BMJ* 2022;379. doi: 10.1136/bmj.o2431 pmid: 36216382

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