



Kent

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Covid-19: Pausing immune suppressing drugs enhances antibody response to boosters, study shows

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Interrupting methotrexate treatment for two weeks after a covid-19 vaccine booster doubles the antibody responses of immune suppressed people, new research¹ has shown.

The improvement in antibody response was maintained for three months, the research published in *Lancet Respiratory Medicine* found. And although the temporary suspension of immune suppressant treatment increases the risk of disease flare ups, most patients could self-manage these.

Methotrexate is the most commonly used immune suppressing drug, with around 1.3 million people in the UK prescribed it for inflammatory conditions such as rheumatoid arthritis and skin conditions such as psoriasis. Until now there has been conflicting advice on whether to continue or interrupt methotrexate treatment after covid-19 vaccination.

Chief investigator Abhishek Abhishek, professor of rheumatology at the University of Nottingham, said, "Implementing these results could vastly improve the protection provided by boosters against covid-19 for millions of people living with these conditions. Covid-19 has left them vulnerable to serious illness, while still having to live with the painful and troubling effects of their conditions. We hope this evidence is the next step in helping them."

The Vaccine Response on off Methotrexate (Vroom) trial planned to recruit 560 patients but was stopped early by an independent oversight committee when interim results showed a clear benefit.

The open label study included 254 patients who were randomly assigned either to continue or to temporarily stop methotrexate treatment immediately after receiving their third dose of the covid-19 vaccine. Around half of the patients had rheumatoid arthritis, 34% had psoriasis with or without arthritis, and 20% had a skin condition alone. Patients were excluded from the trial if they had immune mediated inflammatory diseases for which treatment cannot be interrupted safely. The mean age of the participants was 59 years and 61% were female.

A two week interruption of methotrexate treatment after the booster dose resulted in a 2.19 fold increase in spike antibody response at four weeks (95% confidence interval 1.57 to 3.04). This enhanced antibody response was maintained at 12 weeks. The treatment effect was present across groups of varying ages, methotrexate doses, diseases, and history of SARS-CoV-2 infection.

Interrupting methotrexate for two weeks did not affect quality of life or general health, the study which was funded by the National Institute for Health and Care Research and the Medical Research Council found.

More patients in the suspend methotrexate group self-reported disease flare ups in the first four weeks but most self-managed these and there was no significant difference in seeking NHS help for flares across the two groups. The study was not large enough to evaluate whether suspending medication would result in fewer cases of covid-19 or fewer hospital admissions with covid-19.

Rosemary Boyton, professor of immunology and respiratory medicine at Imperial College London, told a Science Media Centre briefing, "This is a simple, relatively safe, low cost, high benefit intervention. These are very at-risk people who don't make particularly good responses to vaccination. These people need as much boost as they can get. What is most remarkable is the sustained response at 12 weeks. The slower waning is a very encouraging outcome."

Abhishek said patients should consult their hospital specialist teams and a decision on whether to pause methotrexate treatment when getting a covid-19 vaccine would depend on disease stability and previous experience with treatment interruptions. He said all patients benefit from receiving a booster dose, whether or not they pause methotrexate treatment. The results have been sent to the Joint Committee on Vaccination and Immunisation and to specialist societies for them to produce recommendations.

John Iredale, executive chair of the Medical Research Council, said, "This important finding means many people who need to take immune suppressing drugs now have a safe and effective way to improve their immune response to life saving covid-19 vaccines. This study shows yet again how the UK research community's world leading ability to rapidly set up well designed clinical trials can deliver the evidence needed to optimise medical interventions and save lives in the pandemic."

1 Abhishek A, Boyton R, Peckham N, et al. Effect of a 2-week interruption in methotrexate treatment versus continued treatment on covid-19 booster vaccine immunity in adults with inflammatory conditions (VROOM study): a randomised, open label, superiority trial. *Lancet Respir Med* 2022;(June). doi: 10.1016/S2213-2600(22)00186-2.

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