

Effect of a 2-week interruption in methotrexate treatment on COVID-19 vaccine response in people with immune-mediated inflammatory diseases (VROOM study): a randomised, open label, superiority trial

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Publication

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Abstract

Summary

Background

Methotrexate is the first-line treatment for immune-mediated inflammatory diseases and reduces vaccine-induced immunity. We evaluated if a 2-week interruption of methotrexate treatment immediately after COVID-19 booster vaccination improved antibody response against the S1 receptor binding domain (S1-RBD) of the SARS-CoV-2 spike protein and live SARS-CoV-2 neutralisation compared with uninterrupted treatment in patients with immune-mediated inflammatory diseases.

Method

We did a multicentre, open-label, parallel-group, randomised, superiority trial in secondary-care rheumatology and dermatology clinics in 26 hospitals in the UK. Adults (aged ≥ 18 years) with immune-mediated inflammatory diseases taking methotrexate (≤ 25 mg per week) for at least 3 months, who had received two primary vaccine doses from the UK COVID-19 vaccination programme were eligible. Participants were randomly assigned (1:1) using a centralised validated computer program, to temporarily suspend methotrexate treatment for 2 weeks immediately after COVID-19 booster vaccination or continue treatment as usual. The primary outcome was S1-RBD antibody titres 4 weeks after COVID-19 booster vaccination and was assessed masked to group assignment. All randomly assigned patients were included in primary and safety analyses. This trial is registered with ISRCTN, ISRCTN11442263; following a pre-planned interim analysis, recruitment was stopped early.

Finding

Between Sept 30, 2021, and March 7, 2022, we screened 685 individuals, of whom 383 were randomly assigned: to either suspend methotrexate ($n=191$; mean age 58.8 years [SD 12.5], 118 [62%] women and 73 [38%] men) or to continue methotrexate ($n=192$; mean age 59.3 years [11.9], 117 [61%] women and 75 [39%] men). At 4 weeks, the geometric mean S1-RBD antibody titre was 25 413 U/mL (95% CI 22 227–29 056) in the suspend methotrexate group and 12 326 U/mL (10 538–14 418) in the continue methotrexate group with a geometric mean ratio (GMR) of 2.08 (95% CI 1.59–2.70; $p<0.0001$). No intervention-related serious adverse events occurred.

Interpretation

2-week interruption of methotrexate treatment in people with immune-mediated inflammatory diseases enhanced antibody responses after COVID-19 booster vaccination that were sustained at 12 weeks and 26 weeks. There was a temporary increase in inflammatory disease flares, mostly self-managed. The choice to suspend methotrexate should be individualised based on disease status and vulnerability to severe outcomes from COVID-19.

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