External article

10.3310/MTYV5942

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

This page provides information about a publication describing research funded by the Efficacy and Mechanism Evaluation programme under award number NIHR134607, which has been published in a third-party journal. For information about copyright and reproduction of the original publication, please see the publisher's website.

Publication

Abhishek A, Boyton RJ, Peckham N, McKnight Á, Coates LC, Bluett J, *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;**10**:840–50. https://doi.org/10.1016/S2213-2600(22)00186-2

Abstract

Background

Immunosuppressive treatments inhibit vaccine-induced immunity against SARS-CoV-2. We evaluated whether a 2-week interruption of methotrexate treatment immediately after the COVID-19 vaccine booster improved antibody responses against the S1 receptor-binding domain (S1-RBD) of the SARS-CoV-2 spike protein compared with uninterrupted treatment in patients with immune-mediated inflammatory diseases.

Methods

We did an open-label, prospective, two-arm, parallel-group, multicentre, randomised, controlled, superiority trial in 26 hospitals in the UK. We recruited adults from rheumatology and dermatology clinics who had been diagnosed with an immune-mediated inflammatory disease (eg, rheumatoid arthritis, psoriasis with or without arthritis, axial spondyloarthritis, atopic dermatitis, polymyalgia rheumatica, and systemic lupus erythematosus) and who were taking low-dose weekly methotrexate (≤25 mg per week) for at least 3 months. Participants also had to have received two primary vaccine doses from the UK COVID-19 vaccination programme. We randomly assigned the participants (1:1), using a centralised validated computer randomisation program, to suspend methotrexate treatment for 2 weeks immediately after their COVID-19 booster (suspend methotrexate group) or to continue treatment as usual (continue methotrexate group). Participants, investigators, clinical research staff, and data analysts were unmasked, while researchers doing the laboratory analyses were masked to group assignment. The primary outcome was S1-RBD antibody titres 4 weeks after receiving the COVID-19 booster vaccine dose, assessed in the intention-to-treat population. This trial is registered with ISRCT, ISRCTN11442263; following the pre-planned interim analysis, recruitment was stopped early.

Findings

Between Sept 30, 2021 and March 3, 2022, we recruited 340 participants, of whom 254 were included in the interim analysis and had been randomly assigned to one of the two groups: 127 in the continue methotrexate group and 127 in the suspend methotrexate group. Their mean age was 59·1 years, 155 (61%) were female, 130 (51%) had rheumatoid arthritis, and 86 (34%) had psoriasis with or without arthritis. After 4 weeks, the geometric mean S1-RBD antibody titre was 22 750 U/mL (95% CI 19 314–26 796) in the suspend methotrexate group and 10 798 U/mL (8970–12 997) in the

continue methotrexate group, with a geometric mean ratio (GMR) of 2·19 (95% CI 1·57–3·04; p<0·0001; mixed-effects model). The increased antibody response in the suspend methotrexate group was consistent across methotrexate dose, administration route, type of immune-mediated inflammatory disease, age, primary vaccination platform, and history of SARS-CoV-2 infection. There were no intervention-related serious adverse events.

Interpretation

A 2-week interruption of methotrexate treatment for people with immune-mediated inflammatory diseases resulted in enhanced boosting of antibody responses after COVID-19 vaccination. This intervention is simple, low-cost, and easy to implement, and could potentially translate to increased vaccine efficacy and duration of protection for susceptible groups.

Funding

National Institute for Health and Care Research.

Funding

This publication was funded by the Efficacy and Mechanism Evaluation programme as a part of award number NIHR134607.

This article reports on one component of the research award Vaccine Response On/Off Methotrexate (VROOM): does temporarily suspending methotrexate treatment for two weeks enhance COVID-19 vaccine response? A randomised controlled trial. For more information about this research please view the award page [https://fundingawards.nihr.ac.uk/award/NIHR134607]

DOI

https://doi.org/10.1016/S2213-2600(22)00186-2