External article

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Effects of temporarily suspending low-dose methotrexate treatment for 2 weeks after SARS-CoV-2 vaccine booster on vaccine response in immunosuppressed adults with inflammatory conditions: protocol for a multicentre randomised controlled trial and nested mechanistic substudy (Vaccine Response On/Off Methotrexate (VROOM) study)

Publication

Abhishek A, Boyton RJ, McKnight Á, Coates L, Bluett J, Barber VS, *et al*. Effects of temporarily suspending low-dose methotrexate treatment for 2 weeks after SARS-CoV-2 vaccine booster on vaccine response in immunosuppressed adults with inflammatory conditions: protocol for a multicentre randomised controlled trial and nested mechanistic substudy (Vaccine Response On/Off Methotrexate (VROOM) study). *BMJ Open* 2022;**12**:e062599. https://doi.org/10.1136/bmjopen-2022-062599

Abstract

Introduction

It is unknown if a temporary break in long-term immune-suppressive treatment after vaccination against COVID-19 improves vaccine response. The objective of this study was to evaluate if a 2-week interruption in low-dose weekly methotrexate treatment after SARS-CoV-2 vaccine boosters enhances the immune response compared with continuing treatment in adults with autoimmune inflammatory conditions.

Methods and analysis

An open-label, pragmatic, prospective, parallel group, randomised controlled superiority trial with internal feasibility assessment and nested mechanistic substudy will be conducted in rheumatology and dermatology clinics in approximately 25 UK hospitals. The sample size is 560, randomised 1:1 to intervention and usual care arms. The main outcome measure is anti-spike receptor-binding domain (RBD) antibody level, collected at prebooster (baseline), 4 weeks (primary outcome) and 12 weeks (secondary outcome) post booster vaccination. Other secondary outcome measures are patient global assessments of disease activity, disease flares and their treatment, EuroQol 5- dimention 5-level (EQ-5D-5L), self-reported adherence with advice to interrupt or continue methotrexate, neutralising antibody titre against SARS-CoV-2 (mechanistic substudy) and oral methotrexate biochemical adherence (mechanistic substudy). Analysis of B-cell memory and T-cell responses at baseline and weeks 4 and 12 will be investigated subject to obtaining additional funding. The principal analysis will be performed on the groups as randomised (ie, intention to treat). The difference between the study arms in anti-spike RBD antibody level will be estimated using mixed effects model, allowing for repeated measures clustered within participants. The models will be adjusted for randomisation factors and prior SARS-CoV-2 infection status.

Ethics and dissemination

This study was approved by the Leeds West Research Ethics Committee and Health Research Authority (REC reference: 21/HRA/3483, IRAS 303827). Participants will be required to give written informed consent before taking part in the trial. Dissemination will be via peer review publications, newsletters and conferences. Results will be communicated to policymakers.

Trial registration number

ISRCTN11442263.

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