DEAR EDITOR, We would like to thank Dr Murray and colleagues for their interest in our meta-analysis, ‘Cytopenias among patients with rheumatic diseases using methotrexate: a meta-analysis of randomized controlled clinical trials’ [1, 2]. We agree that the results may be of particular interest during the COVID-19 pandemic, as patients and clinicians seek to minimize contact with the healthcare system and may be considering less frequent laboratory monitoring of methotrexate.

We found cytopenias to be a rare side effect of methotrexate in rheumatoid arthritis. We caution that these results from the meta-analysis are limited to patients who were included in phase II/III clinical trials, i.e. patients with few comorbidities.

We have also recently conducted secondary analyses of a double-blind, randomized, placebo-controlled trial where the median age was 66 years, BMI was 32 kg/m² and all patients had multiple comorbidities [3]. The incidence rate of any hematologic adverse event in this trial of patients without systemic rheumatic diseases was 32 cases per 100 person-years in the methotrexate arm, compared with 26 cases per 100 person-years in the placebo arm.

While there were frequent cytopenias in this trial, these abnormalities were primarily mild in nature. Among 2391 subjects taking methotrexate for a median of 23 months of follow-up, only ten cases of severe anaemia were reported, while no cases of severe leukopenia or thrombocytopenia were reported. We are currently performing more detailed analyses of haematologic outcomes in this trial.

The current COVID-19 pandemic has altered how we consider the risk-benefit ratio of frequent laboratory monitoring for methotrexate. Cytopenias appear rare among patients established on methotrexate but are more common in those at a higher risk of severe complications of COVID-19, such as advanced age or multiple comorbidities. We agree with Dr Murray and colleagues that our standard of care has changed during COVID-19 and some of the changes may be permanent.

Funding: This work was supported by the National Institutes of Health [NIH-HL119718, NIH-AR072577].

Disclosure statement: D.H.S. receives research support from institutional contracts with Abbvie, Amgen, Genentech, Janssen and Pfizer, and serves as an epidemiologic consultant to Corrona. The other author has declared no conflicts of interest.

Kathleen M. M. Vanni1 and Daniel H. Solomon1,2

1Division of Rheumatology and 2Division of Pharmacoepidemiology, Brigham and Women’s Hospital, Boston, MA, USA

Accepted 30 April 2020
Correspondence to: Daniel H. Solomon, Brigham and Women’s Hospital, 75 Francis Street, Boston, MA 02115, USA. E-mail: dsolomon@bwh.harvard.edu

References

1 Murray K, Turk M, Veale D. Comment on: Cytopenias among patients with rheumatic diseases using methotrexate: a meta-analysis of randomized controlled clinical trials. Rheumatology 2020 59:e74–e75.

2 Vanni KMM, Lyu H, Solomon DH. Cytopenias among patients with rheumatic diseases using methotrexate: a meta-analysis of randomized controlled clinical trials. Rheumatology 2020;59:709–17.

3 Solomon DH, Glynn RJ, Karlson EW et al. Adverse effects of low-dose methotrexate: a randomized trial. Ann Intern Med 2020; 172:369–80.