

Correspondence on “Associations of baseline use of biologic or targeted synthetic DMARDs with COVID-19 severity in rheumatoid arthritis: results from the COVID-19 global rheumatology alliance physician registry”

Sparks *et al*¹ are to be congratulated on an important and timely study. They found that the use of JAKi was associated with worse outcome of COVID-19 infection, and they interpret this as a harmful effect of the treatment in that particular setting. But this question deserves further consideration. Assuming that the observation is correct, what could the mechanism be? As the authors correctly point out, some JAKi's did show benefits for patients with severe COVID-19 infection.^{2,3} We, therefore, propose an alternative explanation of the observed data.

Some guidance documents,^{4,5} and certainly medical practice traditions, frequently have patients discontinue immunomodulatory treatments when a potentially severe infection is diagnosed, and it seems safe to assume that the vast majority of patients in the study did, in fact, stop their treatment when they became aware of the infection. While this would of course apply to all antirheumatic therapies, there are important differences in the impact this might have. Biologicals have half-lives in the order of weeks, and the effect of stopping the treatment is, therefore, limited in the acute setting. For methotrexate, pharmacodynamic aspects also lead to a long latency in the impact of discontinuing the drug. In contrast, JAKi have short half-lives and discontinuing the treatment will almost immediately lead to the reactivation of the relevant signalling pathways.

We therefore propose, as an alternative possible explanation of the findings by Sparks *et al*, that it is the discontinuation of JAKi when SARS-CoV-2 infection is diagnosed, rather than the treatment itself, that is harmful.

Needless to say, this possibility needs to be tested in clinical studies before leading to changes in practice, and would most likely only be addressed sufficiently in a prospective, randomised trial.

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