Antibody response to a single dose of SARS-CoV-2 mRNA vaccine in patients with rheumatic and musculoskeletal diseases

The immune response to SARS-CoV-2 messenger RNA (mRNA) vaccines in patients with rheumatic and musculoskeletal diseases (RMD) is undefined because these individuals were largely excluded from phase I–III studies. To better understand the immune response to vaccination in this patient population, we studied the antibody response in patients with RMD who completed the first dose of SARS-CoV-2 mRNA vaccination.

Participants with RMD across the USA were recruited to participate in this prospective cohort via social media. Those with prior SARS-CoV-2 were excluded. We collected demographics, RMD diagnoses and immunomodulatory regimens and tested for SARS-CoV-2 antibodies at baseline and prior to the second vaccine dose. Antibody testing was conducted on the semi-quantitative Roche Elecsys anti-SARS-CoV-2 S enzyme immunoassay (EIA) which tests for antibodies against the receptor-binding domain (RBD) of the SARS-CoV-2 spike protein. We evaluated the association between demographic/clinical characteristics and positive antibody response using Fisher’s exact test and Wilcoxon rank-sum test.

We studied 123 participants who received their first SARS-CoV-2 vaccination dose between 8 January 2021 and 12 February 2021; 52% underwent BNT162b2, and 48% underwent mRNA-1273 (table 1). The most common reported RMD diagnoses were inflammatory arthritis (28%), systemic lupus erythematosus (20%), Sjogren’s syndrome (13%) and overlap connective tissue disease (29%). Whereas 28% reported not taking immunomodulatory agents, the remainder reported regimes including non-biologic disease-modifying antirheumatic drugs (DMARDs) (19%), biologic DMARDs (14%) and combination therapy (37%).

At a median (IQR) of 22 (18–26) days after the first vaccine dose, 74% (binomial exact 95% CI, 65% to 81%) had a detectable anti-RBD antibody response (online supplemental table 1). Younger participants appeared more likely to develop an antibody response (p=0.06). No differences were detected between disease groups or overall immunomodulatory therapy categories. However, those on regimens including mycophenolate or rituximab were less likely to develop an antibody response (p=0.001 and p=0.04, respectively) (table 2). Nearly
all patients (94%) on anti-tumour necrosis factor (TNF) inhibitor therapy had detectable antibodies.

In this study of the immune response to the first dose of the SARS-CoV-2 mRNA vaccine in patients with RMD, the majority of participants developed detectable anti-SARS-CoV-2 RBD antibodies; however, patients on regimens including mycophenolate or rituximab were less likely to develop an antibody response. Overall, there were no major differences by diagnosis or being on immunomodulatory therapy (versus not being on therapy), though consistent with prior studies younger patients were more likely to develop antibody responses. Nearly all patients on anti-TNF therapy developed detectable antibody. These associations warrant further investigation.

Rituximab and methotrexate have been shown to reduce humoral responses to influenza and pneumococcal vaccines.\(^1,2\) We found that patients on rituximab were less likely to develop antibody response, yet methotrexate did not negatively impact antibody development. In addition, we found that patients on mycophenolate were less likely to develop antibody response to mRNA vaccination, consistent with observed experience of mycophenolate were less likely to develop antibody development. In addition, we found that patients on rituximab were less likely to develop humoral responses to influenza and pneumococcal vaccines.\(^2,3\) Nearly half of the patients with RMD have expressed tumour necrosis factor (TNF) inhib -

Limitations of this study include a small, non-randomised sample; limited information on immunomodulatory dosage and timing; lack of serial measurements; and use of an EIA designed to detect antibody response after natural infection. Furthermore, these are data on the first-dose response to a two-dose series. Nearly half of the patients with RMD have expressed hesitancy or unwillingness to receive a SARS-CoV-2 mRNA vaccine due to a paucity of data;\(^4\) however, this report can provide reassurance to patients and their providers. We did, however, observe that certain lymphocyte-modulating therapies were associated with poorer humoral vaccine response; potential exploratory strategies to increase immunogenicity in this subgroup may involve adjustment in immunomodulatory therapy, dosage or timing around vaccination.

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Contributors All authors contributed equally to the manuscript.

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REFERENCES
**Supplement Table 1.** Anti-SARS-CoV-2 Spike Protein Receptor Binding Domain Total Antibody Levels\(^1\), stratified by Therapy.

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<th>Therapy</th>
<th>Median</th>
<th>IQR</th>
<th>Range</th>
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<td>None</td>
<td>54.2</td>
<td>13.1 - 154.8</td>
<td>2.4 - 250</td>
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<tr>
<td>Non-biologic DMARD(^4)</td>
<td>28.5</td>
<td>4.8 - 250</td>
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<td>Biologic DMARD(^5)</td>
<td>80.9</td>
<td>55.5 - 204.3</td>
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<td>Corticosteroid-monotherapy(^6)</td>
<td>12.2</td>
<td>7.9 - 133.1</td>
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<td>Combination therapy</td>
<td>28.2</td>
<td>3.5 - 102.4</td>
<td>0.9 - 250</td>
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\(^1\) Manufacturer cut-off; positive ≥0.80 U/mL (Roche Elecsys\(^®\)). Maximum antibody level is 250 U/mL.
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