Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

We believe that, because of the combination of these measurements, CRESS will be an important tool in the search for new, effective therapies for primary Sjögren's syndrome.

HB reports grants and personal fees from Bristol Myers Squibb and Roche, and personal fees from Novartis, Medimmune, and Union Chimique Belge, outside the submitted work. LdW and SA declare no competing interests.

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Antibody kinetics in patients with rheumatic diseases after SARS-CoV-2 mRNA vaccination

Persistence of antibody response after two-dose SARS-CoV-2 mRNA vaccination has been shown for up to 6 months in immunocompetent populations.[1] We previously confirmed a robust SARS-CoV-2 antibody response in most patients with rheumatic and musculoskeletal diseases; however, we found attenuated responses in patients on lymphocyte depleting agents.[2] Although antibody titres among organ transplant recipients 3 months after completion of an mRNA vaccine series were mostly stable,[3] the kinetics of antibody response in other immunosuppressed populations remain to be defined. Here, we present anti-spike antibody titres over a 3-month period in patients with rheumatic and musculoskeletal disease who completed the two-dose SARS-CoV-2 mRNA vaccine series.

We included patients with rheumatic and musculoskeletal disease on immunosuppressive medication who received two doses of mRNA (BNT162b2 [tozinameran] Pfizer–BioNTech or mRNA-1273 [elasomeran] Moderna) SARS-CoV-2 vaccine. Participants were recruited via social media postings by national rheumatic and musculoskeletal diseases organisations and advocacy groups, as well as through clinician referral. Baseline demographics and clinical characteristics were collected via electronic questionnaire. Participants with previous SARS-CoV-2 infection were excluded. Antibody testing was done 1 month and 3 months after dose 2 with the Roche Elecsys anti-SARS-CoV-2 S enzyme immunoassay (EIA); range <0·4 to >250·0 U/mL [positive test result was ≥0·8 U/mL]), which tests for antibodies against the receptor binding domain (RBD) of the spike protein. Participants completed vaccination between Jan 4 and April 21, 2021. Low-positive antibody response was defined as anti-RBD pan Ig of 0·8–50 units per mL; high-positive antibody response was defined as anti-RBD pan immunoglobulin of more than 50 units per mL.[3] This study was approved by the Johns Hopkins Institutional Review Board (IRB00248540), and patients provided electronic informed consent.

We assessed serial samples from 809 participants. 745 (92%) were female, with a median age of 49 years (IQR 39–59). Inflammatory arthritis (355 [44%] participants), overlap connective tissue disease (188 [23%]), and systemic lupus erythematosus (147 [18%]) were the most common rheumatic and musculoskeletal disease diagnoses. Hydroxychloroquine (322 [40%]) and methotrexate (209 [26%]) were the most frequently reported conventional disease modifying antirheumatic drugs, whereas tumour necrosis factor alpha (TNFα) inhibitor therapy was the most common biologic agent (173 [21%]; appendix pp 1–2).

See **Online** for appendix

744 (92%) of 809 participants had a positive anti-spike antibody response at a median of 29 days (IQR 28–32) after dose 2 and 753 (93%) had detectable anti-spike antibody responses at a median of 91 days (87–94) after dose 2. Titres remained stable in 724 (89%) participants between 1 month and 3 months after completion of the vaccination series (table). Titres decreased in 37 (5%) of 809 participants, whereas an increase in titres was observed in 88 (11%) participants.

Among 669 participants with high-positive titres at 1 month, 637 (95%) remained stable and 32 (5%) had a reduction in titres by 3 months. Among 75 participants with low-positive titres at 1 month, 37 (49%) remained stable, 33 (44%) had high-positive responses, and five (7%) had titres that dropped below the threshold of positivity. Among 65 participants with negative antibody response at 1 month, 50 (77%) remained negative, while de novo antibody responses were seen in 15 (23%) participants at 3 months (table). All 15 participants with de novo response reported use of antimetabolite therapy, including azathioprine or mycophenolate. This finding might suggest delayed response in patients on lymphodepleting therapy (appendix p 3). Supporting this observation, among patients with low-positive titres at 1 month and high-positive titres at 3 months, 27 (82%) of 33 were on antimetabolite therapy.

56 (7%) of 809 participants did not have detectable antibody response at 3 months; the most

Published **Online**
September 28, 2021
https://doi.org/10.1016/S2665-9913(21)00282-4

	Negative antibody response at 3 months (n=56)	Low-positive antibody responses at 3 months (n=77)	High-positive antibody responses at 3 months (n=676)
Negative antibody response at 1 month (n=65)	50 (77%)	9 (14%)	6 (9%)
Low-positive antibody response at 1 month (n=75)	5 (7%)	37 (49%)	33 (44%)
High-positive antibody response at 1 month (n=669)	1 (<1%)	31 (5%)	637 (95%)

Data are n (%), where the denominator is the number of patients with responses at 1 month.

Table: **Anti-spike antibody responses 3 months after two doses of SARS-CoV-2 vaccine stratified by antibody responses 1 month after two-dose mRNA vaccine series in patients (n=809) with rheumatic and musculoskeletal diseases**

common immunosuppressive agents in this group included rituximab (33 [59%] of 56), glucocorticoids (26 [46%]), mycophenolate mofetil or mycophenolic acid (16 [29%]), and methotrexate (14 [25%]), which have previously been associated with blunted responses to SARS-CoV-2 vaccination.[2]

Our study is limited by the absence of an immunocompetent control group, data on memory B-cell and cellular responses, and medication doses for all participants. The Roche Elecsys anti-SARS-CoV-2 S enzyme immunoassay is limited by a low ceiling titre of 250 U/mL, precluding detection of decreasing antibody titres in those with titres above this threshold. We included patients without previous known SARS-CoV-2 infection, but because we did not complete anti-nucleocapsid testing, asymptomatic infection at any point in the study cannot be excluded.

In conclusion, we found that rates of seropositivity remained largely stable in most of our population with rheumatic and musculoskeletal disease at 3 months after completion of a two-dose mRNA SARS-CoV-2 vaccination series. We observed increased antibody titres in 6% of participants, which might suggest delayed immune response in those on specific immunosuppressive therapies. Although correlates of protection against SARS-CoV-2 infection are not yet established, one study estimated that an antibody neutralisation level for 50% protection against detectable SARS-CoV-2 infection to be 20% of the mean concentration reported in assays of convalescent serum samples.[4] Breakthrough SARS-CoV-2 infections in fully vaccinated patients with rheumatic and musculoskeletal disease resulting in severe disease and death have been reported, and immunosuppressed status has been associated with an increased risk of infection despite vaccination.[5] These findings have prompted the US Center for Disease Control and Protection to recommend third dose vaccination for patients with moderate-to-severe disease on immunosuppressive drugs. Longitudinal studies to further understand kinetics of antibody titres over time and to determine thresholds for protection could inform the optimal vaccination schedule for patients with rheumatic and musculoskeletal disease on immunosuppressive medication to ensure durable protective immunity.

All authors contributed to the creation of this manuscript in all aspects including data gathering, analysis, writing, and critical revision. DLS reports consulting and speaking honoraria from Sanofi, Novartis, CSL Behring, Jazz Pharmaceuticals, Veloxis, Mallincrodt, and Thermo Fisher Scientific. LC-S reports consultant fees from Janssen, Boehringer-Ingelheim, Mallinckrodt, EMD-Serono, Allogene, Roivant, Octapharma, and ArgenX. All other authors report no competing interests.

This research was made possible with the generous support of the Ben-Dov family. This work was supported by grant number 5T32DK007713 (JLA) and F32DK124941 (BJB) from the National Institute of Diabetes and Digestive and Kidney Diseases; K24AI144954 (DLS) from the National Institute of Allergy and Infectious Diseases; and K23AR073927 (JJP) from the National Institute of Arthritis and Musculoskeletal and Skin Diseases. The analyses described here are the responsibility of the authors alone and do not necessarily reflect the views or policies of the US Department of Health and Human Services, nor does mention of trade names, commercial products or organisations imply endorsement by the US Government.

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