Booster-dose SARS-CoV-2 vaccination in patients with autoimmune disease: a case series

An attenuated humoral response to SARS-CoV-2 vaccination has been observed in some patients with autoimmune disease, and immunosuppressed status has been associated with an increased risk of COVID-19 infection despite vaccination. Recent studies have demonstrated enhanced humoral response to third-dose SARS-CoV-2 vaccination in immunosuppressed transplant patients, but the immunogenicity of booster vaccination in other immunosuppressed populations is unknown. Thus, we sought to describe the humoral response in patients with autoimmune disease who received a booster SARS-CoV-2 vaccine.

Using our prospective cohort of patients with autoimmune disease, we included patients who reported receipt of a single booster dose of SARS-CoV-2 mRNA or adenovirus vector vaccine between 10 April and 11 June 2021. We observed serial anti-spike antibody responses among these participants.

A total of 18 participants received a booster SARS-CoV-2 vaccine dose (table 1). Most (13/18) were women with median (IQR) age of 55 (44–63) years. The most common autoimmune diagnoses included myositis (n=6) and inflammatory arthritis (n=3). Most (14/18) were on antimetabolite therapy; mycophenolate was the most commonly reported immunosuppressive therapy (n=8), with a median (IQR) daily dose of 3000 mg (2500–3000 mg). Participants completed initial vaccination with either Pfizer (n=8), Moderna (n=6) or Johnson & Johnson/Johnson & Jansen (J&J) Ad26.COV2.S (n=4).

Anti-spike antibodies, evaluated via Roche Elecsys anti-RBD pan-Ig were negative in 10 participants (anti-RBD <0.8 U/mL) and low-positive (anti-RBD 0.8–500 U/mL) in six participants at a median of 29 (IQR 28–33) days after completion of initial vaccine series with median anti-spike antibody level (IQR) of <0.4 (<0.4–222 U/mL).

Participants underwent booster vaccine at a median of 77 (IQR 54–94) days after completion of initial series. Booster vaccines included single dose of Moderna (n=8), J&J (n=6) or Pfizer (n=4). Nine participants obtained a different vaccine platform (mRNA vs adenovirus) for the additional dose, while the remainder received the same vaccine type.

Repeat anti-spike antibody testing was performed at a median 30 (IQR 27–36) days after booster dose. Eighty-nine per cent of participants had an augmented humoral response following booster vaccination, with median anti-spike antibody level (IQR) of 2500 (885–2500 U/mL) (online supplemental figure 1). Among those negative following initial vaccine series, 80% were positive following the booster dose. All low-positive participants demonstrated high titre response following booster vaccination. Two patients remained negative following booster dose; neither adjusted peri-vaccination immunosuppression and reported taking anti-CD20 therapy and mycophenolate respectively. Most participants (10/15) continued immunosuppression during the initial vaccine series, compared with the minority (5/18) who continued therapy peri-booster.

This study is limited by observational design, small and inhomogenous sample as well as absence of data on memory B-cell and T-cell response. The augmented effect of booster dose may be confounded by peri-booster pause of immunosuppression. Baseline disease activity or severity was not routinely collected.

Evidence-based approaches to safely optimising immune responses to SARS-CoV-2 vaccination for vulnerable populations are urgently required. While no antibody titre has been defined to correlate with protection, booster dosing may be an option for patients with limited antibody responses to standard vaccine series. The SARS-CoV-2 vaccination schedule may require further refinement in immunosuppressed populations. Further studies are needed to address safety and efficacy of booster vaccination, as well as optimal adjustment in peri-vaccination timing of immunosuppressive therapies; this should be investigated further in a clinical trial setting.

PATIENT AND PUBLIC INVOLVEMENT

Patients were not involved in the design, conduct or dissemination of the study, though this study was motivated by questions frequently posed by patients. The study has a public website (https://vaccineresponse.org/) and email account where we welcomed participants and the public to contact the research team. Results of the study will be shared with national RMD organisations for dissemination to their patient communities once published.
Table 1  Vaccines administered, autoimmune diagnoses, immunosuppression and peri-vaccination management with longitudinal anti-spike antibody responses

<table>
<thead>
<tr>
<th>Age</th>
<th>Sex</th>
<th>Diagnosis</th>
<th>Immunosuppressive therapy</th>
<th>Initial vaccine series</th>
<th>Meds held during initial vaccine</th>
<th>Pre-booster antibody</th>
<th>Booster vaccine type</th>
<th>Days from initial to booster vaccine</th>
<th>Post-booster antibody</th>
<th>Therapy held per-booster*</th>
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<td>Multiple sclerosis</td>
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<td>Pfizer</td>
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<td>J&amp;J</td>
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* Median number (IQR) doses held for mycophenolate 27 (25–28). Fourteen doses of leflunomide held by one patient. Two doses of azathioprine held by two participants. One dose held for abatacept, belimumab, methotrexate and secukinumab respectively.
† Denotes Crohn’s disease or ulcerative colitis.
‡ Denotes missing data.
§ Denotes systemic lupus erythematosus.
¶ Rheumatoid arthritis, ankylosing spondylitis, psoriatic arthritis, reactive arthritis or inflammatory bowel disease associated arthritis.
** Roche Elecsys anti-RBD pan-Ig ≥0.8 U/mL is considered positive (upper limit reported as >2500).

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REFERENCES
Supplemental Figure 1. Anti-SARS-CoV-2 antibody titers pre and post booster vaccine.

Pre-Booster Median <0.4U/mL (IQR <0.4-222). Post-Booster Median >2500U/mL (IQR 885-2500). p-value <0.001
Pre-Booster drawn at 29 days (IQR 28-33) after initial vaccine series. Post-Booster drawn at 30 (IQR 27-36) days after booster dose.