Correspondence on 'Immunogenicity and safety of anti-SARS-CoV-2 mRNA vaccines in patients with chronic inflammatory conditions and immunosuppressive therapy in a monocentric cohort'

Jesse Veenstra
Jie Wang
Kathleen Maksimowicz-McKinnon
Tingting Liu
Bobby Zuniga

See next page for additional authors

Follow this and additional works at: https://scholarlycommons.henryford.com/dermatology_articles
Authors
Jesse Veenstra, Jie Wang, Kathleen Maksimowicz-McKinnon, Tingting Liu, Bobby Zuniga, Iltefat H. Hamzavi, Li Zhou, and Qing-Sheng Mi
Correspondence on ‘Immunogenicity and safety of anti-SARS-CoV-2 mRNA vaccines in patients with chronic inflammatory conditions and immunosuppressive therapy in a monocentric cohort’

Patients with immune-mediated inflammatory diseases (IMID) have largely been excluded in clinical trials of SARS-CoV-2 mRNA vaccines due to both disease status and immunotherapeutics used. A recent study by Geisen et al has shown that patients with IMID using immunotherapeutics exhibited significantly lower antibody titres against the SARS-CoV-2 spike protein (S) after full vaccination with a SARS-CoV-2 mRNA vaccine relative to vaccinated healthy controls (HCs), suggesting a compromised SARS-CoV-2 mRNA vaccine antibody response in this population.1 Furthermore, a separate study by Boyarsky et al found that a proportion of patients with IMID with or without immunomodulatory therapy failed to seroconvert after the first dose of a SARS-CoV-2 mRNA vaccine.2 Here, we quantified SARS-CoV-2 mRNA vaccine-induced anti-S and receptor-binding domain (RBD) antibodies among fully vaccinated HCs and found that antibody levels in patients with IMID using immunotherapeutics were significantly lower than HCs.

A total of 66 HCs and 8 patients with IMID who had been fully vaccinated (BNT162b2 or mRNA-1273) for at least 2 weeks were recruited. All participants received their first vaccination between 13 December 2020 and 5 February 2021 and the second dose between 3 January 2021 and 5 March 2021. Individuals with known prior SARS-CoV-2 infection were excluded. IMID diagnoses included psoriasis, rheumatoid arthritis, systemic lupus erythematosus (SLE), mixed connective tissue disease, hidradenitis suppurativa and inflammatory bowel disease. All patients with IMID were on an immunomodulatory therapy, including biologic and non-biologic disease-modifying antirheumatic drug therapy, corticosteroid or combination therapy (table 1). Demographic information is detailed in online supplemental table S1. Additionally, non-vaccinated non-convalescent healthy individuals (n=8) were included as controls. Fully quantitative anti-SARS-CoV-2 immunoglobulin G (IgG) antibodies were measured with the COVID-SeroIndex ELISA kit (Kantaro and Bio-Techne, USA), assessing both anti-S and RBD antibodies.3

<table>
<thead>
<tr>
<th>Age</th>
<th>Sex</th>
<th>IMID diagnosis</th>
<th>Immunotheapeutic regimen</th>
<th>Anti-S IgG (AU/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>30s</td>
<td>F</td>
<td>HS and LCV</td>
<td>Tofacitinib</td>
<td>16.4</td>
</tr>
<tr>
<td>40s</td>
<td>F</td>
<td>Ulcerative colitis</td>
<td>Infliximab and azathioprine</td>
<td>52.0</td>
</tr>
<tr>
<td>50s</td>
<td>F</td>
<td>RA</td>
<td>Hydroxychloroquine</td>
<td>102.8</td>
</tr>
<tr>
<td>60s</td>
<td>F</td>
<td>SLE</td>
<td>Methotrexate</td>
<td>84.8</td>
</tr>
<tr>
<td>60s</td>
<td>M</td>
<td>Psoriasis and PsA</td>
<td>Ixekizumab</td>
<td>90.5</td>
</tr>
<tr>
<td>60s</td>
<td>F</td>
<td>RA, SLE and MCTD</td>
<td>Methotrexate and prednisone 5 mg</td>
<td>120.9</td>
</tr>
<tr>
<td>60s</td>
<td>F</td>
<td>RA and SLE</td>
<td>Prednisone 5 mg</td>
<td>Undetectable</td>
</tr>
</tbody>
</table>

As expected, all vaccinated HCs achieved seroconversion (anti-RBD positive), which is in line with clinical trial results from mRNA-12735 and BNT162b2.6,4 while one patient with IMID and all non-vaccinated non-convalescent HCs were below the detectable limit (figure 1A). Given a mean age of 55.9 years (range: 33–68 years) among patients with IMID, HCs were split into groups of less than 50 years of age (mean age: 34.4 years; range: 21–49 years; n=55) and 50 years or older (mean age: 56.4 years; range: 50–66 years; n=11). Anti-S-IgG antibody levels were comparable between the <50-year-old and ≥50-year-old HC groups (p=0.19), with a mean of 178.7 AU/mL (95% CI, 163 to 194) and 153.8 AU/mL (95% CI, 114 to

Figure 1 Patients with IMID treated with immunotherapeutics have reduced levels of SARS-CoV-2 vaccine-induced antibody. (A) Semiquantitative anti-RBD IgG levels were measured in 66 HCs and 8 IMID patients who had been fully vaccinated for at least 2 weeks. Non-vaccinated healthy participants were included as controls (n=8). The red dashed line (0.7 CI) indicates the cut-off threshold correlating to the presence or the absence of antibody per manufacturer (Kantaro and Bio-Techne). Individuals with RBD levels above the 0.7 cut-off threshold moved forward for anti-S IgG quantification. (B) Fully quantitative anti-S IgG levels were measured in the study population: healthy: <50 years old (n=55), healthy: ≥50 years old (n=11), IMID (n=8) and control (n=8). Individuals with RBD levels below the 0.7 cut-off level were assigned a value of 0. The red dashed line (25 AU/mL) indicates the threshold correlating to 100% neutralising antibody levels per manufacturer. Horizontal black bars indicate mean IgG levels. Unpaired two-tailed t-test. *p<0.05; ****p<0.0001. Anti-S, anti-spike protein; CI, cut-off index; HCs, healthy controls; IgG, immunoglobulin G; IMID, immune-mediated inflammatory diseases; RBD, receptor-binding domain.

Table 1 Patient-level IMID diagnosis, immunotherapeutic regimen and anti-S IgG level

*Anti-S, anti-spike protein; HS, hidradenitis suppurativa; IgG, immunoglobulin G; IMID, immune-mediated inflammatory disease; LCV, leukocytoclastic vasculitis; MCTD, mixed connective tissue disease; PsA, psoriatic arthritis; RA, rheumatoid arthritis; SLE, systemic lupus erythematosus.
Antibody levels among patients with IMID using immunotherapeutics were significantly lower (85.2 AU/mL (95% CI, 29 to 141)) compared with two HC groups, suggesting a compromised vaccine-induced antibody response among patients with IMID (figure 1B). IMID patient-level demographics, diagnosis, immunotherapeutics regimen and individual anti-S-IgG antibody levels are outlined in table 1. One patient with SLE and after vaccination may be necessary to achieve a meaningful correlate of protection.

Our study shows that fully vaccinated patients with IMID using immunotherapeutic regimens had significantly lower titres of vaccine-induced anti-SARS-CoV-2 antibodies. In contrast to Giesen et al, where all patients with IMID had seroconversion after full vaccination, we observed one patient with IMID who did not mount a detectable antibody response after full vaccination, which was also suggested by Boyarsky et al, although after only a single vaccination. While most patients with IMID did mount a detectable anti-S antibody response after full vaccination, it remains unknown how much protection this provides or if the response is durable. Limitations of the current study and Giesen et al’s findings include a relatively small sample size and the absence of extended longitudinal measurements. Further investigation using greater numbers of patients with IMID and specific immunotherapeutic regimens will be required to assess antibody levels longitudinally and characterize SARS-CoV-2 memory B cell and T cell responses. These data are urgently needed to plan effective vaccination approaches for patients with IMID, including when and if booster doses will be required and if holding certain immunotherapeutics before and after vaccination may be necessary to achieve a meaningful correlate of protection.

Jesse Veenstra 1,2,3, Jie Wang 1,2,3, Kathleen McKinnon-Maksimowicz 4, Tingting Liu 1,2,3, Bobby Zuniga 1,2,3, Iltefat Hamzavi 1, Li Zhou 1,2,3, Qing-Sheng Mi 1,2,3

1Department of Dermatology, Henry Ford Health System, Detroit, Michigan, USA
2Center for Cutaneous Biology and Immunology, Department of Dermatology, Henry Ford Health System, Detroit, Michigan, USA
3Immunology Program, Henry Ford Cancer Institute, Henry Ford Health System, Detroit, Michigan, USA
4Division of Rheumatology, Department of Internal Medicine, Henry Ford Health System, Detroit, Michigan, USA

Correspondence to Dr Qing-Sheng Mi, Immunology Program, Henry Ford Health System, Detroit, Michigan, USA; qmi1@hfhs.org

Contributors JV: study conception, drafting the manuscript and data analysis. KM-M: study conception and manuscript editing. JW, TL and EZ: sample processing, data generation and analysis. IH: patient recruitment. LZ: study conception, manuscript editing and funding. Q-SM: study conception, data analysis, manuscript editing and funding.

Funding This publication presents independent research funded by the NIH/NIAMS R01AR063611 (Q-SM), Henry Ford Immunology Program T71017 (Q-SM) and T71016 (LZ).

Competing interests None declared.

Patient consent for publication Not required.

Ethics approval This study was approved by the Henry Ford Health System Institutional Review Board (#12826). All individuals completed informed consent prior to participation in the study with understanding that their information and blood samples would be used for research purposes.

Provenance and peer review Not commissioned; internally peer reviewed.

Supplemental material This content has been supplied by the author(s). It has not been vetted by BMJ Publishing Group Limited (BMJ) and may not have been peer-reviewed. Any opinions or recommendations discussed are solely those of the author(s) and are not endorsed by BMJ. BMJ disclaims all liability and responsibility arising from any reliance placed on the content. Where the content includes any translated material, BMJ does not warrant the accuracy and reliability of the translations (including but not limited to local regulations, clinical guidelines, terminology, drug names and drug dosages), and is not responsible for any error and/or omissions arising from translation and adaptation or otherwise.

This article is made freely available for use in accordance with BMJ’s website terms and conditions for the duration of the covid-19 pandemic or until otherwise determined by BMJ. You may use, download and print the article for any lawful, non-commercial purpose (including text and data mining) provided that all copyright notices and trade marks are retained.

© Author(s) (or their employer(s)) 2021. No commercial re-use. See rights and permissions. Published by BMJ.

Additional supplemental material is published online only. To view, please visit the journal online (http://dx.doi.org/10.1136/annrheumdis-2021-220736).

JV and JW contributed equally.


Received 6 May 2021
Accepted 8 May 2021
Ann Rheum Dis 2021;0:1–2. doi:10.1136/annrheumdis-2021-220736

ORCID iDs
Jesse Veenstra http://orcid.org/0000-0002-3576-855X
Qing-Sheng Mi http://orcid.org/0000-0001-9732-1975

REFERENCES