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Clinical discussion: COVID-19 vaccinations in patients with autoimmune disorders (AID)

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Overview

- COVID-19 and risk of severe disease
- COVID-19 vaccination and disease modifying therapies
- Timing of vaccinations
- Conclusions

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COVID-19 and risk of severe disease

COVID-19 Overview: risk for severe disease

- On March 11, 2020, WHO declared the COVID-19 outbreak (a respiratory illness caused by SARS-CoV-2 virus) a pandemic[1]
- A number patient risk factors may increase risk of severe disease, these factors include[2]

- Older age
- Obesity
- Diabetes
- Hypertension
- Cancer
- Coronary heart disease
- Chronic pulmonary or kidney disease
- Use of corticosteroids
- Immunocompromised condition
- Use of immunosuppressant medications

COVID-19, coronavirus disease 2019; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; WHO, World Health Organization.

1. Cucinotta D et al. Acta Biomed 2020;91:157-160. 2. People with Certain Medical Conditions. Centers for Disease Control and Prevention. Updated March 29, 2021. Accessed October, 2021. https://www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/people-with-medical-conditions.html.

COVID-19 Overview: risk for severe disease

- In patients with rheumatic disease, several studies have shown there is no clear association between treatment with b/tsDMARDs and increased risk of severe COVID-19[1-4]
- The same risk factors apply in AID patients:[5]

- Older age
- Obesity
- Diabetes
- Hypertension
- Cancer
- Coronary heart disease
- Chronic pulmonary or kidney disease
- Use of corticosteroids
- Immunocompromised condition
- Use of immunosuppressant medications

AID, autoimmune disorders; b/tsDMARDs, biologic/targeted synthetic disease-modifying antirheumatic drugs; COVID-19, coronavirus disease 2019. 1. Landewe RB et al. *Ann Rheum Dis* 2020;79:851-858. 2. Gianfrancesco M et al. *Ann Rheum Dis* 2020;79:859-866. 3. Fredi M et al. *Lancet Rheum* 2020; 2(9):e549-e556. 4. Salvarani C et al. *Ann Rheum Dis* 2020;79:986-988. 5. People with Certain Medical Conditions. Centers for Disease Control and Prevention. Updated March 29, 2021. Accessed October, 2021. https://www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/people-with-medical-conditions.html.

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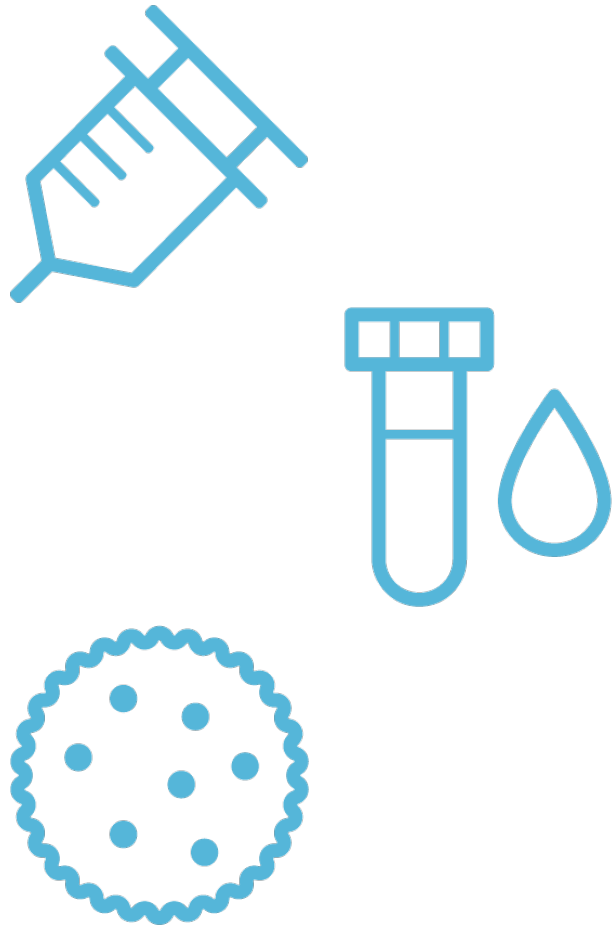
COVID-19 vaccination and disease modifying therapies

Issues with vaccination in patients with AID

- Vaccination **recommendations**
- **Timing** of vaccination
- Timing of immunotherapy **administration**
- Limited role for post-vaccination **serology**



AID, autoimmune disorders. Prof. Van Pesch opinions.

Vaccination in AID patients

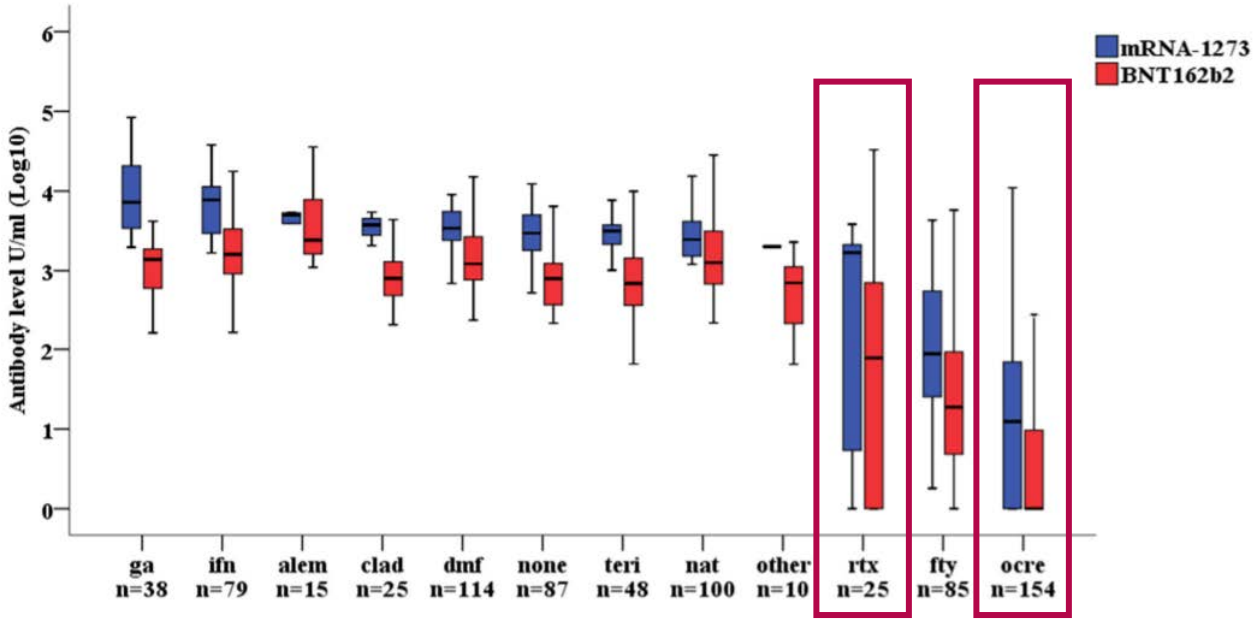
The expected response to COVID- 19 vaccination for patients receiving systemic immunomodulatory therapies is likely to be blunted in its magnitude and duration compared to the general population

- No contraindication across all AID
- Should occur preferably in a stable phase of the disease

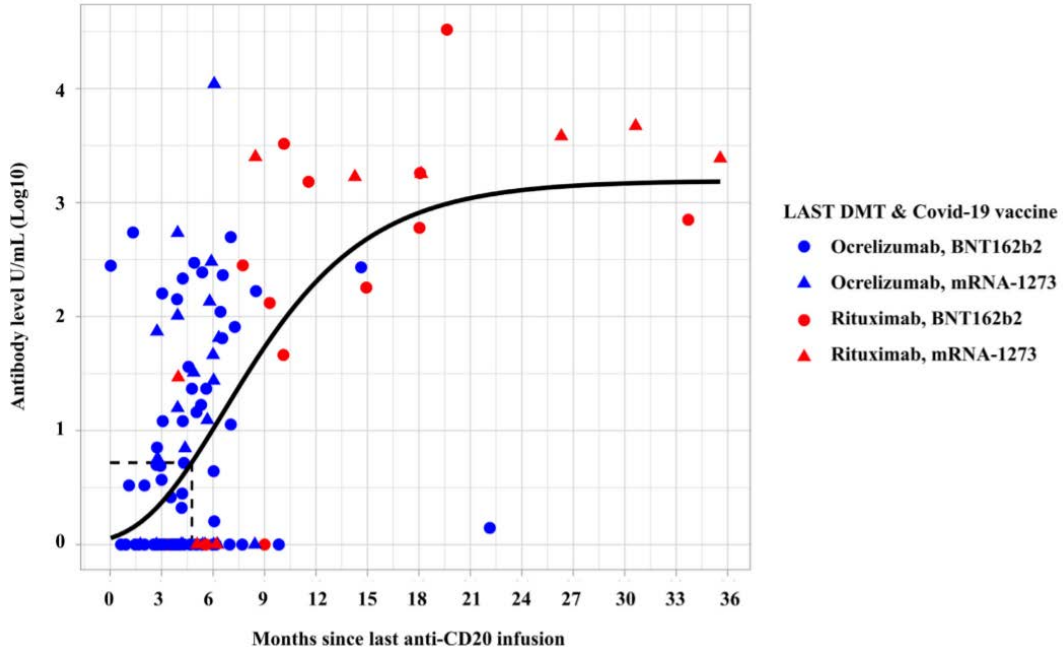
AID, autoimmune disorders; COVID-19, coronavirus disease 2019.
Curtis JR et al. Arthritis Rheumatol. 2021;73(10):e60–e75.

MS DMTs, ALC and COVID-19 vaccination

- Post vaccination RBD antibody levels by DMT in relation to vaccine type



- Post-vaccination RBD antibody levels in patients treated with anti-CD20 therapies according to the time passed since the last infusion

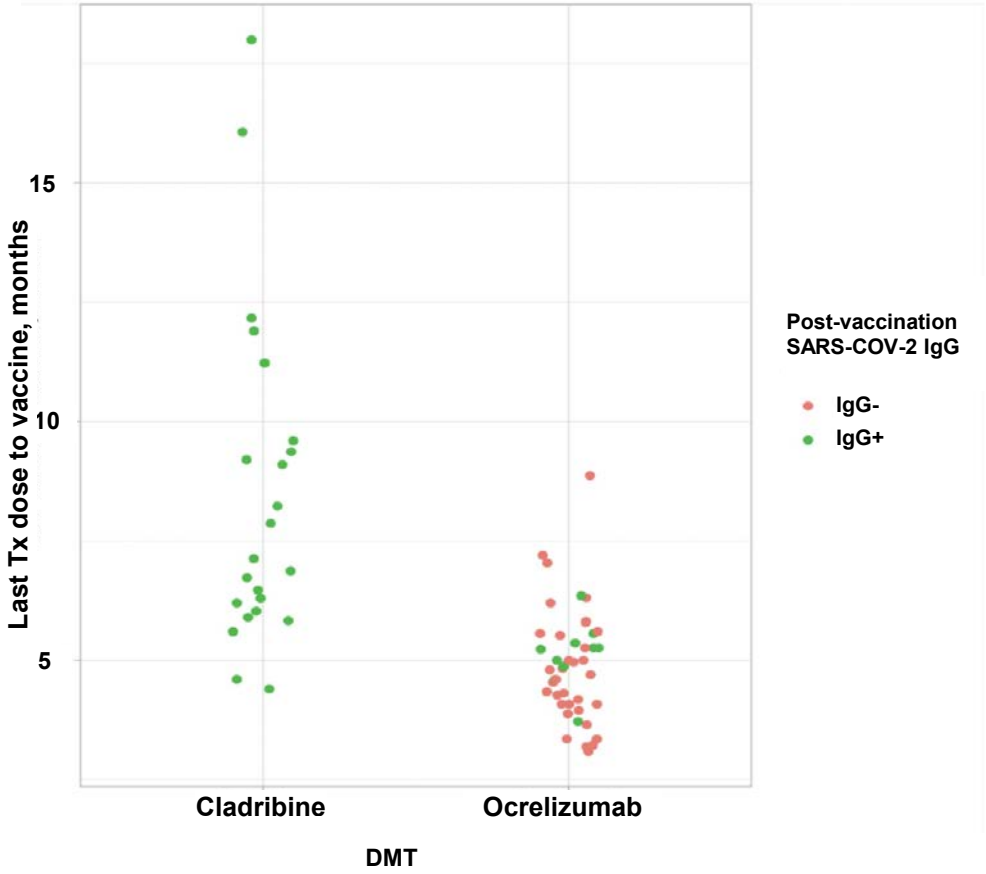


In pwMS, anti-CD20 treatment and fingolimod led to a reduced humoral response to mRNA-based SARS-CoV-2 vaccines. The mRNA-1273 may be preferentially considered for patients under anti-CD20 treatment or fingolimod.

COVID-19, coronavirus disease 2019; DMTs, disease-modifying therapies; pwMS, patients with Multiple Sclerosis; RBD, receptor-binding domain; ga, glutamer acetate; ifn, interferon; alem, alemtuzumab; clad, cladribine; dmf, dimethyl-fumarate; teri, teriflunomide; rtx, rituximab; fty, fingolimod; ocre, ocrelizumab

Sormani MP et al. *EbioMedicine (000).* 2021;103581. Figures reproduced with permission from *EbioMedicine*

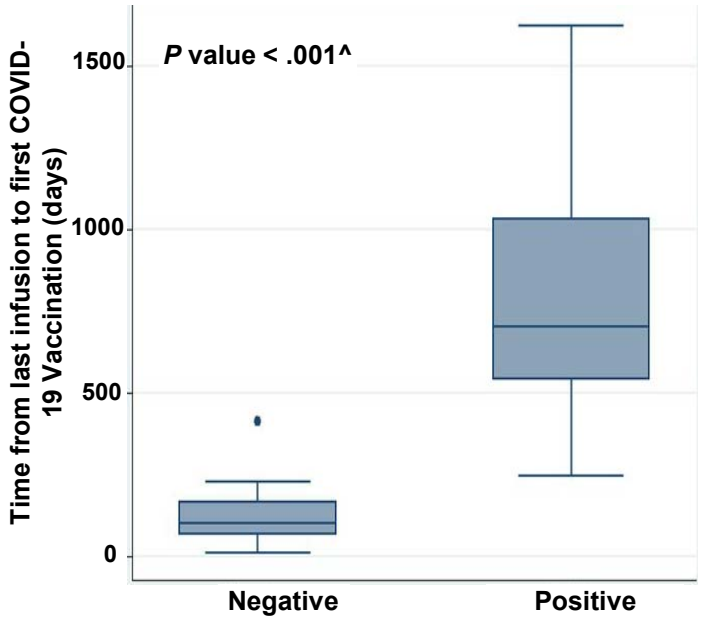
Timing of COVID-19 vaccination and anti-CD20 treatment



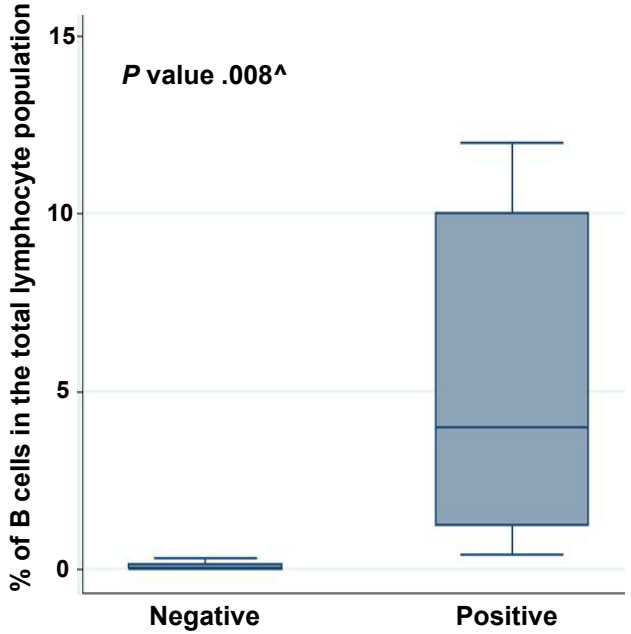
Time in months from last treatment dose to COVID-19 vaccination for patients with MS treated with cladribine or ocrelizumab in relation to post-vaccination SARS-CoV-2 IgG[1]

Anti-CD20

Vaccine responsiveness and time from last infusion[2]



Vaccine responsiveness and B cells status[2]



COVID-19, coronavirus disease 2019; DMT, disease modifying treatment; IgG, immunoglobulin G; MS, multiple sclerosis; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

1. Achiron A et al. *Ther Adv Neurol Disord.* 2021;14:17562864211012835. 2. Spiera R et al. *Ann Rheum Dis.* 2021;80:1357-1359. Figures adapted from *Ann Rheum Dis.* & *Ther Adv Neurol Disord.*

Immunological factors influencing seroconversion rate in patients treated with B-cell depleting therapies (BCDT)

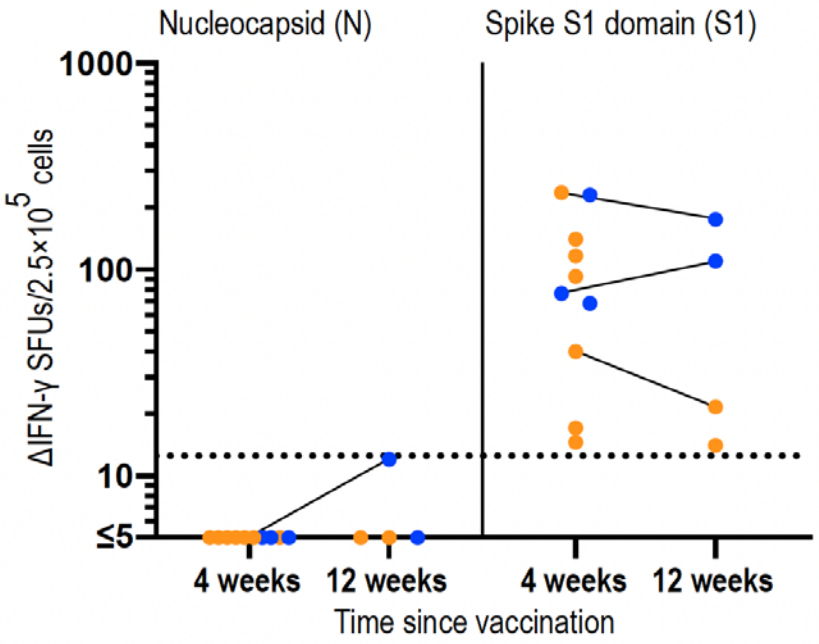
- Lower baseline (pre- vaccination) levels of IgM
- Low CD19 and CD20 counts
- Shorter interval from the last BCDT

► Age, BMI and total treatment duration did not differ between seroconverts and non-seroconverters

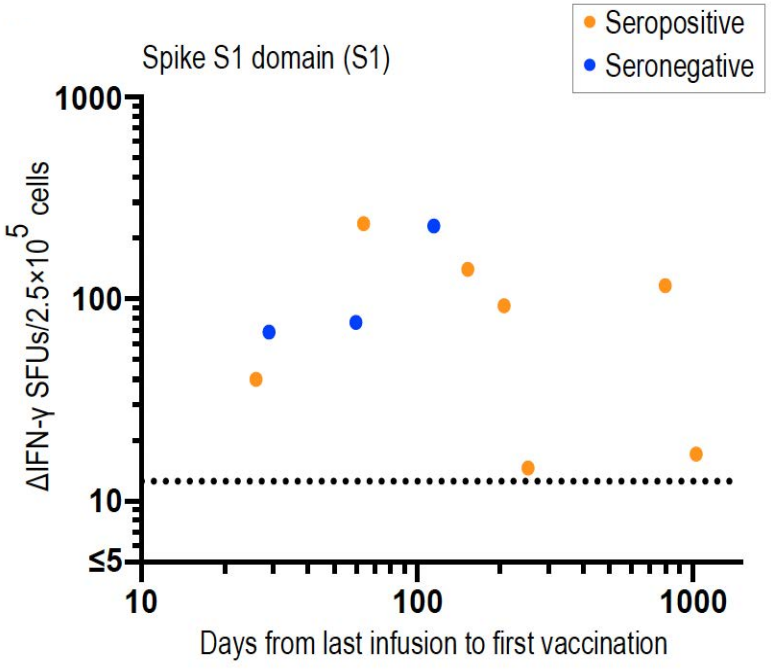
BMI, body mass index; IgM, immunoglobulin M.

Ali A et al., *Vaccine.* 2021;39(41):6111–6116.

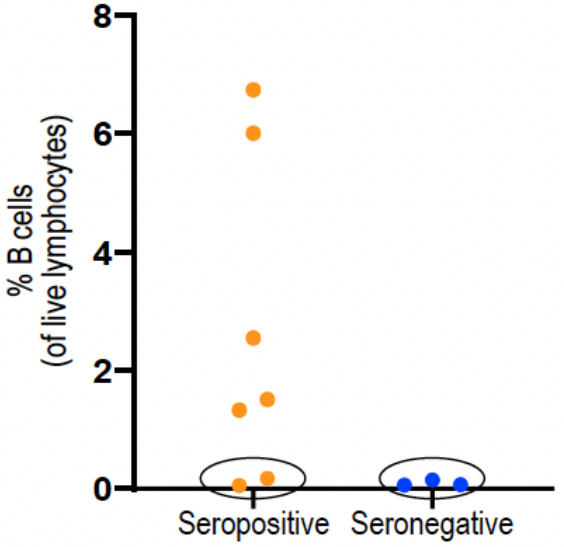
Development of humoral and cellular immunological memory following anti-SARS-CoV-2 vaccination in patients with BCDT



Serology status and number of ΔIFN-γ SFUs after stimulation with N or S1 peptides four (n = 10) and twelve (n = 4) weeks after SARS-CoV-2 vaccination in pwMS on anti-CD20



Serology status and number of ΔIFN-γ SFUs after stimulation with S1 peptides 4 weeks after vaccination (n = 10) and days from last anti-CD20 infusion to first vaccine dose

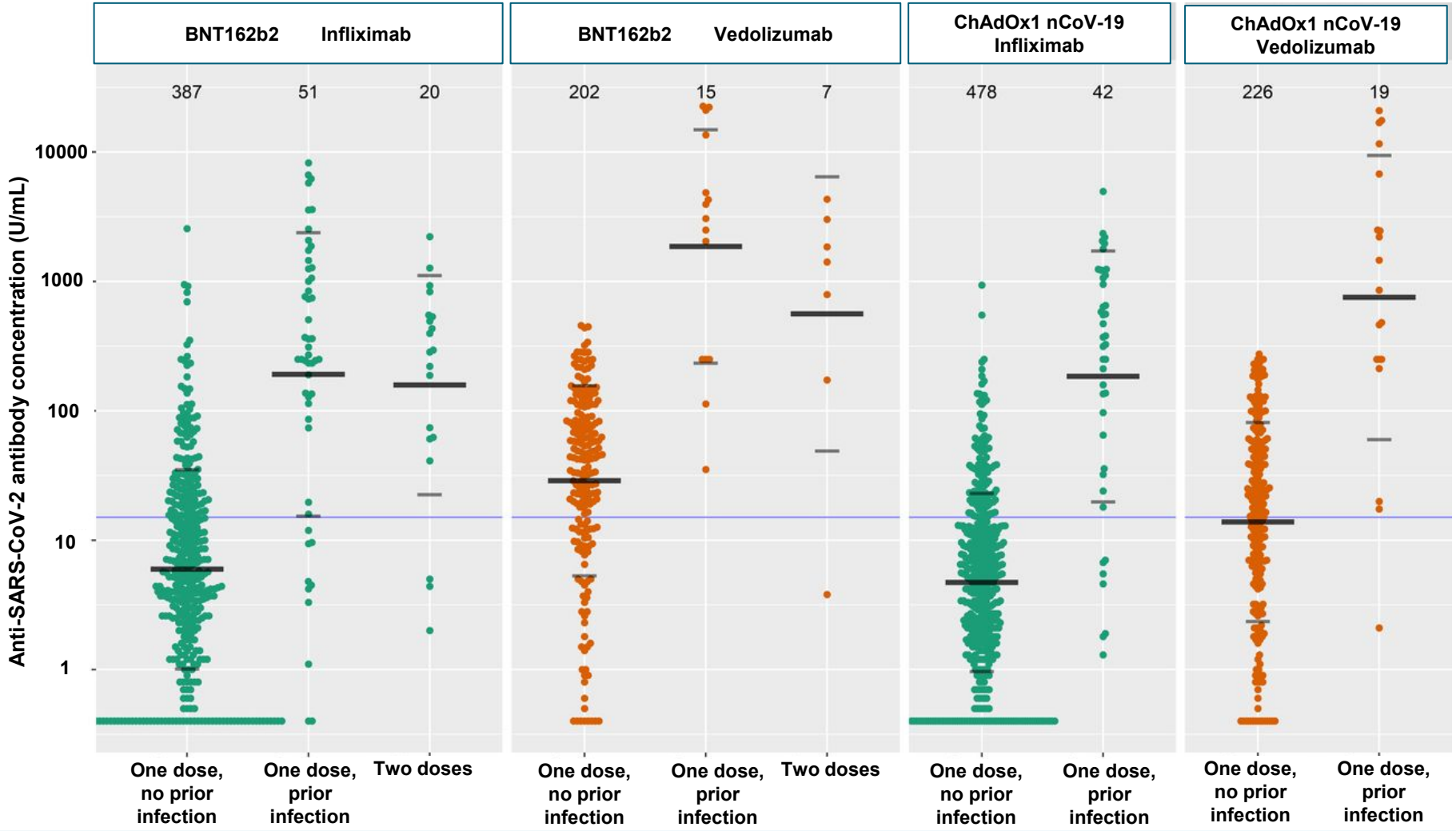


Percentages of B cells in seropositive (n = 7) and seronegative (n = 3) pwMS 4 weeks after vaccination

BCDT, B-cell depleting therapies; IFN; interferon; pwMS, persons with multiple sclerosis; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; SFU, spot forming unit.

Högelin KA et al. *iScience.* 2021;24(9):103078. Figures reproduced with permission from *iScience.*

Anti-SARS-CoV-2 spike antibody concentration, stratified by biological therapy (infliximab vs vedolizumab), prior infection and number of doses and type of vaccine



Vaccines = BNT162b2 and ChAdOx1 nCoV-19. SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

Kennedy NA et al. *Gut.* 2021;70(10):1884-1893.

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Timing of vaccination

Timing of vaccination in patients on immunotherapies

Medications	COVID-19 vaccine administration timing considerations
Hydroxychloroquine, sulfasalazine, leflunomide, apremilast, IVIG	Do not delay or adjust vaccine administration timing
Methotrexate, mycophenolate mofetil, Azathioprine, cyclophosphamide (IV or oral), TNFi, IL- 6R, IL- 1R, IL- 17, IL- 12/23, IL- 23, belimumab, JAK inhibitors, abatacept (IV or SC), oral calcineurin inhibitors, GCs (prednisone-equivalent dose <20 mg/day)	Do not delay or adjust vaccine administration timing
Rituximab	Assuming that a patient's COVID- 19 risk is low or able to be mitigated by preventive health measures (e.g., self- isolation), schedule vaccination so that the vaccine series is initiated ~4 weeks prior to next scheduled rituximab cycle

COVID-19, coronavirus disease 2019; GC, glucocorticoids; IL, interleukin; IV, intravenous; IVIG, intravenous immunoglobulin; JAK, Janus kinase; SC, subcutaneous; TNFi, tumor necrosis factor inhibitor.

Curtis JR et al. *Arthritis Rheumatol.* 2021;73(10):e60–e75.

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Conclusions

General considerations: vaccination of people who are immunocompromised

- Vaccinating people who are immunocompromised can be challenging. It can be difficult to determine the extent to which a person is immunocompromised, because it depends on the underlying disease, medical treatment and other factors. The person may have:[1]
  - reduced protection from previous vaccination
  - reduced response to vaccines, so they may need extra doses
  - an increased risk of vaccine-preventable diseases or complications
  - an increased risk of adverse events, particularly from live vaccines

When considering vaccinating people on immunosuppressive therapy, it may be important to review the:
mechanism, and duration of the effect on the immune system, of the medicine or other treatment
consequence of using combination therapies for example, corticosteroids and other immunosuppressive therapies such as disease-modifying anti-rheumatic drugs, which can contribute to the nature, extent and length of the immunocompromising condition
anticipated duration of the person's immunocompromised state, whether due to the therapy or the underlying disease

Healthcare professionals and investigators should apply clinical judgment and consider the risks and benefits of administering a vaccine in immunocompromised patients

1. AU Immunization Handbook. https://immunisationhandbook.health.gov.au/vaccination-for-special-risk-groups/vaccination-for-people-who-are-immunocompromised URL accessed October 2021.

Open research questions

- What measures of immunity correlate with clinical protection from SARS-CoV-2?
- At what rate does immunity decay post-vaccination (and differences across vaccines)?
- Need to understand the factors linked to vaccination non-response
- How to potentiate long-term immunogenicity?
- Optimal vaccination strategies timing of second vaccinations, booster doses, the use of adjuvants and/or switching between vaccines with different mechanisms of action

SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.