CRA Recommendation on Covid-19 Vaccination in Persons with Autoimmune Rheumatic Disease

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The Canadian Rheumatology Association guideline panel suggests using COVID-19 vaccination in persons with autoimmune rheumatic disease (conditional recommendation, low certainty of the evidence about effects).

- This recommendation is based on evidence for currently approved COVID-19 vaccines: BNT 162b2 (Pfizer-BioNTech) and mRNA-1273 (Moderna)
- The panel agreed that for the majority of patients the potential benefits will probably outweigh the potential harms in people with ARDs. Some patients at low risk for symptomatic COVID-19 infection and severe COVID-19 (e.g. young otherwise healthy patients who are able to follow public health measures), or patients who find the uncertainty of potential harms important, might choose to wait until more direct information is available.
- Persons with autoimmune rheumatic diseases should be informed that direct evidence of benefits and safety of the COVID-19 vaccine in people with autoimmune rheumatic disease is not yet available.
- Persons with autoimmune rheumatic diseases who meet local eligibility criteria for COVID-19 vaccination should not be denied access to vaccination and should not be required to take additional steps compared to people without autoimmune rheumatic diseases to obtain their vaccination.

View the Evidence Profiles and Evidence-to-Decision Framework.

Justification

The CRA panel suggests using COVID-19 vaccination due to moderate certainty of large anticipated desirable effects, low certainty of trivial anticipated undesirable effects, increased health equity, and probable acceptability and feasibility. This recommendation places a relatively high value on the large desirable anticipated effects based on moderate certainty evidence, and a relatively lower value on the trivial undesirable anticipated effects based on low certainty evidence.

Detailed justification

The CRA panel decided on a conditional recommendation for COVID-19 vaccination. The panel balanced the moderate certainty in the vaccine benefits (prevention of symptomatic and severe/critical COVID-19 infection) against the low certainty of evidence for harms. Although the magnitude of the best estimate of harms was judged to be trivial, the uncertainty in the evidence led to a conditional recommendation. The panel was clear

that for the majority of patients the benefits will outweigh the uncertainty in potential harms in people with ARDs. Some patients at low risk for COVID-19 infection and severe COVID-19 (e.g. young otherwise healthy patients who are able to follow public health measures), or patients who find the uncertainty of potential harms important, might choose to wait until more direct information is available. Voting was unanimous on the direction of the recommendation (favouring the vaccine), but was not unanimous on the strength of the recommendation. Two panelists felt a strong recommendation for the vaccine should be made. The remaining panelists felt that if direct evidence of vaccine safety and efficacy in people with autoimmune rheumatic diseases was available, a strong recommendation could be supported. This is a living recommendation and will be reassessed when important new evidence becomes available.

Subgroup considerations

- People taking rituximab: Based on serological studies from other vaccines, rituximab is expected to decrease immunogenicity. Prior guidelines for other vaccines in patients with ARDs have recommended that immunization be deferred to ⩾5 months after the last dose and at least 4 weeks prior to the subsequent dose of rituximab [2].
- People taking other DMARDs: Some other DMARDs may reduce protection from the vaccine. Given the large magnitude of benefit of the COVID-19 vaccines, it is likely that the benefits of the vaccine will still be large for most ARD patients. Continuing medications will often be the safest option to prevent disease flares until more evidence is available. This is in line with guidance from the British Society of Rheumatology [5]. Recent guidance from the American College of Rheumatology recommended holding some medications (methotrexate, JAK inhibitors, abatacept) around the time of COVID-19 vaccination [45]. The CRA COVID-19 guideline panel did not feel that this guidance could be endorsed at this point but will review the full guidance document and evidence review once published. Any decision to hold medications should be discussed between a patient and their rheumatologist or healthcare team.
- Additional considerations apply for pregnant and breastfeeding women. These were not covered in the scope of this guideline.

Implementation considerations

- As vaccine access is determined by provincial health authorities, it will be essential to ensure people with ARDs do not face unnecessary additional barriers to vaccine access. For instance, people with ARDs should not be required to obtain a physician letter as proof of an informed decision discussion. A decision tool, co-developed by the Canadian Rheumatology Association and the Canadian Arthritis Patient Alliance to support decision-making for the COVID-19 vaccine in people with ARDs is available at: https://rheum.ca/decision-aid/.
- People with ARDs may have mobility limitations and appropriate access to vaccine clinics should be ensured.

Monitoring and evaluation

- Monitoring of vaccine uptake should occur in people with ARDs, including populations at risk of inequity. Low uptake may point to barriers to access or hesitancy.
- The frequency of serious adverse events, disease flares, and COVID-19 infection/serious outcomes should be followed in patients with ARDs who do and do not receive the vaccine.

Research priorities

The following research areas were considered a high priority:

- Observational evidence on the frequency of harms (in particular serious adverse events/serious disease flares) in people with ARDs: If very infrequent, may lower the importance of these outcomes
- Evidence comparing the frequency of serious adverse events and autoimmune adverse events in people with ARDs: if not different with sufficient certainty, the panel may decide not to rate the quality of evidence for harms down for indirectness
- Evidence on the benefits (both clinical outcomes and serological studies) in people with ARDs on different medications: May help identify subpopulations of patients with lower benefits and inform decisions regarding whether to hold medications around the time of vaccination.
- Evidence on patient values preferences for the benefits and harms across different patient populations
- Understanding vaccine hesitancy and barriers to vaccine access faced by persons with ARDs
- Understanding vaccine benefits and harms in populations at risk for inequities. We additionally encourage the collection of data that documents vaccine access difficulties for patients facing barriers to accessing vaccination, to support advocacy for improved prioritization protocols and vaccine delivery.

REFERENCES

1 Furer V, Rondaan C, Heijstek MW, Agmon-Levin N, van Assen S, Bijl M, et al. 2019 update of EULAR recommendations for vaccination in adult patients with autoimmune inflammatory rheumatic diseases. *Ann Rheum Dis*. 2020;79(1):39-52.

2 Papp KA, Haraoui B, Kumar D, Marshall JK, Bissonnette R, Bitton A, et al. Vaccination Guidelines for Patients With Immune-Mediated Disorders on Immunosuppressive Therapies. *J Cutan Med Surg*. 2019;23(1):50-74.

3 Polack FP, Thomas SJ, Kitchin N, Absalon J, Gurtman A, Lockhart S, et al. Safety and Efficacy of the BNT162b2 mRNA Covid-19 Vaccine. *N Engl J Med*. 2020;383(27):2603-15.

4 Baden LR, El Sahly HM, Essink B, Kotloff K, Frey S, Novak R, et al. Efficacy and Safety of the mRNA-1273 SARS-CoV-2 Vaccine. *N Engl J Med*. 2020.

5 British Society for Rheumatology. COVID-19 guidance 2020 [Available from: https://www.rheumatology.org.uk/practice-quality/covid-19-guidance.

6 COVID-19 vaccine tracker.

7 Ribeiro AC, Laurindo IM, Guedes LK, Saad CG, Moraes JC, Silva CA, et al. Abatacept and reduced immune response to pandemic 2009 influenza A/H1N1 vaccination in patients with rheumatoid arthritis. *Arthritis Care Res (Hoboken)*. 2013;65(3):476-80.

8 Arad U, Tzadok S, Amir S, Mandelboim M, Mendelson E, Wigler I, et al. The cellular immune response to influenza vaccination is preserved in rheumatoid arthritis patients treated with rituximab. *Vaccine*. 2011;29(8):1643-8.

9 Eisenberg RA, Jawad AF, Boyer J, Maurer K, McDonald K, Prak ET, et al. Rituximab-treated patients have a poor response to influenza vaccination. *J Clin Immunol*. 2013;33(2):388-96.

10 Oren S, Mandelboim M, Braun-Moscovici Y, Paran D, Ablin J, Litinsky I, et al. Vaccination against influenza in patients with rheumatoid arthritis: the effect of rituximab on the humoral response. *Ann Rheum Dis*. 2008;67(7):937-41.

11 Ribeiro AC, Guedes LK, Moraes JC, Saad CG, Aikawa NE, Calich AL, et al. Reduced seroprotection after pandemic H1N1 influenza adjuvant-free vaccination in patients with rheumatoid arthritis: implications for clinical practice. *Ann Rheum Dis*. 2011;70(12):2144-7.

12 Favalli EG, Ingegnoli F, Cimaz R, Caporali R. What is the true incidence of COVID-19 in patients with rheumatic diseases? *Ann Rheum Dis*. 2021;80(2):e18.

13 Fredi M, Cavazzana I, Moschetti L, Andreoli L, Franceschini F, Brescia Rheumatology C-SG. COVID-19 in patients with rheumatic diseases in northern Italy: a single-centre observational and case-control study. *Lancet Rheumatol*. 2020;2(9):e549-e56.

14 Liu M, Gao Y, Zhang Y, Shi S, Chen Y, Tian J. The association between severe or dead COVID-19 and autoimmune diseases: A systematic review and meta-analysis. *J Infect*. 2020;81(3):e93-e5.

15 Michelena X, Borrell H, Lopez-Corbeto M, Lopez-Lasanta M, Moreno E, Pascual-Pastor M, et al. Incidence of COVID-19 in a cohort of adult and paediatric patients with rheumatic diseases treated with targeted biologic and synthetic disease-modifying anti-rheumatic drugs. *Semin Arthritis Rheum*. 2020;50(4):564-70.

16 Andersen KM, Mehta HB, Palamuttam N, Ford D, Garibaldi BT, Auwaerter PG, et al. Association Between Chronic Use of Immunosuppresive Drugs and Clinical Outcomes From Coronavirus Disease 2019 (COVID-19) Hospitalization: A Retrospective Cohort Study in a Large US Health System. *Clin Infect Dis*. 2021.

17 Dougados M, Soubrier M, Antunez A, Balint P, Balsa A, Buch MH, et al. Prevalence of comorbidities in rheumatoid arthritis and evaluation of their monitoring: results of an international, cross-sectional study (COMORA). *Ann Rheum Dis*. 2014;73(1):62-8.

18 Hitchon CA, Boire G, Haraoui B, Keystone E, Pope J, Jamal S, et al. Self-reported comorbidity is common in early inflammatory arthritis and associated with poorer function and worse arthritis disease outcomes: results from the Canadian Early Arthritis Cohort. *Rheumatology (Oxford)*. 2016;55(10):1751-62.

19 Urowitz MB, Gladman DD, Farewell V, Su J, Romero-Diaz J, Bae SC, et al. Accrual of Atherosclerotic Vascular Events in a Multicenter Inception Systemic Lupus Erythematosus Cohort. *Arthritis Rheumatol*. 2020;72(10):1734-40.

20 Strangfeld A, Schafer M, Gianfrancesco MA, Lawson-Tovey S, Liew JW, Ljung L, et al. Factors associated with COVID-19-related death in people with rheumatic diseases: results from the COVID-19 Global Rheumatology Alliance physician-reported registry. *Ann Rheum Dis*. 2021.

21 Gianfrancesco M, Hyrich KL, Al-Adely S, Carmona L, Danila MI, Gossec L, et al. Characteristics associated with hospitalisation for COVID-19 in people with rheumatic disease: data from the COVID-19 Global Rheumatology Alliance physician-reported registry. *Ann Rheum Dis*. 2020;79(7):859-66.

22 Hurd K, Barnabe C. Systematic review of rheumatic disease phenotypes and outcomes in the Indigenous populations of Canada, the USA, Australia and New Zealand. *Rheumatol Int*. 2017;37(4):503-21.
23 Puges M, Biscay P, Barnetche T, Truchetet ME, Richez C, Seneschal J, et al. Immunogenicity and impact on disease activity of influenza and pneumococcal vaccines in systemic lupus erythematosus: a systematic literature review and meta-analysis. *Rheumatology (Oxford)*. 2016;55(9):1664-72.
24 Shimabukuro T. COVID-19 vaccine safety update: Advisory Committee on Immunization Practices (ACIP) January 27, 2021 [Available from: https://www.cdc.gov/vaccines/acip/meetings/slides-2021-1-27-21.html.
25 Israeli Vaccination Monitoring Commitee Summary Report, January 10, 2021 [Available from: https://www.health.gov.il/English/MinistryUnits/HealthDivision/PublicHealth/Epidemiology/Pages/default.aspx.
26 Rothery C, Bojke L, Richardson G, Bojke C, Moverley A, Coates L, et al. A discrete choice experiment to explore patients' willingness to risk disease relapse from treatment withdrawal in psoriatic arthritis. *Clin Rheumatol*. 2016;35(12):2967-74.
27 van Herwaarden N, van der Maas A, Minten MJ, van den Hoogen FH, Kievit W, van Vollenhoven RF, et al. Disease activity guided dose reduction and withdrawal of adalimumab or etanercept compared with usual care in rheumatoid arthritis: open label, randomised controlled, non-inferiority trial. *BMJ*. 2015;350:h1389.
28 Hazlewood GS, Loyola-Sanchez A, Bykerk V, Hull PM, Marshall D, Pham T, et al. Patient and Rheumatologist Perspectives on Tapering DMARDs in Rheumatoid Arthritis: A Qualitative Study. *Rheumatology (Oxford)*. 2021;[submitted].
29 Stamp LK, Chan SJ, Marra C, Helme C, Treharne GJ. Tapering biologic therapy for people with rheumatoid arthritis in remission: A review of patient perspectives and associated clinical evidence. *Musculoskeletal Care*. 2019;17(3):161-9.
30 Durand C, Eldoma M, Marshall DA, Bansback N, Hazlewood GS. Patient Preferences for Disease-modifying Antirheumatic Drug Treatment in Rheumatoid Arthritis: A Systematic Review. *J Rheumatol*. 2020;47(2):176-87.
31 ANZMUSC. An Australian Living Guideline for the Pharmacological Management of Inflammatory Arthritis. 2020;Version 0.4.
32 Adamichou C, Bertsias G. Flares in systemic lupus erythematosus: diagnosis, risk factors and preventive strategies. *Mediterr J Rheumatol*. 2017;28(1):4-12.
33 Sandmann F, Davies N, Vassall A, Edmunds WJ, Jit M. The potential health and economic value of SARS-CoV-2 vaccination alongside physical distancing in the UK: transmission model-based future scenario analysis and economic evaluation. *medRxiv*. 2020:2020.09.24.20200857.
34 Nixon SA. The coin model of privilege and critical allyship: implications for health. *BMC Public Health*. 2019;19(1):1637.
35 Crenshaw K. Demarginalizing the Intersection of Race and Sex: A Black Feminist Critique of Antidiscrimination Doctrine, Feminist Theory and Antiracist Politics. *University of Chicago Legal Forum*. 1989:139-68.
36 O'Neill J, Tabish H, Welch V, Petticrew M, Pottie K, Clarke M, et al. Applying an equity lens to interventions: using PROGRESS ensures consideration of socially stratifying factors to illuminate inequities in health. *J Clin Epidemiol*. 2014;67(1):56-64.

37 Government of Canada. Recommendations on the use of COVID-19 vaccines 2021 [Available from: https://www.canada.ca/en/public-health/services/immunization/national-advisory-committee-on-immunization-naci/recommendations-use-covid-19-vaccines.html.

38 Pianarosa E, Chomistek K, Hsiao R, Anwar S, Umaefulam V, Hazlewood G, et al. Global Rural and Remote Patients with Rheumatoid Arthritis: A Systematic Review. *Arthritis Care Res (Hoboken)*. 2020.

39 Safiri S, Kolahi AA, Hoy D, Smith E, Bettampadi D, Mansournia MA, et al. Global, regional and national burden of rheumatoid arthritis 1990-2017: a systematic analysis of the Global Burden of Disease study 2017. *Ann Rheum Dis*. 2019;78(11):1463-71.

40 Sallam M. COVID-19 vaccine hesitancy worldwide: a systematic review of vaccine acceptance rates. *medRxiv*. 2021:2020.12.28.20248950.

41 Lazarus JV, Ratzan SC, Palayew A, Gostin LO, Larson HJ, Rabin K, et al. A global survey of potential acceptance of a COVID-19 vaccine. *Nature Medicine*. 2020.

42 Valeria Valerio HCS, Emily G McDonald, Alyson Turner, Charles Frenette, Marie Hudson, Brian J Ward, Ines Colmegna. High Frequency of COVID Vaccine Hesitancy Among People Immunized for Influenza. *[unpublished]*.

43 Boucher VG, Pelaez S, Gemme C, Labbe S, Lavoie KL. Understanding factors associated with vaccine uptake and vaccine hesitancy in patients with rheumatoid arthritis: a scoping literature review. *Clin Rheumatol*. 2020.

44 Campochiaro C, Trignani G, Tomelleri A, Cascinu S, Dagna L, Group C-VS. Potential acceptance of COVID-19 vaccine in rheumatological patients: a monocentric comparative survey. *Ann Rheum Dis*. 2021.