CDC/IDSA COVID-19 Clinician Call

COVID-19 Outcomes in Immunosuppressed Individuals with Autoimmune Disease; Variants Q&A

March 27, 2021

Q&A

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1. **What are the recommendations about COVID-19 vaccine in patients with rheumatologic diseases that can be exacerbated with the vaccine and possible need steroid treatment?**

   There are 2 early papers looking at vaccine adverse effects in people with autoimmune diseases. So far, the data is quite reassuring, and does not show more disease exacerbations or more severe adverse effects (admittedly, there is much more work to do in this area):

   https://ard.bmj.com/content/early/2021/03/24/annrheumdis-2021-220272

   https://ard.bmj.com/content/early/2021/03/24/annrheumdis-2021-220231

2. **Should immunosuppressive drugs such as mycophenolate, etc. be held during the acute infection and if so when should they be restarted after recovery?**

   We do recommend holding medications such as mycophenolate in patients with non-life-threatening rheumatic disease. The ACR guidance on holding and re-starting medications provides detailed recommendations regarding the various therapies.

   https://www.rheumatology.org/Portals/0/Files/ACR-COVID-19-Clinical-Guidance-Summary-Patients-with-Rheumatic-Diseases.pdf

3. **Should rheum meds e.g., methotrexate, or other mAbs be held during COVID infection? And what about around the time of vaccination?**

   This is a great ACR resource that will be updated regularly regarding which medications to hold and for how long for people on immunosuppression: https://www.rheumatology.org/Portals/0/Files/COVID-19-Vaccine-Clinical-Guidance-Rheumatic-Diseases-Summary.pdf.

4. **Any data on vaccine response with patients on TNFi?**

   The data is still very preliminary, but immune responses (IgG to spike protein) look only minimally attenuated in those on anti-TNF.

5. **How long following the most recent rituximab infusion is the increased likelihood of mortality due to COVID observed?**

   This is a good question. We unfortunately do not have data on rituximab timing, but we presume that risk persists while B cells (CD19 levels) remain undetectable.

6. **Can you try to reconcile why JAK inhibitor baricitinib appears to be beneficial when combined with remdesivir, but the cohort study suggests JAK inhibitor may increase risk for bad outcomes.**

   This is a good question. JAKi decrease the immune response to viral infections (as evidenced by serious zoster infections; systemic review summarizing some of this data https://pubmed.ncbi.nlm.nih.gov/32931985/). I suspect early in infection where the innate immune response is important, JAKi is harmful; later in infection when there is an aberrant immune response leading to organ damage, JAKi may have a role (ACTT-2 study).

7. **For patients who are on rituximab, should they have different recommendations for COVID-19 vaccines, given the effect of rituximab on the vaccine-elicited immune response?**

   There is unfortunately a high likelihood that these patients will not develop a humoral immune response to the vaccine. We await the T cell response data. For now, ACR recommends trying to vaccinate people before they receive their next dose to the extent possible.

8. **Is there any data on the response to COVID vaccination following rituximab?**

   Yes, unfortunately the very preliminary data shows that these patients do not form IgG anti-spike protein responses. We await the T cell response data.

9. **Given the worse COVID related outcomes in pts taking JAK1 inhibitors, coupled with the new data of significant adverse risks on Xeljanz (JAK1), is it recommended for pts on JAK1 -Xeljanz in particular- to switch to alternate RA therapy, such as anti-IL-6?**

   This is a good question. For many patients, JAKi is not first or even second line therapy, so options are often limited. In patients who do have other options, it is reasonable to present available data and reach a shared decision about therapy.

10. **Steroids have demonstrated mortality benefit in severe covid-19. What is the recommendation for steroid dosing in patients who are already on prednisone when they acquire the infection?**

    If patients develop mod/severe COVID, current recommendations are these patients receive standard RECOVERY dosing of dexamethasone. There is very little data, however, in this patient population.

11. **Should a higher dose of corticosteroids be used on those patients who have been on chronic steroids? Is it safe to add toci to steroid when they develop respiratory failure?**

    This is a good question, and unfortunately, we have no data. Most of these patients should at least receive standard doses of dexamethasone and toci; however, I would not mix biologics (so if someone is on TNFi, I would not add toci) because of serious concern for infection

12. **How long following the most recent rituximab infusion is there is a decreased IgG response to COVID vaccination?**

    We will be studying this in the assembled cohort that I showed - stay tuned!

13. **Will you recommend more the RNA vaccines or adenovirus-based vaccines to autoimmune diseases?**

    There is at least one study examining this. At the current time, the ACR does not recommend one vaccine over another.

14. **I wonder if the Rtx group would also be the group where the protein loss where the more significant. Wouldn't be predictable the response to vaccination be lower in one who is losing proteins, whether in urinary loss or low liver production?**

    Yes, it is reasonable to postulate that some of these patients may lose immunoglobulin through urine. However, many rituximab patients are on maintenance therapy for vasculitis and do not have active liver or kidney disease, so I suspect this is a generalized effect.

15. **Any new data on autoantibodies?**

    Here is a nice recent paper regarding autoantibody responses in people with severe COVID-19: https://www.nature.com/articles/s41586-021-03234-7.

16. **What do you recommend on patient on IVIG and vaccination?**

    These patients should receive vaccination; no special precautions at this time.

17. **Are mRNA vaccines more or less safe and effective for these patients?**

    Data is still very preliminary, but published studies so far do not a show safety signal https://ard.bmj.com/content/early/2021/03/24/annrheumdis-2021-220231 and https://ard.bmj.com/content/early/2021/03/24/annrheumdis-2021-220272

18. **What are the reasons/explanations, if any, for those diagnosed with "APA" to experience more prolonged, "allergic-like" reactions to the Moderna mRNA vaccine?**

    This will need to be closely studied; so far this is not a signal we have seen in the limited literature to date. It may be that the underlying autoimmune disease is not related to the allergic reaction, but we need more data to know for sure.

19. **Does the condition itself inhibit or slow production of antibodies to immunize "APA" patients against Covid?**

    We do worry that immune stimulation from vaccine can precipitate a disease flare in patients with autoimmunity. Interestingly, prior RCTs that have examined this issue for influenza and other vaccines have not shown a significant signal. Early data, such as the studies above, show that patients with SLE and other conditions do make antibodies to spike protein after COVID-19 vaccine. Some immunosuppressants might slightly attenuate this response.

20. **Are there studies underway or study results re: levels of antibody production following full vaccination in "APA" patients as there are re: transplant patients? If so, what are the results?**

    See the two studies above; more are coming very soon.

21. **Were those "APA" patients who received full vaccination told to wait longer than 2 weeks before relaxing some CDC-recommended Covid safety protocols when gathering with other fully vaccinated persons told this due to medical knowledge that their condition could inhibit or slow production of antibodies to safely immunize them to the fullest against Covid offered by vaccine or for other reasons? If for other reasons, what are these?**

    The ACR will periodically update its vaccine guidance, hopefully including post-vaccine procedures for people with autoimmune diseases. This might be a helpful resource moving forward: https://www.rheumatology.org/Portals/0/Files/COVID-19-Vaccine-Clinical-Guidance-Rheumatic-Diseases-Summary.pdf.