GUTHY JACKSON Charitable Foundation

# FAQs

## NMOSD & COVID-19: Immune Suppression & Vaccination

**Updated: March 1, 2021**

*We hope everyone is well and coping with the challenges of the COVID-19 pandemic. With information changing on a daily basis, the Foundation continues to do all it can to aid the NMOSD community in navigating the many questions at hand. The Foundation does not provide clinical care or vaccine recommendations or policies, but we are hopeful these Frequently Asked Questions (FAQs) will assist NMOSD patients in making informed decisions with their doctors, healthcare teams, caregivers and families.*

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1. **Question: Do NMOSD or therapies used to treat NMOSD increase the risk of SARS-CoV-2 infection ?**

   ***Answer —*** In limited clinical studies performed since the onset of the COVID-19 pandemic,[A] no increased risk of COVID-19 infection has been observed in patients with NMOSD, regardless of which therapeutic agents were being used as treatment. These important and reassuring results may be due to several reasons, including preventive measures taken by patients and healthcare providers to guard against infection, and that the underlying immunology of NMOSD itself does not appear to increase risks of COVID-19 infection or disease.

2. **Question: Are NMOSD patients on immunosuppressive therapies more likely to have severe COVID-19 ?**

   ***Answer —*** No clinical studies published to date have found a heightened risk of severe disease (e.g., hospitalization, ICU admission or death) due to COVID-19 in patients with NMOSD as compared to other members of the community—regardless of which therapeutic regimen is used in their NMOSD treatment. As above, this reassuring finding likely involves good precautionary practices by patients, families, caregivers and healthcare providers.

3. **Question: Should persons on immunosuppressive therapy for NMOSD be vaccinated for COVID-19 ?**

   ***Answer —*** There are several good reasons why NMOSD patients should be vaccinated:

   a. The U.S. National Institutes of Health and U.S. Centers for Disease Control & Prevention recommend that persons using immunosuppressive therapies receive an mRNA or non-live COVID-19 vaccination. Being vaccinated also protects those not yet vaccinated.

   b. Many of the current vaccines provide protection against severe outcomes of COVID-19 disease (e.g. hospitalization, intensive care unit or death). Even if not perfect against the variant strains, vaccines still offer a best chance to prevent or reduce risks of severe illness in COVID-19 disease if infected by a variant virus. Bottom line: variant or not, it is best to be vaccinated and greatly increase your chances of having no or mild disease compared with not being vaccinated, which can increase your chances of having severe (or worse) COVID-19 outcomes.

c. Early data suggest many of the current vaccines are highly likely to increase the speed of clearance of the virus if you become infected. As above, here is the essential point: if vaccines can shorten the time for the virus to stay in the body, the lower the chances the virus can mutate into a concerning variant. So not only can vaccines protect against severe COVID-19 disease outcomes, they likely restrict the generation of viral mutants or variants, which is helpful to personal and public health.

d. Globally, more than 100 million individuals have now been vaccinated against COVID-19 disease. While the clinical trials focused on vaccinations in healthy persons, at this point many people with autoimmune diseases or those being treated with immunosuppressive agents (transplant recipients, cancer chemotherapy, asthma, and autoimmune diseases) have already been vaccinated. To date, the incidence of reported severe allergic reaction is very rare (the currently estimated rate is 2.5 per 1 million vaccinated); nearly all of these reactions occurred in persons already known to be highly allergic to other vaccines and environmental factors. These reactions almost always occurred within the 15-30 minute observation period recommended after vaccination. These persons recovered after a brief treatment and reported no subsequent issues. Thus, there is now a large real-world experience supporting the FDA and CDC guidance that current COVID-19 vaccines are extremely safe, even among those who have comorbidities (underlying diseases) or those on immune- modifying treatment regimens. Studies of COVID-19 vaccines in persons on immune suppressive therapies are also continuing to move forward.

e. All of the COVID-19 vaccines that have current regulatory approval or authorization are allowed to be used in patients taking medicines routinely used to treat NMOSD.[B–G]

**4. Question: Are some COVID-19 vaccines safest for use in persons taking immunosuppressive therapy ?**

***Answer —*** There are four COVID-19 vaccine platforms: 1) genetic [mRNA, DNA]; 2) viral vector (live/attenuated); 3) recombinant (protein only); 4) inactivated (whole inactivated virus). Of those vaccines receiving emergency use authorization or approval to date, the U.S. National Institutes of Health and U.S. Centers for Disease Control & Prevention recommend that persons taking immunosuppressive therapy receive COVID-19 vaccinations that use an mRNA (e.g. BioNTech-Pfizer or Moderna-NIH) or non-live viral vector (e.g. Oxford-AstraZeneca or Johnson & Johnson) platform. Some experts recommend mRNA vaccines be used over the viral–vectored vaccines in persons using immunosuppression therapy if possible, for two reasons: 1) greater reported efficacy; and 2) to minimize any risk related to viral DNA functioning. Other vaccines still being tested are recombinant (e.g. NovaVax), and are in theory expected to be safe for use in persons using immune suppressive therapies.

**5. Question: Do immunosuppressing drugs used in NMOSD lower effectiveness of COVID-19 vaccines ?**

***Answer —*** Different immunosuppressive medicines used in NMOSD therapy may have varying impacts on vaccine responses. It is important to note that even when using immunosuppressive therapy that may impede vaccine responses, some protection is better than no protection and there are good strategies that offer a best chance for vaccine effectiveness. For example, vaccinations may be given prior to starting immunosuppressive therapy, or in a vaccine "window" for best effectiveness. However, being vaccinated as soon as possible is likely to be best to reduce risk of severe COVID-19 outcomes. Decisions regarding vaccination (type, timing, etc.) are best made in consultation with an NMOSD specialist or healthcare provider. General themes of vaccine use with distinct therapeutic classes are summarized below: [B-G]

a. C5 inhibitors (e.g. eculizumab, ravulizumab) do not inhibit antibody production. Based on how such agents work, they are unlikely to diminish a response to any of the COVID-19 vaccines currently approved or authorized, regardless of when administered. As with any vaccination, please consult your healthcare provider to decide the best COVID-19 vaccine schedule and type for you.

b. A body of published data suggests that B cell and/or antibody responses to vaccines may be diminished with use of B cell depletion (e.g. inebilizumab, rituximab). For this reason, many experts suggest it is best to vaccinate prior starting such therapy, or at a pause in dosing toward the end of a 6 month cycle of therapy (e.g. wait 7-14 days after vaccination for next treatment dose). However, this scheduling is not always practical, and being vaccinated as soon as possible is likely more important than timing the vaccine with use of B cell depletion. Please consult your healthcare provider to select the best vaccination schedule and type of COVID-19 vaccine for you.

c. A body of published data suggest IL-6 receptor inhibition (e.g. satralizumab, tocilizumab) does not significantly impede classical vaccines; this is likely true for COVID-19 vaccines (note: data not yet available). With use of IL-6 receptor inhibition, vaccination may be best the third week in a once-per month treatment schedule (or 7 days prior to the next drug dose) but with no pause in therapy. However, this scheduling is not always practical, and being vaccinated as soon as possible may be more important than timing the vaccine in use of IL-6R inhibition. As with any immunization, please consult your healthcare provider to select the best vaccination schedule and type of COVID-19 vaccine type for you.

d. Azathioprine appears to have only a modest impact on immune responses to vaccines, allowing a good chance for protective immunity to COVID-19 disease, particularly severe disease or death. As this drug is often taken daily, it is best to be vaccinated as soon as possible with no pause in treatment. Please consult your healthcare provider to select the best vaccination schedule and COVID-19 vaccine type for you.

e. Mycophenolate appears to have only a modest impact on immune response to vaccines, allowing a good chance for protective immunity to COVID-19 disease, particularly severe disease or death. As this drug is often taken daily, it is best to be vaccinated as soon as possible with no pause in treatment. Please consult your healthcare provider to select the best vaccination schedule and COVID-19 vaccine type for you.

f. While low dose oral steroids are unlikely to interfere with vaccine response, high–dose intravenous (IV) steroids are likely to have a greater suppression of immune responses to COVID-19 or other vaccines. It is best to avoid vaccinating within 7 days of the latest IV steroid dose. Please consult your healthcare provider to select the best vaccination schedule and COVD-19 vaccine type for you.

g. Plasmapheresis (plasma exchange; PLEX) is designed to remove pathogenic antibodies or other large proteins from the bloodstream. Unfortunately, it also removes beneficial antibodies, including those that may neutralize the SARS-CoV-2 virus, and monoclonal antibody (biologic) drugs such as eculizumab, inebilizumab or satralizumab. Patients should discuss with their neurologist whether or how they might need to re-establish their biologic therapy levels following PLEX.

***Note***: specific information pertaining to each of the COVID-19 vaccines with current or pending approval or emergency use authorization is referenced below. [H-K]

6. **Question: Do COVID-19 vaccines or other vaccinations increase the risk of having an NMOSD relapse ?**

***Answer —*** At the present time there is no direct evidence that COVID-19 or any other vaccines cause relapses. It may be best to minimize chances of fever or allergic response to vaccines in NMOSD. Patients may wish to discuss with their NMOSD specialists the idea of pre-medicating with an antipyretic (e.g. a fever-reducer such as Tylenol) and antihistamine (such as Benadryl, Claritin, Zyrtec, etc.) at normal doses 1 hour prior to vaccination. This may be especially useful for the second dose of COVID-19 vaccines requiring two doses.

7. **Question: Are antibodies the only immune response generated following a COVID-19 vaccination ?**

***Answer —*** It is important to emphasize that vaccines induce their significant immune protection against COVID-19 through T cells and interferons, not just by creating antibodies. So, COVID-19 vaccines are likely to be at least partially protective against severe COVID-19 disease even in the setting of B cell depletion that limits strong B cell or antibody responses.

8. **Question: Are variants of the virus more likely to develop in persons on immunosuppressive therapy ?**

***Answer —*** It may be reassuring to NMOSD patients that many of the variants of concern to date have been isolated from younger, healthy individuals, often with no signs or symptoms of COVID-19 disease. Other variants of the virus have been isolated from persons with severe infections lasting a month—or longer. Most RNA viruses, including the SARS-CoV-2 virus that causes COVID-19, intentionally make mistakes when they replicate their "genetic material" (that is RNA). This RNA replication process is called error-prone proofreading: the virus intentionally makes mistakes in its RNA that are not corrected. This process generates many mutants, a few of which may provide a mutant with a competitive advantage to infect more people, cross over to infect animal reservoirs, etc. The essential point is that the virus does not appear to target immunosuppressed persons—it mutates by design regardless of its host.

9. **Question: Are the mutated SARS-CoV-2 viruses likely to completely resist COVID-19 vaccination ?**

***Answer —*** There are several reasons for optimism that the current COVID-19 vaccines likely provide good if not excellent protection against most emerging variant strains. First, immune responses to COVID-19 vaccines tend to cross-protect against many forms of the SARS-CoV-2 virus and even other coronaviruses. Second, spike protein variants of concern thus far have few mutations within their T cell antigens (epitopes); and even fewer mutations are seen in other key antigens (e.g., such as the N, M or E proteins); Third, COVID-19 vaccines induce many different types of antibodies, some of which are highly likely to protect against the variants; Fourth, the immune system learns over time and may keep pace with any viral mutations. For example, in a process known as affinity maturation, B cells & antibodies become better at protecting against antigens such as viral proteins over time. If so, vaccines may give the immune system a head start in the race against COVID-19. Collectively, based on early data to date, even if somewhat reduced, the COVID-19 vaccines are likely to confer significant protection against SARS-CoV-2 virus variants—yet another reason to be vaccinated as soon as possible.

10. **Question: Are studies ongoing to improve COVID-19 vaccine efficacy against variant virus strains ?**

***Answer —*** Yes, and not just by creating next-generation vaccines designed to target the variant strains. Many different ways of using current vaccines to help best protect against COVID-19 are also being investigated These include additional booster dose(s) of vaccines; higher doses of vaccines; and possibly even mixing vaccine types to expand effectiveness and/or durability of

COVID-19 vaccines that are not identical. It should also be emphasized these concepts are only experimental at the present time, and not currently approved or recommended.

**11. Question: Are vaccines the only way to protect against COVID-19 infection or severe outcomes ?**

***Answer —*** Vaccines have the greatest promise for protecting against becoming infected and also reducing the spread of COVID-19 if used by a large enough proportion of the population. Until "herd immunity" has been achieved, masking, distancing, disinfecting and washing hands are the simplest and best proven forms of behavior that help protect NMOSD patients, families and caregivers against COVID-19.

**12. Question: Are there additional resources available to learn more about NMOSD and COVID-19 ?**

***Answer—*** Absolutely. Please visit the Guthy-Jackson Charitable Foundation website for further information and special *GJCF Breakout Sessions* focusing on COVID-19 science and medicine: GuthyJacksonFoundation.org

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*Reference Information*:


[A] Fan et al. [2020] *Neurology/Neuroimm Neuroinflamm* paper finding no increased risk of greater COVID-19 infection or disease in NMOSD patients as compared to the general population. In addition, no increased risk of COVID-19 infection or disease was observed in NMOSD patients regardless of therapy for NMOSD.

[B] CDC Advisory Committee on Immunization Practices (ACIP) [2021]. Guidelines for Vaccine Immunization in Persons with Altered Immune Competence.

[C] CDC Vaccines & Immunizations [2021]. Interim Clinical Considerations for use of mRNA COVID-19 Vaccines Currently Authorized in the United States.

[D] National Health Service, United Kingdom [2021]. COVID-19 Vaccination Program.

[E] World Health Organization [2021]. COVID-19 Vaccines.

[F] Infectious Diseases Society of America [2021]. FAQs of Vaccination in Special Populations

[G] National Multiple Sclerosis Society [2021]: COVID-19 Vaccine Guidance

[H] FDA Fact Sheet [2021]: Pfizer-BioNTech COVID-19 Vaccine

[I] FDA Fact Sheet [2021]: Moderna-NIH COVID-19 Vaccine

[J] FDA Fact Sheet [2021]: AstraZeneca-Oxford COVID-19 Vaccine

[K] FDA Fact Sheet [2021]: Johnson & Johnson / Janssen COVID-19 Vaccine