**Information on COVID-19 and Friedreich's Ataxia**

There has now been significant progress toward a safe and effective vaccine for COVID-19. At least three companies have now completed late stage (phase 3) clinical trials of a vaccine. There are at least 3 more vaccines under development. These different types of vaccines are not interchangeable and thus there may be reasons to consider which may be the safest or most effective based on your individual concerns. There are no special concerns with COVID vaccines for persons with FA. However, those with advanced disease may be especially vulnerable to COVID-19 complications; thus, while weighing the current safety and efficacy data, the risk/benefit balance is in favor of vaccination. While FARA does not make medical recommendations and does not endorse any particular vaccination, as a resource for the community we have researched COVID vaccines and reached out to FA experts to create this information document on COVID-19 vaccines.

**What is Immunity?** Protection from an infectious disease. If you are immune to a disease, you can be exposed to it without becoming infected. Immunity can be acquired through previous infection with a disease or through **Immunization**, which is the process by which a person becomes protected against a disease through vaccination.

**What is a Vaccine?** A product that stimulates a person's immune system to produce immunity to a specific disease, protecting the person from that disease. Vaccines are usually administered through needle injections, but can also be administered by mouth or sprayed into the nose.

**How and when will COVID-19 vaccines become available?** In the US, at least at first, COVID-19 vaccines may be used under an Emergency Use Authorization (EUA) from the U.S. Food and Drug Administration (FDA). EUAs have a different timeline for review due to the public health emergency. Once the FDA authorizes or approves use of COVID-19 vaccine(s), limited quantities will become available, but supply will increase substantially in 2021. In the UK and EU, G20 leaders have pledged an equitable distribution of COVID-19 vaccines, with the UK and Germany each announcing plans to begin vaccinations in their countries in December if the reviews of the potential vaccines are positive, and Spain expects to start vaccinations in January. Italy and Belgium may start vaccinating in January, too, or perhaps as early as late December.

**Who will be eligible to receive the vaccine?** The initial supply will be limited and during an initial period it may be that some groups will be vaccinated first based on scientific data and ethical considerations. For example, if there is limited supply, it may be recommended that first responders or medical personnel are vaccinated first. The first available vaccines have been tested in adults and therefore, at first, COVID-19 vaccines may not be authorized, approved, or recommended for children.

**What are the differences between the types of vaccines?** In the past, vaccines were usually bits of the virus that caused the disease, which triggered the body to produce antibodies, and thus immunity, to that specific virus. However, the first few vaccines that are being developed for COVID-19 are using new technologies. Because viruses are naturally good at getting genetic material into human cells, they can be used to carry the genetic code ("the gene") for a COVID-19 protein into human cells. But while these

viruses are good at carrying genetic material into cells, they are highly modified and unable to make people sick.

**Virus Vaccines**. The AstraZeneca/Oxford (AZ) vaccine being developed in the UK contains a modified adenovirus, one of the family of viruses that cause colds. NOTE: This is not the virus generally used to delivery gene therapy. This vaccine requires two doses to get a good response. The initial results of the clinical trial with the AstraZeneca/Oxford vaccine were somewhat confusing, as an initial lower dose of the vaccine followed by a higher dose seemed to provide better immunity than two higher doses. This may be an anomaly that won't occur in larger clinical trials. It is theoretically possible that at least some people may develop immunity to the adenovirus used in the AZ vaccine. If antibodies develop, this could lead to reduced effectiveness of the vaccine. And previous exposure and thus immunity to adenovirus viruses may make this vaccine less effective for some people. But the overall safety and effectiveness of the vaccine will be tested and will continue to be monitored after the release of the vaccine.

**mRNA vaccines**. A new technology was used by both the Pfizer and Moderna to create the first vaccines that use messenger RNA, or mRNA. The mRNA directs cells to produce COVID virus protein and the immune system then responds by making protective antibodies to the COVID-19 virus. Note: The mRNA vaccines don't use any type of virus for delivery, the mRNA is inside lipid nanoparticles to protect it until it is taken up into the cell. Both of these vaccines require two doses to be effective. They also need to be stored cold, but Pfizer's vaccine has to be stored at ultra-cold temperatures, which has raised practicality concerns about how it can be shipped and distributed. Until we know the detailed methodology of distribution it will be hard to provide firm answers on availability and access. In addition, because these vaccines are based on a completely new technology, there are no long-term data on safety, efficacy in different age groups, and whether they will generate long term immunity.

**Are there any special considerations for FAers regarding COVID vaccines?** Individuals should discuss COVID vaccines with their health care provider.

Currently, there is no reason to believe that the adverse effects of any of these vaccines is different in FA patients than in the general population. However, at this time there are no public data on adverse effects in any population, and it will be hard to fully ascertain in advance any potential side effects of any of the vaccines. Note that the experts we consulted suggested that, once the vaccines are approved, the risk-benefit ratio in FA patients are weighted in favor of vaccination given the higher vulnerability of FA patients to COVID 19 complications.

Some general considerations to be aware of include the long-term effects of treatment with virus, as, for example, the adenovirus present in the AZ vaccine or an AAV virus in a vaccine being developed at Massachusetts General Hospital, and the possible immune responses to vaccines in general. Additionally, we currently do not have data on the durability of these vaccines in any population.

Most of the gene therapy approaches currently under development for the treatment of FA are using Adeno-Associated Viruses (AAVs). AAVs were discovered because of their association with adenovirus, but they do not have the same genetic or protein makeup. Therefore, it is unlikely that an antibody response to adenovirus used in the AZ vaccine would generate a similar immune response to AAV. The specific type of AAV used in either gene therapy or in a COVID vaccine may also influence whether a subsequent immune response could be a concern. Thus, a conservative approach may be to avoid AAV-based vaccines if equally effective and safe non-viral vaccines are available. With the information available, there is currently no reason to expect that a patient's eligibility for an FA gene therapy trial

using an AAV vector or the patient's safety in such a trial would be impacted by having received COVID 19 vaccines that do not use AAV vectors.

If currently enrolled in a clinical trial, individuals should speak to their study coordinator for more information before getting vaccinated. Each clinical trial is likely to have specific protocols regarding vaccinations.

**Anyone considering receiving a COVID vaccination should discuss the matter with his or her physician. FARA does not endorse or recommend any particular vaccination.**

*Please note: This is an evolving situation. The comments provided are based on information available at the time of posting- December 7, 2020.*

**References:**


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