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December 2020 update: Information from the American College of Rheumatology Regarding Vaccination Against SARS-CoV-2

Background

As of this writing, there are 5 SARS-CoV-2 vaccines completing phase 3 studies and over 50 vaccines in some stage of human clinical testing. Two companies with vaccine candidates have applied for emergency use authorization (EUA) from the US Food and Drug Administration (FDA). On December 11th, Pfizer and BioNTech's vaccination became the first vaccine given emergency approval for prevention of SARS-CoV-2 and distribution has begun. The science is briskly evolving, and the latest developments can be accessed at www.cdc.gov. An additional up-to-date source on the wide array of vaccine candidates can be found at the New York Times.

This document will address vaccine development and patient education.

Vaccine Development

Types of vaccines

The vaccines currently in phase 3 trials fit into one of three basic categories: mRNA vaccines, protein subunit vaccines and adenovirus vector vaccines. All accomplish the goal of induction of immunity but achieve that goal through different techniques.

Messenger RNA vaccines include mRNA (wrapped in a lipid nanoparticle) that gets incorporated into human cells upon vaccination. In the case of SARS-CoV-2, this mRNA typically encodes for the viral spike protein. The mRNA instructs the host cell to produce the spike protein, which stimulates an immune response that will ultimately provide protection against SARS-CoV-2.

Protein subunit vaccines contain purified viral protein (often the spike protein) subunits which are often accompanied by an adjuvant to boost the immune response. The protein is processed by the immune system to trigger a protective immune response.

Vector vaccines use a separate viral vector that has been engineered to code for proteins from the SARS-CoV-2 virus. Two of the vaccines in phase 3 trials use a replication-defective adenovirus vector that has been altered to code for the SARS-CoV-2 spike protein. Once the vector infects the host cell, its DNA enters the host cell nucleus. The host then produces the protein from SARS-CoV-2 which elicits an immune

response and protection against COVID-19. Note that the adenovirus does not modify the host genome.

It is noteworthy that no vaccines using live, attenuated SARS-CoV-2 virus are in phase 3 trials.

Where vaccine development stands (as of Dec 12, 2020)

The 5 phase 3 vaccines in the US, and their latest developments as of 12/12/20, include the following:

-Pfizer and BioNTech have collaboratively produced an mRNA vaccine that has been given emergency use approval by the FDA.
-Moderna has produced an mRNA vaccine and has applied for an EUA from the FDA.
-AstraZeneca reported initial results on their vector vaccine in late November and testing continues.
-Novavax's protein subunit vaccine was granted fast track designation by the FDA in early November but clinical trial results have not been released.
-Janssen is wrapping up a 1 dose vaccination study and preparing for a 2 dose vaccination series study of their vector vaccine.

How is the efficacy of a vaccine calculated?

As reports of vaccination success surface, it is important to understand how the "success rate" is calculated.

The formula is the following:
(% who get COVID in control group) - (% who get COVID in vaccine group) / (% who get COVID in control group).

Efficacy data presented so far from the respective vaccine candidate trials are preliminary and not final. These studies are very large, with over 30,000 participants and as more data are analyzed, the reported efficacy may change.

Are there plans to study patients taking immunosuppressive drugs?

There are plans for further studies on the effect of immunosuppression on SARS-CoV-2 vaccination, but no data are available at this time. The ACR is developing a guidance document on the use of SARS-CoV-2 virus vaccination in patients with rheumatic disease that will be available in first quarter 2021.

Should patients who receive the vaccine continue their immunosuppressive therapy before and after vaccination?

At this point no data are available to guide the management of immunosuppressive therapy in the context of SARS-CoV-2 vaccination. The CDC does offer vaccination guidance in immunosuppressed individuals, although this document does not specifically discuss SARS-CoV-2 vaccination (www.cdc.gov).

Should patients who have previously contracted and recovered from COVID-19 receive the SARS-CoV-2 vaccination?

No guidance currently exists in this scenario. However, for other conditions such as herpes zoster, immunization after disease presentation is currently recommended. As more information or formal recommendations are available, this document will be updated.

How to talk to patients about a SARS-CoV-2 vaccine

The risk of COVID-19 vs. the risk of a vaccine

Comprehensive safety checks are required as part of the process leading to FDA approval of a new vaccine. As with all vaccines that have passed rigorous testing and licensure procedures, the benefits of vaccination (preventing or reducing the severity of infection) are expected to far outweigh any risk from the vaccine. We anticipate recommending all patients, including rheumatology patients, receive an approved COVID-19 vaccine.

If a vaccine based on live, attenuated SARS-CoV-2 virus is developed – again, none is in Phase III testing in the US – it could be an exception. In general, patients taking immunosuppressive medicines, especially chronic prednisone at 10 mg/d or higher, and possibly patients taking biologics, should avoid live-attenuated vaccines until and unless those vaccines have been demonstrated to be safe in those populations.
We understand that questions regarding the impact of nucleic acid or viral vector vaccines on our patients' autoimmune disease activity are important. However, no information is available at this time to answer those questions.

Partial vs. absolute protection

Most vaccines offer incomplete protection against infection and this is likely to be the case with SARS-CoV-2 vaccines as well. However, even partial protection will be of benefit both to patients and the general public. Partial protection may mean that most but not all persons develop immunity, or that some recipients develop weak immunity that makes the consequences of infection less severe than they would have been otherwise.

Durability of protection

Seroconversion (development of antibodies) following natural infection with SARS-CoV 2 takes place between 5-14d after onset of symptoms. Antibody titers appear to correlate with clinical severity but their appearance does not clearly correlate with an abrupt decline in viral load. Also, in some cases, IgM/IgG antibody levels decline rapidly. There is wide variability in the quality of commercially available kits used to measure antibody responses against SARS-CoV-2. Thus, it remains unclear how long protection against re-infection lasts following natural infection with SARS-CoV-2. The same questions apply to durability of protection against SARS-CoV-2 following vaccination. All individuals (including rheumatology patients and staff members engaged in their care) receiving vaccines against SARS-CoV-2, or recovering from COVID-19 infection, should be counseled that the durability of protection remains to be determined, and that prior infection and measurable IgM and IgG antibody responses may not confer reliable or durable protection from reinfection.

Herd immunity

When a large portion (estimated to necessarily be as high as ~70% in the case of SARS-CoV-2) of the individuals in a population are immune to a virus, it becomes difficult for that virus to spread within that population. This phenomenon, known as herd immunity, helps protect individuals who are not immunized, even though they are not immune. This is especially important to members of a population who are poor candidates for vaccines, and to patients who are at risk of severe disease should they contract the virus. Therefore, we highly encourage all employees of rheumatology practices to receive vaccination for the protection of their patients. Some providers and organizations may consider vaccination of employees, and/or other measures to mitigate viral spread, a requirement for (continued) employment.

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