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April 2021 update: Information from the American College of Rheumatology Regarding Vaccination Against SARS-CoV-2

Background

As of 4/25/2021, three vaccines have been granted emergency use authorization (EUA) fromthe US Food and Drug Administration (FDA) to prevent COVID-19 caused by SARS- CoV-2. There are at least 18 vaccines in Phase 3 testing worldwide with over 200 additional vaccine candidates in development. The science is briskly evolving, and the latest developments can be accessed at www.cdc.gov.

This document will discuss vaccine development and patient education.

Clinical Questions

The ACR has produced a guidance document on the use of SARS-CoV-2virus vaccination in patients with rheumatic disease that is available here: https://www.rheumatology.org/Portals/0/Files/COVID-19-Vaccine-Clinical-Guidance-Rheumatic-Diseases-Summary.pdf

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 immuneresponse and protection against COVID-19. The adenovirus does not modify the host genome.

It is noteworthy that no vaccines using live, attenuated SARS-CoV-2 virus are inphase 3 trials*

Where vaccine development stands (as of April 25, 2021)

The 5 phase 3 vaccines in the US, and their latest developments include the following:

- Pfizer and BioNTech have collaboratively produced an mRNA vaccine that was given emergency use approval by the FDA. Vaccinations are in progress acrossthe United States.
- Moderna has produced an mRNA vaccine that was granted emergency use approval by the FDA. Vaccinations are in progress across the United States.
- Janssen (Johnson and Johnson) has produced a single shot adenovirus-based viral vector vaccine that was given emergency use approval by the FDA. There have been very rare reports of thrombosis and thrombocytopenia (“TTS syndrome”) in women aged 18-59 with this vaccine, leading to the CDC to place a brief pause on administration of the vaccine. The pause has since been lifted and the CDC and FDA have placed a warning on giving this vaccination but otherwise have not placed any new restrictions on its use. Further details can be found at www.cdc.gov.
- Novavax has developed a two-shot protein subunit vaccine that has demonstrated positive results in the UK and US. Novavax has applied for EUAoutside of the US and is anticipated to apply for EUA with the FDA.
- AstraZeneca's two-shot adenovirus viral vector vaccine has been approved for use in the UK but is still completing a US based study. The process for EUA in the US has not yet been completed.

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 symptomatic COVID in control group) - (% who get symptomatic COVID invaccine group) / (% who get symptomatic COVID in control group).

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 ofinfection) are expected to far outweigh any risk from the 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, andpossibly patients taking biologics, should avoid live-attenuated vaccines until and unlessthose vaccines have been demonstrated to be safe in those populations.

Partial vs. absolute protection

Most vaccines offer incomplete protection against infection and this is likely to be thecase 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 mostbut not all persons develop immunity, or that some recipients develop weak immunitythat 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-CoV2 takes place between 5-14d after onset of symptoms. Antibody titers appear to correlate with clinical severity, and in some cases, IgM/IgG antibody levels decline rapidly. 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 thatthe durability of protection unclear, and that prior infection and measurable IgM and IgG antibody responses may not confer reliable or durable protection from reinfection.

Additional Resources

The science behind vaccination against SARS-CoV-2 is evolving very rapidly and manyresources exist to stay up to date. Both the CDC (www.cdc.gov) and the AMA (www.ama-assn.org) have vast resources for both providers and patients.

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