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DUKE INFECTION CONTROL OUTREACH NETWORK

COVID-19 Vaccine Q&A

Introduction

There's a light at the end of the tunnel. Dr. Jerome Adams said "this is the beginning of the end" when speaking about the COVID vaccine rollout. On December 11th, the FDA announced an Emergency Use Authorization (EUA) for the Pfizer/BioNTech COVID-19 vaccine, for prevention of COVID-19 for individuals 16 years or older. On December 14th, the initial shipments of the first COVID-19 vaccine went out across the whole nation. Then, on December 18th, the FDA announced a second EUA for a vaccine created by Moderna.

The November DICON newsletter highlighted some information on the candidate vaccines and Dr. William Schaffner spoke regarding the COVID vaccines at our annual DICON/DASON Symposium. Dr. Marci Drees recently presented a webinar elaborating on the leading COVID-19 vaccine candidates. Now that most of us are going to be face to face with the vaccine recipients, and receiving the vaccine ourselves, there are several frequently asked questions upon which we'd like to comment.

Q#1. What is an mRNA vaccine? How does it work? Do they work? Will they alter my genetic code?

A: mRNA translates information stored within genetic material into proteins which cells use to carry out everyday functions. The Pfizer and Moderna vaccines use mRNA like a blueprint. When the mRNA is injected into a subject's arm, it enters into the muscle cell's cytoplasm allowing the cell to synthesize the spike protein of SARS-CoV-2. The spike protein is then presented to the immune system, which forms antibodies, and protects against disease from the real coronavirus. A great graphical representation of this process is available from the Royal Society of Chemistry.

These mRNA vaccines are greatly effective, with 94-95% efficacy at preventing COVID-19 disease in phase 3 clinical trials consisting of over 43,000 and 30,000 participants (Figure 1).[1]

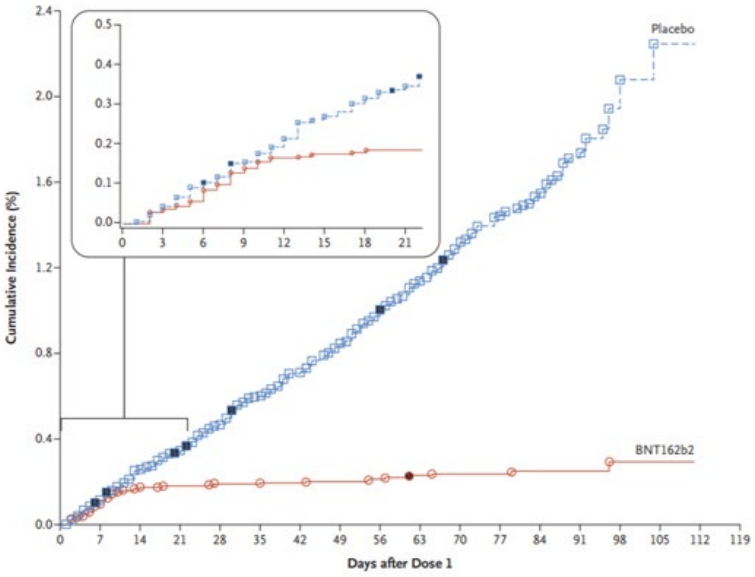

Figure 1. Vaccine efficacy data from Pfizer COVID-19 vaccination[1]

They also demonstrate efficacy at preventing severe COVID, and are >90% effective at preventing any COVID-19 disease in published subgroup analyses (age, race, sex, and risk factor for severe disease). Albeit, due to the small number of participants and cases in some of these subgroups, not all the individual subgroup analyses are statistically interpretable.

Some are worried that an mRNA vaccine could cause genetic mutations, or alter genetic code. The mRNA that is injected does not enter into the cell nucleus, or interact with DNA in any way. The only way for RNA to become DNA is through a process called reverse transcription, which human cells are incapable of performing.

Q#2. This seems like a new technology; how can you be sure that it is safe?

A: While these vaccines are the first developed mRNA vaccines, the technology used to create them has been researched for decades. It's more accurate to say that the science behind these vaccines, while innovative, is not novel.

In previous vaccine studies the overwhelming majority of adverse events occurred within 6 weeks of vaccination.

Therefore, the FDA previously published expectations for any vaccine EUA submission to include phase 3 data with a median participant follow-up of at least two months after completing the full vaccination regimen. Both the Pfizer and Moderna vaccines have met this target observation period.

Severe adverse events reported for both the Pfizer and the Moderna vaccines were balanced between the placebo and vaccine groups. Minor solicited adverse events and those occurring fewer than 7 days from injection with the Pfizer vaccine were higher in the vaccine groups. The most common local reactions were pain at injection site (78% in Pfizer and 90% in Moderna), and swelling or lymphadenopathy (6% and 10%). Systemic reactions most commonly manifested following the second dose and included fatigue, headache, and muscle aches. Reactions were more frequent in younger cohorts (<55 years old in the Pfizer study and <65 years in the Moderna study). Notably, 45% of the <55-year-old group took an antipyretic medication after the 2nd dose in the Pfizer study.

Furthermore, in the Pfizer study, with approximately 19,000 participants in the vaccine group and a median follow-up time of 2 months, the study has a >83% probability of detecting at least one adverse event, if the true incidence is 0.01% (1 in 10,000). So, if it is a really rare adverse event, it may not be seen in the clinical trial. Therefore, post-authorization safety monitoring will be very important in detecting these rare events. There are reporting systems in place to monitor for rare events following vaccine administration, including the Vaccine Adverse Event Reporting System (VAERS). VAERS has been around since 1990 and anyone can access it and enter a report. The benefit of this system is the ability to detect safety signals rapidly and gather high numbers of reports since patients and providers alike can enter a report. The downside to VAERS is that just because events occur after a vaccination, this temporal relationship does not necessarily imply causality. So, this database has to be routinely analyzed and any significant signal should be followed by individual case investigation.

V-safe is a new monitoring system created specifically for the COVID vaccines by the CDC. It is a smartphone-based tool that uses text messages with web surveys embedded in them to provide personal health check-ins after the vaccination. They will contact vaccine recipients daily for the first week then weekly for the next 5 weeks. Any events reported to V-safe will be entered into VAERS by the V-safety monitors. Vaccine Safety Datalink (VSD) is another system, founded in 1990, that is used to monitor safety. VSD uses electronic health data from 9 major health organizations across the US to detect safety issues. Clinical Immunization Safety Assessment (CISA) is resource provided by the CDC for vaccine providers that provides consultation service for complex vaccine safety questions on an individual case level basis.

Q#3. I've heard that people have had allergic reactions after being vaccinated. If I have allergies should I receive the vaccine?

A: As of this writing there have been eleven reported cases of allergic reactions to the COVID-19 vaccine in the United States, with two reports of anaphylaxis. While there are several anecdotes thus far, we do not yet know the risk of these severe allergic reaction. However, a 3 year review on severe adverse events after vaccinations reported in the VSD found the rate of anaphylaxis after vaccination to be 1.31 per million vaccine doses given.[2] For comparison, the lifetime risk of being struck by lightning is only one in 15,000, and the risk of contracting severe COVID-19 disease if infected is estimated at 1 in 10 to 1 in 20.

The CDC recommends forgoing vaccination only for those who have a history of allergic reaction to an ingredient of the COVID-19 vaccine. The most likely culprit allergen in both the Pfizer and Moderna vaccines is the lipid polyethylene glycol—the main component in Miralax. Because the vaccine contains no egg products or preservatives, persons with a history of food allergies or allergy to other vaccines may receive either available COVID-19 vaccine.

Q#4. Isn't it better to build immunity naturally through infection, rather than vaccination?

A: People often have a misconception that immunity derived through natural infection is healthier, or safer, than immunity derived from vaccination. There is no evidence to support this idea. It seems to be primarily driven by recall bias, particularly for infections which are no longer commonly encountered, such as measles, which can be a lethal or highly morbid disease for children. Because we don't often see cases of measles, but hear about perceived

adverse effects from vaccination, the risks of infection slip from our mind, and seem to outweigh the benefits of vaccination.

In the first week of vaccine availability, over 600,000 health care workers were vaccinated for COVID-19 in the United States. No deaths occurred as a result of vaccination, and only one patient was hospitalized for observation following an allergic reaction. In contrast, in the same week over 120,000 Americans were hospitalized due to COVID-19 with roughly 20,000 deaths reported. Over the course of the pandemic over 300,000 Americans have died from COVID-19—a fatality rate of 1 in 1,000 persons. Furthermore, a sizeable percentage of COVID-19 survivors will also go on to develop long-term symptoms as a consequence of natural infection. These simple numbers show clearly that the vaccine provides immunity in a much safer way than acquiring immunity naturally.

Q#5. If I get the vaccine, can I stop wearing this mask?!
A: There is a slight difference in preventing disease from SARS-CoV-2 which is vaccine efficacy and preventing transmission of SARS-CoV-2, from asymptomatic cases or asymptomatic transmission. The studies conducted by Pfizer and Moderna do not directly address the question of asymptomatic transmission. However, in the FDA brief from Moderna, there is data suggesting vaccination may reduce asymptomatic transmission. There were 2/3 fewer asymptomatic infections in the vaccine group following the 1st dose (relative risk 0.37, 95% CI: 0.29, 2.33), with no data as yet reported following the 2nd dose. This is encouraging as this will be what gives us the ability to stop wearing masks. However, current recommendations are to continue practicing social distancing, hand washing and mask wearing after vaccination.

Q#6. I'm pregnant. Is it safe for me to get the vaccine? What if I want to breastfeed?
A: The COVID-19 vaccines currently available have not been tested in pregnant women. However, the American College of Obstetricians and Gynecologists recently released a Practice Advisory in favor of vaccinating pregnant and lactating patients for COVID-19. They recommend that COVID-19 vaccines "not be withheld from pregnant individuals" and "should be offered to lactating individuals similar to non-lactating individuals." This recommendation is driven primarily by evidence demonstrating pregnancy as an independent risk factor for developing severe illness in COVID-19 infection.

A conversation with the patient and their clinical team is recommended but not required prior to vaccination. FDA recommends that all pregnancies that occur within 30 days after vaccination should be followed for pregnancy outcomes.

A combined developmental and perinatal/postnatal reproductive toxicity study of mRNA-1273 (Moderna vaccine) in rats was submitted to FDA on December 4, 2020. FDA review of this study concluded that mRNA-1273 given prior to mating and during gestation periods at dose of 100 µg did not have any adverse effects on female reproduction, fetal/embryonal development, or postnatal developmental except for skeletal variations which are common and typically resolve postnatally without intervention.

Q#7. What is herd immunity? Can I rely on herd immunity to protect me without receiving the vaccine myself?
A: Herd immunity is the principle that individuals who are susceptible to an infectious disease can be protected from infection once a proportion of the entire population has been immunized, either through vaccination or natural infection. The percentage of the population or threshold needed to establish herd immunity can be determined from a simple formula:

$$\%\ immunized\ to\ reach\ herd\ immunity = 1 - \frac{1}{R_0}$$

R_0, the basic reproduction number, describes the number secondary infections arising from one infected individual. The value of R_0 depends on multiple factors, both intrinsic and extrinsic to the disease, which we have discussed in prior newsletters. From the formula, it is clear that the more contagious infections (high values of R_0) require a larger proportion of immunized individuals to reach herd immunity. In the case of COVID-19, R_0 value estimates range from 2.5 – 6.[2] This means 60 – 84% of the population would need to develop immunity to protect the unvaccinated from SARS-CoV-2. The COVID-19 vaccines make such a target attainable, and in a manner far safer than through natural infection. For those more interested in herd immunity, a more thorough discussion with interactive graphics (allowing the user to create models with theoretical R_0 and vaccine efficacy values) can be found here.

Recent surveys estimate 63% of the American population is willing to receive a SARS-CoV-2 vaccine. Through December 11th, the CDC estimates 28% percent of the population (91 million Americans) has been previously infected. The combined totals of these estimates suggest we can reach a state of protective herd immunity, but also demonstrate the importance of promotional campaigns to encourage vaccination. Vaccines only work when injected into arms, not when sitting in pharmaceutical vials!

References

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