Interpreting the Interim Pfizer/BioNTech COVID-19 Vaccine Data

Interview with Wayne Koff, Ph.D.
President and CEO
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Wayne Koff is the founding President and CEO of the Human Vaccines Project (HVP). Earlier today, following Pfizer’s and BioNTech’s announcement that their mRNA-based COVID-19 vaccine candidate had an interim efficacy of more than 90%, HVP Editor Kristen Jill Abboud discussed the implications of these results with Koff. An edited version of the conversation appears below.

This special issue also includes reactions from several experts in the field and a summary of the ongoing Phase III efficacy trial, including trial demographics and next steps.

Put these results in context for us. What does this level of efficacy mean and how does it compare to the efficacy of other vaccines?

These are incredibly exciting results. It is a remarkable achievement to show these results from a large, international efficacy trial in less than a year since the identification of the virus. Having a vaccine with 90% efficacy would be similar to some of the best pediatric vaccines we have, so this is really encouraging.

There aren't any licensed vaccines based on the mRNA platform. What are the implications for other vaccine candidates based on this platform, for SARS-CoV-2 or other pathogens?

I think this is the other key observation that has come out of this initial data. There has
been tremendous promise for a long time on the potential of mRNA as a vaccine platform, but this is really the first time that this level of efficacy has been observed with an mRNA vaccine candidate. This opens the door for the potential of mRNA vaccines for other respiratory diseases, such as RSV, for which we don’t have a vaccine, or influenza, for which the annual vaccine is only around 60% effective. This also provides an opportunity to explore using mRNA for vaccines for non-communicable diseases as well, such as cancer vaccines. It is exciting news for the potential of mRNA vaccines.

Obviously, these data are only preliminary so there are many questions remaining. What are the most critical data that we should be watching for as the trial reaches its final endpoint?

As the companies have pointed out, this is an initial look at the efficacy of the vaccine. The trial will not meet its endpoint until there are 164 disease endpoints among the trial volunteers, which could come relatively quickly given the expansiveness of the pandemic. The key issue will be safety. Ensuring that the vaccine is as safe as possible is really paramount, and that will be a critical part of the Emergency Use Authorization (EUA) or licensure application. After considering safety, there are still many other questions. The demographic of the populations enrolled in the trial will be critical, and, specifically, the data among the elderly, which is the population at the highest risk of severe disease. Related to that, we will want to understand whether this vaccine protects equally well against mild and severe disease.

Another important issue, which the companies will only have data on after some time, is the durability of the vaccine-induced immune responses. Ideally, a vaccine would have life-long protective immunity. There are some licensed vaccines that work extremely well in terms of durability—smallpox and yellow fever vaccines are the examples of this. Whereas other vaccines, including those for influenza, pertussis, and mumps, are less effective in terms of durability. That is one of the questions we will have to wait to answer as vaccine trial participants are followed for a longer period of time.

Another important question is whether there are any data yet on the identification of potential correlates of protection: are neutralizing antibody titers the key assay that we need to be looking at for other vaccines? Once you have a vaccine that has shown efficacy and is made available, either through licensure or EUA, you may need to do bridging studies for other vaccines that are based on that correlate.

Is it likely that correlates can be determined after 164 infections or will more data/follow-up be required?

I think there will be a huge amount of work immediately to try to figure out the correlate. It might be that we need to have larger numbers to determine it, or we might get lucky and it may simply be the neutralizing antibody titer.
This vaccine is a two-shot regimen that must be stored at ultra-cold temperatures. How does this complicate deployment efforts?

This will certainly be an issue for delivery and deployment of this vaccine on a global scale. The ideal vaccine would be one shot and not have issues with cold chain storage. But there have been advances in cold-chain storage in recent years, as well as with the technologies associated with GPS systems and use of drones to deliver vaccines, so this ultimately will become an engineering problem.

What are the implications of this early result for the other vaccines in efficacy trials, even those that aren’t using an mRNA delivery system? Does this raise the expectations for the efficacy of other candidates as well?

If you look at the data from non-human primates and the immunogenicity data in people from Phase I trials, the levels of neutralizing antibodies are relatively similar for all the platforms. Some vaccines are inducing higher levels of neutralizing antibodies than others, but most of the leading candidates are in the same ballpark, which bodes well for all the candidates if the neutralizing antibody titer is in fact the correlate.

Prior to these preliminary results, I assumed we were going to see efficacy in the range of between 50-80% based on all the data. If it turns out that this result holds up and there is really over 90% efficacy, and if the vaccine works as well in the elderly as in young adults—two really big questions—then we will have an amazing result from this unprecedented effort.

Interview by Kristen Jill Abboud

Reactions from the Field

Moncef Slaoui, M.S., M.B.A., Ph.D., Scientific Head of Operation Warp Speed

“These data are very encouraging as they demonstrate the feasibility of vaccination against COVID and that protection can be achieved at a very high level. This level of efficacy will, I hope, help alleviate the concerns and hesitancy that developed over the past several months.”

Michael Osterholm, Ph.D., MPH, Director, Center for Infectious Disease Research and Policy, University of Minnesota

"While these results are positive and encouraging, I think we need to further clarify what it means to find a vaccine efficacy of 90%. Was that for severe illness, hospitalization, and even death? Or was it for preventing limited clinical
illness in populations with few underlying risk factors for severe disease? These are the results I'm anxiously awaiting before we can determine the public health significance of the 90% finding."

*Osterholm is now part of U.S. President-elect Biden's newly formed COVID-19 Advisory Council.*

Sarah Gilbert, BSc, Ph.D., Professor of Vaccinology, Jenner Institute, University of Oxford

"It's great news that the first interim analysis has shown such a high level of protection. There is a lot more detail to come, and it will be for the regulatory authorities to review all the data thoroughly. We now know that it is possible to make a vaccine to protect people against SARS-CoV-2, which is something we did not know for certain yesterday."

Stanley Plotkin, M.D., Emeritus Professor of Pediatrics, University of Pennsylvania, Human Vaccines Project Board Member Emeritus

"This is very positive news for control of the COVID-19 epidemic, although we need to know about protection of the mucosa and duration of protection. This is also a validation of the mRNA technology, which bodes well for its use to develop vaccines against other diseases."

Stacey Schultz-Cherry, Ph.D., Full Member, Department of Infectious Diseases, St. Jude Children's Research Hospital

"The Pfizer results showing no serious safety concerns and greater than 90% efficacy in preventing disease in healthy adults is great news as we continue to battle this pandemic. While promising, it is important to continue assessing long-term safety, how long the protection will last, and if it will prevent viral spread."

Richard Hatchett, M.D., CEO, Coalition for Epidemic Preparedness Innovations

“Key challenges of course are the supply and cold chain requirements, which could limit broad availability of the vaccine in many settings, but, overall a historically important day, both in the struggle against COVID-19 and for mRNA vaccines as a whole.”

Jaap Goudsmit, M.D., Ph.D., Chief Scientific Officer of the Human Immunomics Initiative, Adjunct Professor of Epidemiology and Immunology, Harvard T.H. Chan School of Public Health
“It is a great accomplishment to get a vaccine that induced a neutralizing antibody response to the receptor binding site and protects in the first months after vaccination to an unexpected level of 90%. We have to wait and see if the vaccine response is durable and even more importantly if the vaccine can be produced at scale.”

Michelle Williams, Sc.D., S.M., Dean of the Faculty, Harvard T.H. Chan School of Public Health

"These are exciting results and hopefully we will see this and other COVID vaccines available in the near future. It will also be important to ensure that the vaccine is safe and effective in those most vulnerable, including the elderly and those living in low and middle-income countries.”

John Moore, Ph.D., Professor of Microbiology and Immunology, Weill Cornell Medical College

"A 90% efficacy rate was higher than many of us hoped/expected to see. Yes, there remain many unknowns that will need to be addressed over time as more data emerge. To misquote Winston Churchill, ‘This is not the end, but it is the beginning of the end.'"

Michel De Wilde, Ph.D., MDW Consultant

“A vaccine efficacy readout 10 months after the virus is discovered is not only unprecedented, it is extraordinary. While some caution remains in order, a vaccine is clearly feasible.”

Barry Bloom, Ph.D., Joan L. and Julius H. Jacobson Research Professor of Public Health, Harvard T.H. Chan School of Public Health

"The results are very encouraging for the mRNA vaccine platform in general, and it is good that there is a capability of producing about 1.2 billion doses for 2021. Since no short term serious adverse events were seen, the principal concern is the duration of the protective response.”

Julie McElrath, M.D., Ph.D, Senior Vice President and Director, Vaccine and Infectious Disease Division, Fred Hutchinson Cancer Research Center

"The 90% or greater efficacy against COVID-19 induced by the Pfizer/BioNTech vaccine candidate is an astonishing finding from the earliest interim analysis and represents a remarkable achievement for everyone involved in the trial."
Barney Graham, M.D., Ph.D., Deputy Director, Vaccine Research Center, NIAID, NIH

“This is more efficacious than you would expect a respiratory virus vaccine to be, based on influenza, and closer to what we see for measles. Just reserve a little caution for durability. These are data within two months after vaccination.”

Trial Summary

**Study sponsor:** BioNTech

**Study conducted by:** Pfizer

**The SARS-CoV-2 vaccine candidate tested in this study:** BNT162b2 (variant RBP020.2): a modRNA encoding P2 S

**Number of volunteers:** Phase III study enrolled 43,538 participants, 38,955 of whom have received a second dose of the vaccine candidate as of November 8, 2020

**Age groups:** Phase II/III: ≥12 years of age (stratified as 12-15, 16-55, or >55 years of age)

**Demographics:** Approximately 42% of global participants and 30% of U.S. participants have racially and ethnically diverse backgrounds

**Results summary:** According to the press release, the vaccine candidate was found to be more than 90% effective in preventing COVID-19 in participants without evidence of prior SARS-CoV-2 infection in the first interim efficacy analysis. Analysis evaluated 94 confirmed cases of COVID-19 in trial participants. No serious safety concerns have been observed. The case split between vaccinated individuals and those who received the placebo indicates a vaccine efficacy rate above 90%, at 7 days after the second dose. This means that protection is achieved 28 days after the initiation of the vaccination, which consists of a 2-dose schedule. Safety and additional efficacy data continue to be collected. Clinical trial to continue through to final analysis at 164 confirmed cases in order to collect further data and characterize the vaccine candidate's performance against other study endpoints.

The Phase III clinical trial of BNT162b2 began on July 27.

**Next steps:** Submission for Emergency Use Authorization (EUA) to the U.S. Food and Drug Administration (FDA) planned for soon after the required safety
milestone is achieved, which is currently expected to occur in the third week of November (when data from two months post-final dose from at least half the study volunteers will be available, per FDA guidance).

Previous clinical data was published in *The New England Journal of Medicine* and *Nature*.