CDC/IDSA COVID-19 Clinician Call Q&A

The COVID-19 Vaccine

7/18/2020

1. **Is there too much focus on S and RBD? Live-attenuated approach has proved great for MMR and polio why not pursue this?**

   Some live attenuated vaccines are also being proposed. But they also pose challenges for administration during an active outbreak of COVID because you would not want to the attenuated vaccine strains and the wild type virus to recombine. (Dr. Edwards)

   I agree with Dr. Edwards' response. And we have other effective vaccines that focus on a single protein such as the HPV vaccine. (Dr. Orenstein)

2. **Given the development of MSIC in children who have had COVID-19, is there concern for similar syndromes in vaccine recipients?**

   There are concerns about the role of antibody in enhancing disease, but these will need to be carefully assessed in clinical trials and post-licensing studies. (Dr. Edwards)

3. **Given RNA vaccine was never used in human, is there any safety concern related to RNA vaccine?**

   It has been given to humans in several Phase 1 studies already for other antigens including influenza, CMV and MERS, with good immune responses and no worrisome side effects. (Dr. Edwards)

4. **Can you comment on whether you believe the FDA Guidance Document describing development requirements for a COVID-19 vaccine will lead to an effective vaccine testing?**

   I am very encouraged by the guidance document. The parameters have been well articulated, and they appear thoughtful and appropriate. This is a very helpful document. (Dr. Edwards)

   I again agree with Dr. Edwards' response. I think the FDA Guidance document is particularly helpful a minimum level of effectiveness will be needed to gain FDA approval. (Dr. Orenstein)

5. **Is there an inexpensive, rapid way to assess TH1 response to vaccine candidates?**

   Not sure that I can adequately address that. Will try and find a T cell immunologist who can help with that question. (Dr. Edwards)

6. **Any upfront plans for specific vaccine trials in immunocompromised patients?**

   Not at this time and to my knowledge. This might be a very good group for the monoclonal antibodies that are also being generated and tested in NIH funded programs. (Dr. Edwards)

7. **Will phase 3 participants studied about whether they were previously infected? If yes how? It seems challenging with the notion that in some cases antibodies to common antigens wane. If they are studies and felt to have had prior infection will they be excluded?**

   All Phase 3 participants will have a pre vaccination titer determined so that the study will know who has been previously infected. They will not however be screened before enrollment. The immune responses and duration of the immune responses will be compared between those with prior infection and those without. (Dr. Edwards)

8. **What is the presumed efficacy of PPE in health care workers and how will this impact size of vaccine study that includes large number of health care workers?**

   The vaccinated health care workers will be required to wear PPE and this will reduce the risk for infection and will increase the sample size needed to enroll. 30K will be enrolled in the NIH funded trials with the projection that it will include an adequate number of HCW who become infected. A number of HCW have also acquired disease outside of the hospital in the community where they are not wearing the same PPE. (Dr. Edwards)

9. **Knowing that the different races have different physiology and as such will face different risk factors which may be worst in some races than others, what are the factors considered for the safety of blacks or people of African descent?**

   All subjects enrolled in the trial will be carefully assessed for local and systemic reactions after vaccination and for reactions in the post vaccination period. We do not expect a difference in the reactions but will have to carefully assess to comprehensively address the question. (Dr. Edwards)

   I again agree with Dr. Edwards' response. The question raised gives one more reason to assure clinical trials include participation of representatives on racial and ethnic minority groups to carefully assess this issue. (Dr. Orenstein)

10. **Question to Walt - given that we see high seroprevalence in some areas - recent report from NY between 50 and almost 70% in populations in the Bronx and Queens - will that be taken into account in vaccine prioritization? Will we have additional population based seroprevalence studies after the spikes in the sunbelt and CA?**

    I am not aware of plans to eliminate trials in areas hard hit by the COVID-19 pandemic. But what is clear is there will be screening antibody testing to exclude people who have evidence of prior infection. (Dr. Orenstein)

11. **Are you worried about increased risk-taking behavior after vaccination (risk compensation)?**

    Yes, we are always worried about that. But that will be an important part of the consent process. I think that will also be complicated by the fact that the vaccine is quite reactogenic and the participants may figure out if they got vaccine or placebo. (Dr. Edwards)

    One always needs to be worried about this issue. Thus, in counseling enrollees in trials, they need to understand that they could be receiving a placebo and not the vaccine (hence fully susceptible) and that we do not know how well the vaccine will work, which is why the trail is being done in the first place. We hope it will work and there are data suggesting it should be we won't know that until the phase 3 trials are finished. (Dr. Orenstein)

12. **What is being done to anticipate/deal with vaccine hesitancy?**

    We need to listen to the specific concerns of the vaccine hesitant, address their specific questions, show them how carefully vaccine safety is being monitored, and devote attention to improving communication with them. (Dr. Edwards)

    "I agree with Dr. Edwards' response regarding vaccine trials. But the big issue with vaccine hesitancy will come when FDA approved vaccines become available. That's why we need to be doing work now trying to anticipate these. The Johns Hopkins Center for Biosecurity has developed an outstanding document trying to address this issue: https://www.centerforhealthsecurity.org/our-work/publications/the-publics-role-in-covid-19-vaccination

PDF: https://www.centerforhealthsecurity.org/our-work/pubs_archive/pubs-pdfs/2020/200709-The-Publics-Role-in-COVID-19-Vaccination.pdf (Dr. Orenstein)

13. **What about vaccine "atheist" persons? Would they spread the disease further despite the vaccine? Any comment on herd immunity, esp. since children are not being involved in th trials or initial post approval period? Thanks**

    There are several parts to the question. The concerns about vaccine hesitancy are good ones and need to be addressed. See my response above, the projections with the R0 of the virus that herd immunity will need about 70% of the population to be immune. Studies in children and pregnant women are being planned and the proposals are being written. They will not be started before the Phase 2 trials are complete. (Dr. Edwards)

    I agree with Dr. Edwards' response. It's not clear how critical children are in disseminating the virus. A great article in today's (7-19-20) New York Times discusses a study in Korea, which suggests particularly that middle and high school children may be playing an important role in transmission. Studies hopefully will be performed in children, but they are not the top priority group at the present time. (Dr. Orenstein)

14. **Given that the observed epidemic has most heavily impacted LatinX/AA and low-wage, hourly workers, shouldn't those groups be considered "high-risk" and prioritized for COVID-19 vaccination? Those are "essential workers," with much higher rates of infection than healthcare workers**

    I would anticipate that they will be considered in the high-risk groups as well. (Dr. Edwards)

    They are considered one of the higher risk groups although thus far it looks like healthcare workers and other essential workers are likely to be at the top of the list. But this issue will be carefully discussed both by the National Academy of Medicine Committee, helping the ACIP in setting priorities. (Dr. Orenstein)

15. **We have seen the current administration hi-jack the scientific process. How will the ACIP and FDA prevent the politicization of the vaccine availability and use?**

    I am encouraged that the FDA guidance document outlines a science driven approach and the ACIP already has a very active COVID vaccine working group to outlined how it will be used and monitored. (Dr. Edwards)

    I agree with Dr. Edwards' response. It will be important to assure policies are developed without political interference. The ACIP process is an open process. But it is important that other organizations advocate that the ACIP process be supported. (Dr. Orenstein)

16. **Dr. Orenstein said ACIP would not compromise safety in approval - but I thought the FDA approved vaccines, and the ACIP made recommendations for their use. With an upcoming election, is there a concern that the Executive Branch which oversees the FDA might insist on approval of a vaccine that does not meet ACIP's standards? (I am pro-vaccine and anti-meddling.)**

    See my comment above. (Dr. Edwards)

    You are correct that the FDA in approving a vaccine for use makes the determination of safety. But the ACIP also uses safety data in making its recommendations. For example, the initial rotavirus vaccine, in post-licensure monitoring, turned out to cause intussusception in roughly 1 in 10,000 vaccinees. Even though the vaccine was still licensed, the ACIP decided to withdraw its

recommendation for that rotavirus vaccine. The oral polio vaccine (OPV) caused paralytic polio in about 1 in 2.5 million doses (about 1 in 750,000 first doses). Even though the vaccine was licensed and approved by FDA, the ACIP decided in 2000 to go to an all inactivated polio vaccine (IPV) schedule. Thus, the ACIP usually weighs the risks and benefits of vaccines and even if licensed, if it judges the risks outweigh the benefits, they may not recommend its use. (Dr. Orenstein)

17. **As to safety follow-up, how long is follow up with a non-vaccinated placebo group realistic once efficacy is unequivocally established?**

    Good question. That will likely need to be truncated if we find an effective vaccine. We may have to use the background rates from databases to compare adverse events in vaccinated groups after the placebo groups receive vaccine. (Dr. Edwards)

    I agree with Dr. Edwards' comments. But this is all the more reason to assure there is adequate post-licensure monitoring of vaccine safety and I discussed in my presentation how that is usually done. What is critical is for primary care providers to report adverse events following vaccines and then investigators can determine if the reports warrant more comprehensive evaluations. (Dr. Orenstein)

18. **Will those positive with Covid19, need to get the vaccine?**

    The use in people already infected in the past is not clear at this time. The immune response in those subjects and previously uninfected vaccinees can be assessed in the ongoing Phase 3 trials. (Dr. Edwards)

    I agree with Dr. Edwards' response. (Dr. Orenstein)

19. **When will the vaccine be available and which areas - emergency/hospital/pharmacy/out-patients' clinics, will it be available at?**

    Not sure when vaccine will be available but would expect that delivery systems would be rapid and hopefully equitable and efficient. (Dr. Edwards)