CDC/IDSA Clinician Call:
Bivalent COVID-19 Boosters: What You Need to Know;
Plus Update on Monkeypox
September 10, 2022
Q&A

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1. **An immunocompromised transplant patient has been testing positive for antibodies to the nucleocapsid since March, although, to her knowledge, she has never had covid. What is the likelihood of each of these 3 items to explain it?**
   • Evusheld. She had her second 300 mg dose 2 weeks before her first positive nucleocapsid Ab test. Does Evusheld contain Abs to the N protein?
   • IVIG. She has been receiving monthly infusions since late fall 2021. Does IVIG contain Abs to the N protein?
   • She really did have an infection. Although she is on MMF, tacrolimus and prednisone, and IVIG she had an asymptomatic case around Feb/early March.

   Daniel Gluckstein: Probably from the IVIG. An Italian study found spike and nucleocapsid Ab in commercial IVIG - Pisani G, Cristiano K, Simeoni M, Martina A, Pati I, Carocci A, Gaggioli A, Marino F, Adriani D, Pupella S, Candura F, De Angelis V. Detection of antibodies against SARS-CoV-2 both in plasma pools for fractionation and in commercial intravenous immunoglobulins produced from plasma collected in Italy during the pandemic. Blood Transfus. 2022 May;20(3):198-205. doi: 10.2450/2021.0055-21. Epub 2021 May 27. PMID: 34059195; PMCID: PMC9068351.

2. **When should we consider giving the bivalent booster to the high risk elderly who received their 2nd booster who were then recently infected (within the last month)?**

   Kathryn Edwards, MD: would wait until 3 months after the covid infection.

3. **Does CDC consider "up to date" to include the Bivalent booster (asking as our large medical group is debating whether to mandate the bivalent booster for our clinical staff)?**

   Priti Patel, MD, MPH: I will address CDC's up to date definition in my presentation, but yes, it does now incorporate the most recent booster recommended for the individual.

4. **Do you have a recommendation/position if people who have had prime/boost with Moderna stay with the bivalent Moderna and same for Pfizer? Or can people switch from Pfizer to Moderna an vice versa for the bivalent? Is there any data for/against? Thanks.**

   Kathryn Edwards, MD: can use either the Moderna or the Pfizer mRNA vaccines interchangeability after priming with either of the vaccines

5. **Why did Pfizer bivalent boosters receive EUA for 12+ yrs old and Moderna did not? This has created a significant confusion in my organization and increases risk for errors.**

   Kathryn Edwards, MD: The Pfizer submission to FDA was for >12 years and the Moderna submission was for > 18 years

6. **Why is there no observation time post bivalent covid booster vaccination?**

   Kathryn Edwards, MD: Immediate allergic reactions after the booster doses are very uncommon.

7. **Are there links between boosters for COVID and arrythmias?**

   Kathryn Edwards, MD: there have been no links appreciated in VAERS or VSD.

8. **Is it possible that the severely immunocompromised may need a double dose of the bivalent vaccines in order to be adequately protected, as was the case with needing an extra dose for the primary series and an extra booster back before the bivalent? Would this fall under clinical judgment on a case by case basis**?

   Kathryn Edwards, MD: The immune responses in immunocompromised individuals are heterogenous to the primary series and likely will be the same with the boosters. Data on immunogenicity will need to be obtained to address this question.

9. **Is there any evidence that Paxlovid improves symptoms, shortens the course of the illness, prevents long covid or makes someone non-infectious sooner**?

   Mark A Swancutt, MD, PhD: In the EUA documents for Paxlovid, there is evidence that it decreases the time course of symptomatic illness. It is unclear if it makes people less infectious.

10. **What is the evidence that people who have had prime mRNA and a boost who developed symptomatic Omicron need a bivalent? Shouldn't their Omicron infection essentially provide the same if not better than a bivalent boost immunologically**?

    Mark A Swancutt, MD, PhD: This is a good hypothesis. There is no data for prevention of disease in patients with previous omicron disease versus no disease. However, serological virological neutralization data shows an increase in neutralization titer against BA.4/BA.5 and other variants in patients >55 years old. Pre-clinical data from mouse studies show protection against infection from challenge with BA.5 variant in immunized mice (this is not mice with past infection).

11. **What about unvaccinated patients or those people who have only received one dose: can they get the bivalent vaccine**?

    Mark A Swancutt, MD, PhD: The preliminary recommendation is that the one dose of the bivalent vaccine boost replaces other boosters but follows the primary series of any of the approved primary vaccines (Pfizer-bioNTech, Moderna, Novavax, and Janssen). See slide 37 under Dr. Marks' talk.

12. **Is there a CDC policy for immunocompromised people and the bivalent COVID vaccine that we can follow**?

    Mark A Swancutt, MD, PhD: There are no current updated final recommendations on the CDC website. There are some slides in the ACIP slide set under "clinical considerations" that do discuss this. This is not a final recommendation, but the preliminary recommendation is that immunocompromised patients should receive a booster after all previous vaccines that they have received.

13. **What happens if a 15y/o receives a bivalent Moderna booster**?

    Kathryn Edwards, MD: it is not approved for that age, but if inadvertently given, unlikely there will be any adverse reactions. May want to report to VAERS however.

14. **Should the severe immunocompromised patient try to get Pfizer bivalent vs Moderna due to strength**?

    Kathryn Edwards, MD: there should be no preference.

15. **So, will the recommendations back off lesions in sensitive mucosal areas as a reason for treatment**?

    Sapna Bamrah Morris, MD, FIDSA: No— sorry— I just did not mention it until the end

16. **What is the shortest interval in an individual for COVID's second booster and COVID natural infection in terms of safety and efficacy? (This question is about one individual and not public health wise.)**

    Kathryn Edwards, MD: I would space the vaccine at least 3 months after natural infection.

17. **Can a parent choose mono Moderna to boost a child aged 13? Or is bivalent Pfizer the only option for those parents**?

    Kathryn Edwards, MD: Would use the Pfizer bivalent booster but Moderna will be submitting data to FDA to reduce the age limit.

18. **Do you have concerns with this being called a booster instead of an up-dated vaccine? At what time should we be considering replacing the Wuhan strain with a more current one in the primary vaccine?**

    Mark A Swancutt, MD, PhD: I cannot answer this question, but the vaccines in the original vaccines (the primary series) provide significant protection against severe disease, ICU admission, and death against the later omicron variants.

19. **What is the status/progress of a "universal" COVID vaccine? This has been the "Holy Grail" but frustrating and elusive**.

    Mark A Swancutt, MD, PhD: This is much discussed, but the universal vaccine for COVID-19 is not under development right now.

20. **Comments on the need for a yearly booster?**

    Mark A Swancutt, MD, PhD: This is a hypothesis only. It is more desirable than several boosters per year as a goal.

21. **Any outcome data on efficacy of Evusheld?**

    Mark A Swancutt, MD, PhD: The Provent III trial shows a 77% reduction in risk of developing symptomatic disease in preliminary data.

22. **What are the recommendations for the bivalent vaccine in Pregnant and Breast Feeding individuals?**

    Peter Marks, MD, PhD: As with the original COVID-19 vaccines, these vaccines can be given to pregnant and breast feeding individuals, and given the adverse outcomes during pregnancy with COVID-19, consideration should be given to the administration of the bivalent vaccine boosters.

23. **When will Evusheld be updated to include monoclonal antibodies to Omicron variants?**

    Mark A Swancutt, MD, PhD: Evusheld at present protects mice in preclinical studies against BA.1, BA1.1, and BA.2. The exact answer to the question is unknown.

24. **Please comment on a second dose of Evusheld for those who received it more than 6 months ago.**

    Mark A Swancutt, MD, PhD: The interval of every 6 months is for routine updates based upon pharmacokinetics of the antibodies. There is no reason (no contraindication) to not give dose at some interval after 6 months, meaning one can administer a second dose after month 6 and be comfortable about it.

25. **What level of concern does the BJ.1 subvariant represent as far as prospects for antibody evasion?**

    I haven't seen any data on BJ.1 subvariant. The answer is unknown.

26. **Is there any time frame to have available the bivalent booster for pediatric patients?**

    Kathryn Edwards, MD: The manufacturers are working on those studies but not yet available.

27. **The guidelines now say boosters with original vaccines NOT recommended anymore. What if I haven't received bivalent shots yet but I have a patient in my clutches who needs a booster? is it ok to give them original vaccine with the plan to give the new one in 2 months?**

    The preliminary discussion is to give booster after the primary series. Yes, it is "okay", but the gap would be 2 months. This becomes an issue of how well one can time the receipt of vaccine by your clinic.

28. **Shouldn't we try to look at the bivalent vaccine for patients who have not completed their initial 2 or 3 dose series especially for immunocompromised who are required to get 3 primary monovalent shots first?**

    The current recommendation is to administer the primary series prior to administering the bivalent vaccine. This is not a direct answer to your question. The data given at CDC ACIP do not address this question by vaccinating patients "early".

29. **Dr. Edwards, would you recommend bivalent booster with Pfizer (total 30 mcg) or Moderna (total 50 mcg) to a 19 yo who developed mild and self-limited myocarditis following the second Pfizer dose?**

    Kathryn Edwards, MD: I would not give him the bivalent booster since he had myocarditis with the second dose. Not enough data to suggest whether Novavax would be safer. myocarditis has been seen with Novavax as you likely know.

30. **For people who had myocarditis with primary series, would you use Novavax for booster although not authorized?**

    Kathryn Edwards, MD: Novavax has been associated with myocarditis after vaccination so no data to suggest that it would be safer. At this time, I would not revaccinate this individual with the booster.

31. **Dr. Edwards: Does incidence (and risk) of COVID-19-associated myocarditis remain higher than vaccine-associated myocarditis?**

    Kathryn Edwards, MD: This is not totally clear at this time. Some studies from UK suggest that it is not, but no data currently available at this time from the US.

32. **Do we have real world information on the side effects of the new Omicron specific vaccine? I know there won't be long term data but data on immediate effects? fever? fatigue? chills?**

    Kathryn Edwards, MD: total doses are the same and the reaction assessment very similar.

33. **Is there any limit of booster doses now, or if for example an immunocompromised or other patient has had TWO boosters already are they eligible for what would be a THIRD booster (bivalent) at least two months after their second booster? (It might be helpful to have flowcharts for these different scenarios.)**

    Priti Patel, MD, MPH: CDC has some great flowcharts in slides that were presented at ACIP. I can ask Dana, if possible, to email out to attendees.

34. **I believe that prior to the bivalent booster, immunocompromised were recommended to receive a three dose primary series followed by two booster doses (for a total of five doses) with at least THREE OR FOUR months between their first and second booster. Now it seems they are eligible for the bivalent booster TWO months after their last booster, whether that was their fourth or fifth dose. Is this correct? If so, why the change (reduction in interval between boosting)?**

    The interval could be longer than 2 months and that may make sense in certain circumstances.

35. **For a younger person who received 2 immunizations and 1 booster, who got COVID 19 recently, when can they get bivalent immunization?**

    If they are 12 years or older (and thus eligible for the bivalent booster), they could consider waiting 3 months after symptom onset or positive test before getting the booster dose. That timeframe could be modified if there are other concerns related to community transmission levels or other factors.

36. **Is the recommendation to stay with the manufacturer that you used for first 3 shots if now getting the 2nd booster (as a bivalent booster)? or is recommendation to mix and match (they were showing mix and match were recommended if one does the monovalent)....does the same logic apply for the bivalent?**

    Priti Patel, MD, MPH: No specific preference. As we have said at other times in the past, the best vaccine is the one that is available. There is likely to be differential availability between the two different bivalent booster options in the near-term. Beyond that, it could be patient preference based on their experience receiving one vs. the other.

37. **Excellent points on preventing pediatric deaths through vaccination from Dr. Marks and Dr. Edwards! Dr. Patel: can the alarmingly low coverage levels in all age groups (NO age group is over 50% in up to date status) and associated risk of severe outcomes be part of CDC's key messages?**

    Priti Patel, MD, MPH: Great point, thank you!! We have a lot of work to do to get people optimally protected.

<u>Monkeypox Update:</u>

38. **Does anyone have any data regarding IgG and IgM levels that are estimated to be protective following monkeypox vaccination, and if any IgA data is available for those who received intradermal vaccination?**

    Peter Marks, MD, PhD: Not aware of any data in this regard that could be informative at this time.

39. **Is there a reported cases of monkeypox in children**?

    Kathryn Edwards, MD: There have been cases of monkeypox reported in children.

40. **What is the recommendation for monkeypox vaccination in those who have has the disease**?

    Peter Marks, MD, PhD: If an immunocompetent individual has experienced monkeypox it is not necessary to vaccinate. Natural infection probably provides superior immunity.

41. **Is there a monkeypox vaccine for the immunocompromised that cannot take the live vaccine**?

    Sapna Bamrah Morris, MD, FIDSA: Jynneos is safe for immunocompromised. It is non replicating.

42. **Is there any data on Hospitalizations/mortality attributed to monkeypox**?

    Sapna Bamrah Morris, MD, FIDSA: Coming soon— we are still gathering data