CDC/IDSA COVID-19 Clinician Call

Omicron – Continued: Plus Monoclonal Antibody Therapy Updates
December 18, 2021

Q&A

Below the Q&A transcript from the December 18, 2021 Clinician Call. The views and opinions expressed here are those of the presenters and do not necessarily reflect the official policy or position of the CDC or IDSA. Involvement of CDC and IDSA should not be viewed as endorsement of any entity or individual involved.

1. **Should transplant patients who had 3 doses of Pfizer vaccine get a booster? Would Moderna be better or Pfizer again?**

   There is a difference in the number of vaccines recommended for immunocompromised, based on Janssen versus mRNA vaccines. We're trying to see what data are available to inform these updated recommendations and can update as needed. Right now- an immunocompromised patient who received J&J as their first dose is only recommended to get a booster at 2 months (and now we prefer an mRNA vaccine). (Dr. Oliver)

2. **Any consideration on considering fully vaccinated as having 3 shots of a mRNA Vaccine and a second shot of mRNA after a J&J?**

   CDC does not have immediate plans to update the fully vaccinated definition to include a booster dose but will continue to evaluate the evidence. Data show that the currently approved or authorized COVID-19 vaccines remain effective against hospitalization and death for the predominant circulating variants in the United States. CDC will continue to monitor emerging data on vaccine effectiveness and immunogenicity against the omicron variant and data on waning of immunity following a primary series to inform updates to the definition. While CDC recommends that everyone should receive booster vaccination when eligible, ensuring that everyone has access to and completes a primary COVID-19 series remains the priority. (Dr. Oliver)

3. **Are third shots (booster shots) planned for children 12-15 year old's that have reached or are coming up 6 months post vaccination? Especially now with Omicron?**

   Pfizer has announced they are studying this. We will monitor data from the clinical trial, as well as what VE from the 2-dose primary series is over time and will discuss as soon as data are available. (Dr. Oliver)

4. **What advice/counselling do we give to any concerned patients who have already received the J and J vaccine primary or booster?**

   If this is regarding TTS: TTS is typically seen within 2 weeks after the J&J vaccine. If patients are concerned, they can be informed to seek medical care if they develop any signs/symptoms of a blood clot. (but very unlikely if beyond that 2 week window). If you mean for other doses of vaccines: If they have a J&J vaccine primary series: they should get an mRNA vaccine boost 2 months later. If they've already received a boost, we don't have recommendations for any additional doses. (Dr. Oliver)

5. **What efficacy is known/expected of bam/ete against omicron?**

   I have a slide on that. Unfortunately, it does not look good, but we can walk through it live. (Dr. Wolfe)

6. **Please can you help me understand why CDC doesn't recommend that people who start with J&J vaccine get 2 mRNA vaccines, given that people who start with mRNA can get 2 MRNA and 1 J&J?**

   Data show that a boost with an mRNA vaccine after a JnJ vaccine led to similar levels of antibodies (and neutralizing antibodies) after a primary series with mRNA vaccines. We will closely monitor VE (especially in the setting of Omicron) but right now, the recommendations are for a single mRNA vaccine boost 2 months after a JnJ vaccine. (Data here: https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2021-10-20-21/04-COVID-Atmar-508.pdf) (Dr. Oliver)

7. **Any risk in patients who got J&J who subsequently received mRNA vaccines? Sorry meant to add any higher risk of TTS who first got J&J followed by mRNA vaccines?**

   The higher rates of TTS we've seen are after JnJ vaccine. We do not have concerns for TTS after receiving an mRNA vaccine. Studies in the US and abroad (the UK) have not seen any safety issues with an mRNA vaccine boost after an adenovirus vector (J&J or AZ) vaccine (Dr. Oliver).

8. **Any advice about timing to give boosters or additional doses to patients that have received AZ, mix/match, or Sinovac, Sinopharm?**

   We have guidance for this now- it is here: Essentially, they can get a Pfizer booster dose 6 months after completion of their primary series. https://www.cdc.gov/vaccines/covid-19/clinical-considerations/covid-19-vaccines-us.html?CDC_AA_refVal=https%3A%2F%2Fwww.cdc.gov%2Fvaccines%2Fcovid-19%2Finfo-by-product%2Fclinical-considerations.html#people-vaccinated-outside-us (Dr. Oliver)

9. **How soon might NOVAVAX be slotted for FDA review?**

   Novavax was just EUL (emergency use listed) by WHO. They have not submitted data to FDA to review to date. (Dr. Oliver)

10. **Some European immunization guidelines (esp. the German "STIKO") recommend Moderna vaccines/boosters NOT to give in pt <30 yrs. of age. Why the discordance?**

    This is due to a slightly higher risk of myocarditis after a Moderna vaccine, compared to after the Pfizer vaccine. In my understanding, they are recommending Pfizer over Moderna in this younger population due to myocarditis concerns, not recommending adenovirus vector vaccines. (Dr. Oliver)

11. **We have many patients who got Astra Zeneca abroad. Should we stay within class, or give them mRNA as well?**

    In the US, we would still preferentially recommend an mRNA vaccine regardless of their primary series. In addition: CDC guidance for boosters when people got a COVID vaccine outside the US has to be an FDA-approved product (so only the Pfizer vaccine at this time). https://www.cdc.gov/vaccines/covid-19/clinical-considerations/covid-19-vaccines-us.html?CDC_AA_refVal=https%3A%2F%2Fwww.cdc.gov%2Fvaccines%2Fcovid-19%2Finfo-by-product%2Fclinical-considerations.html#people-vaccinated-outside-us (Dr. Oliver)

12. **Does the same apply to AstraZeneca and other Adenovirus-vectored vaccines? How about a person who got JnJ, should we not allow them to take 2 mRNA doses rather than just one? Clear guidance from CDC would be much appreciated.**

    For someone who received an AZ vaccine- we recommend a single Pfizer vaccine as a booster (must be an FDA-approved product, so Pfizer only for now). Guidance on clinical considerations.
    Then we only recommend 1 mRNA vaccine after J&J. The NIH trial showed similar antibody levels for an mRNA booster after a single J&J vaccine or mRNA series. (Sara Oliver)
    https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2021-10-20-21/04-COVID-Atmar-508.pdf

13. **Will the Janssen TTA data be submitted for peer review?**

    Yes! A publication is under review with a journal right now and will hopefully be published in the next several weeks. (Dr. Oliver)

14. **How long after the 2nd dose can someone take the booster?**

    If the primary series was a J&J vaccine: they should get a booster at 2 months. If the primary series was an mRNA vaccine: they should get a booster at 6 months after the 2nd dose. (Dr. Oliver)

15. **We have many folks who have ready access to mRNA vaccines but will not take them for various reasons. They will only take a non mRNA vaccine. May we still offer J&J with good counseling?**

    We have this guidance - certainly if people are well informed about the risk of TTS and still elect to receive a J&J vaccine, they can: Persons who elect to receive a Janssen COVID-19 vaccine should be informed, as part of the pre-vaccination discussion with the vaccine provider, about the risk and symptoms of TTS that could occur in the 2 weeks after vaccination, the need to seek immediate medical care should symptoms develop, and the availability of mRNA COVID-19 vaccines. (Dr. Oliver)

16. **An individual who received J&J and an mRNA booster, should they receive an additional mRNA dose?**

    We will closely monitor VE, especially in the setting of Omicron, and can update vaccine recommendations as needed. But at this time, no recommendations beyond the 1-dose primary series + single booster. (Dr. Oliver)

17. **If sotrovimab supply runs out, any thought about recommending outpatient remdesivir (daily x 3 days) as an alternative for omicron in high-risk patients?**

    I think this is a really good question, and actually one where the data is pretty strong, if you think back to Josh Hill's paper presented at IDWeek. logistically its tough, but i suspect you could incorporate it into your policy for those at the most risk. (Dr. Wolfe)

18. **Dr. Brooks, do the SARS-COV-2 variants compete with each other? Do you anticipate Omicron dominating number of cases and delta disappearing?**

    We don't yet but it is beginning to appear that Omicron is displacing Delta. Whether Omicron recovery reduces risk for subsequent Delta infection is also unknown. (Dr. Brooks)

19. **Could you comment on comparative R value for Omicron?**

    In South Africa, we estimate that the effective reproduction number for Omicron is about 4 times for the background circulating variants (mostly Delta). This higher number for Omicron reflects a combination of different transmissibility and immune evasion. This *not* the same as saying the R0 is 4 times higher because we don't yet know exactly how much the difference is driven by immune evasion. The laboratory data to date are fairly consistent with our estimates from the surveillance data, which suggest immune evasion of about 25-50% (i.e., 50-75% protection conferred by prior infection / vaccination). If this is the case, then Omicron is almost certainly more transmissible than Delta, but that may not be the case if the generation interval is substantially shorter. (Dr. Pulliam)

20. **Is there any evidence for the waning of clinical (not antibody) immunity in those who were immunized early-December 2020 to February 2021? Are we seeing increased hospital admissions or deaths in this early group of vaccine recipients?**

    Yes- several publications. Summary of data presented in slides here, but also published in MMWRs. https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2021-10-20-21/10-COVID-jones-508.pdf (Dr. Oliver)

21. **Interesting that it looks like they have 2 waves annually so far, is Gauteng the most populated area in SA?**

    Yes, Gauteng is the most populous province. Each of our waves has been driven by the spread of a new variant. I'm not sure if the 6-month pattern will hold moving forward, but I agree it's interesting. (Dr. Pulliam)

22. **What is the vaccination acceptance in province of Gauteng? Any information on hospitalization in that province?**

    The plot in this thread gives some insight into admissions: https://twitter.com/hivepi/status/1471721404747948039 (Dr Harry Moultrie is a Senior Epidemiologist at the National Institute for Communicable Diseases in South Africa). In terms of vaccination coverage, about 40% of adults in Gauteng are fully or partially vaccinated. Vaccination data is available at https://sacoronavirus.co.za/latest-vaccine-statistics/ (slide 9 shows vaccination coverage by province) (Dr. Pulliam)

23. **When will the new monoclonal antibody Sotrovimab be available in the US? Since it's one of the two that still work for Omicron.**

    The US has produced 55,000 courses of treatment. More will be available after Jan 3. You can read more here: https://www.phe.gov/emergency/events/COVID19/investigation-MCM/Sotrovimab/Pages/Update-17-Dec21.aspx. (Dr. Brooks)

24. **Assume you mean Fully Vaccinated = 2 and NOT a booster? Please clarify this point.**

    Definition of fully vaccinated is completion of a primary series: 2-dose mRNA vaccine or single dose J&J vaccine. (Dr. Oliver)

25. Can you please clarify fully vaccinated? Does that include boosted or not?

The definition for 'fully vaccinated' is the primary series only: 2 doses of mRNA vaccines, or 1 dose of J&J. Boosters are recommended, but not included in the 'fully vaccinated' definition. We'll continue to monitor emerging data against omicron and can discuss/update as needed. (Dr. Oliver)

26. What type of vaccine(s) is available in Oslo?

The Euro surveillance paper didn't say, and I don't know. Maybe check Our World in Data or the Danish "Stats Serum Institute" website. (Dr. Brooks)

27. Do we know anything yet about omicron severity in pregnant people (vaccinated or unvaccinated)?

I've not seen it carved out specifically but recognizing there's very few hospitalized cases that have been studied in detail, probably a bit early to know. The breakthrough data makes me REALLY want to have them vaccinated though, for mum's sake and babies! (Dr. Wolfe)

28. How long will the booster be effective? Most studies to date have included people more than 4 weeks out.

We are closely monitoring VE of a booster, especially in the setting of Omicron in the future. Right now, only around 20-25% of people have received a booster but will have data on VE and duration over time. (Dr. Oliver)

29. If an individual has had 1 shot of J&J, followed by 2 shots of mRNA, should there be any consideration of giving an additional (third) dose of mRNA to afford ideal protection against Omicron? In other words, should we treat them as if they did not even have the 1 initial shot of J&J?

The current recommendations are if they received 1 dose of J&J initially, they should receive a single booster 2 months later (and we now prefer that booster to be an mRNA vaccine). There aren't recommendations for additional doses beyond that. We will closely monitor VE (especially with Omicron) and can update vaccine recommendations as needed. But the current data suggest a great boost in antibody levels with an mRNA vaccine after J&J (similar to after an mRNA vaccine series) (Dr. Oliver)

30. Is the omicron variant a blessing in disguise, given its transmissibility and, especially, its association with mild disease?

I would suggest exactly the opposite. If you play out models with increased transmissibility, yet milder illness, unfortunately the sheer weight of numbers quickly lead to the lower % of sick people being a higher absolute number. Apply that also to our strained HCW population, and i think it may actually be worse. I do hope I'm wrong. (Dr. Wolfe)

31. What do we know about Omicron and long COVID?

I've seen nothing yet, but nor has anyone been tracked long enough to make reasonable comment. No reason to suggest it would be different but will be months to recognize. (Dr. Wolfe)

32. Boosters recommended for 16-17 yo as well I understand?

Yes- current recommendation: Adolescents aged 16-17 years may receive a single booster dose of Pfizer-BioNTech COVID-19 Vaccine at least 6 months after completion of the primary series, based on their individual benefits and risks. (Dr. Oliver)
https://www.cdc.gov/vaccines/covid-19/clinical-considerations/covid-19-vaccines-us.html?CDC_AA_refVal=https%3A%2F%2Fwww.cdc.gov%2Fvaccines%2Fcovid-19%2Finfo-by-product%2Fclinical-considerations.html

33. Please comment on when to get a booster if one has already gotten a booster. Many people are asking if "another" booster is needed ASAP. CDC needs to clear on its message about time between boosters. Absolutely not clear now.

No recommendations beyond a single booster right now. We will closely monitor VE especially in the setting of Omicron but right now the recommendations are a primary series + single booster for those 16 and over. (Those with mod/severe immunocompromise can get an 'additional dose', but that isn't considered a booster). (Dr. Oliver)

34. Given Omicron and continued Delta, shouldn't we be promoting early treatment (some mAbs and fluvoxamine ... and soon Paxlovid) as a prevention strategy?

I think we have to see how the FDA view it - i suspect favorably. I think the early treatment is exactly how we should be prioritizing ALL of these treatments you mean. But that involves EARLY testing, EARLY notification to centers, and then facilitating getting drug to patients. That's the logistics that remain tough! (Dr. Wolfe)

35. Can I get the link to crisis standards of care as it relates to likely increased infections and impact on healthcare workforce management?

Sure! See: https://www.cdc.gov/coronavirus/2019-ncov/hcp/mitigating-staff-shortages.html. I should note that this is for the healthcare sector**.** (Dr. Brooks)

36. Are there any tools available (e.g., apps linked to latest CDC recs.) to help people walk through the sometimes complex branching logic of knowing things like when to isolate, for how long, when to boost & with what, etc.?

That's a great idea- I'll mention to our team. I'm not aware of an app right now that walks through our recommendations. This website is the best 'go to' for the current recommendations.
https://www.cdc.gov/vaccines/covid-19/clinical-considerations/covid-19-vaccines-us.html?CDC_AA_refVal=https%3A%2F%2Fwww.cdc.gov%2Fvaccines%2Fcovid-19%2Finfo-by-product%2Fclinical-considerations.html (Dr. Oliver)

37. Can persons be co infected with delta and omicron or "reinfected" within 90 days of each other?

I'm not sure about co-infection, but reinfection probably can occur within 90 days. We use the 90-day cutoff to reduce the chance that we're including individuals with long-term shedding among our suspected reinfections. Looking at the time between successive positive tests plots that I showed, I think there is a small tail of people who are reinfected after <90 days. (Dr. Pulliam)

38. Any information on how Omicron might differently affect immunocompromised hosts?

Not that we know yet. But please remember that many/most of the infections to date have been in younger adults, travelers, local populations where immunocompromised are generally not well represented. I've not personally seen data comparing these groups. (Dr. Wolfe)

39. The "reinfections"- are any of these patients vaccinated?

Unfortunately, in South Africa, we're not able to link vaccination status to the data sets that we use to analyze reinfections, so we don't know. There do seem to be a large number of breakthrough infections as well, but we don't know about breakthrough infections in people with prior infection as well, unfortunately. (Dr. Pulliam)

40. Does CDC have data on deaths "related" to all the vaccines available in the US? It seems it would be important and appropriate to know this comparison now that CDC has made a preference recommendation.

Safety data presented at every COVID ACIP meeting. We summarized at this recent one: https://www.cdc.gov/vaccines/acip/meetings/slides-2021-12-16.html 9 deaths from TTS, 1 reported previously from GBS after J&J vaccine. None from myocarditis. Safety data in 5-11 was covered at that ACIP meeting as well. (Dr. Oliver)

41. How is it being determined that a patient is reinfected vs. prolonged shedding with positive PCRs due to persistent initial infection? We are seeing patients that remain positive for 10-12 weeks.

Our analysis requires that positive tests be at least 90 days apart. (Dr. Pulliam)

42. If a person takes Astra Zeneca mAb – and then wishes to get vaccinated – how long would they have to wait to take the vaccine?

Great question - officially we just don't know. I would encourage them to be maximally vaccinated first, as I think there's sometimes some cellular benefit first. But remember, that early on these will likely be targeted to heavily immunosuppressed patients, so probably the proven (small) benefit now, outstrips the unlikely antibody production that will come over a few weeks with vaccine. If we get it into a broader population, your question is certainly highly relevant. (Dr. Wolfe)

43. Is there any data yet that could tell us if an Omicron infection might be protective against a delta infection?

I have wondered that too; what if as Omicron (hopefully) passes Delta is still around. Unknown yet - time will tell. (Dr. Brooks)

44. Out of curiosity, when is Molnupiravir expected to receive EUA?

FDA has it under consideration for authorization based on their advisory committee recommendation. Date of authorization not known but hopefully soon for Molnupiravir and PAXLOVID. (Dr. Brooks)

45. **How soon after the AZ monoclonal antibody infusion did the cardiac events occur?**

    They're IM injections. Good question, I actually don't have the timelines for the individual events. (Dr. Wolfe)

46. **Any timely updates on oral antiviral therapies for COVID-19 and Omicron variant?**

    FDA is in the process of considering authorization of both, hopefully soon. (Dr. Brooks)

47. **What is coronavirus OC 43?**

    This review may help: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7204879/. OC43 is one of four "endemic" coronaviruses that generally cause mild disease and are a frequent cause of seasonal "common colds". (Dr. Brooks)

48. **Are preterm infants included in the EUA? Is there neonatal data regarding safety or even severity to indicate need for Bam-Este in this population?**

    Preterm infants are included if their weight is over 1 kg. (Dr. Patel)

49. **Any word if sotrovimab is pursuing a pediatric EUA?**

    My understanding is yes, they are pursuing an EUA. (Dr. Patel)

50. **How will we know when we shouldn't regionally use CAS-IMD or BAM-ETE?**

    We have looked to the HHS comment released yesterday that once you're beyond 20% you should start swinging over to Sotrovimab, which they are planning to send out shortly. But the supply of that is still very low. I would encourage you to look at your state for the % of Omicron or know which labs locally can find s-drop drop out or sequencing to give you locally relevant data. (Dr. Wolfe)

51. **I know it was briefly mentioned, but hoping to hear more about the oral agents, i.e., Molnupiravir, Paxlovid.**

    Same - so the distribution of both is not clear. Nor is the FDA approval yet set for Paxlovid. We have looked at efficacy of Molnupiravir and decided internally to direct people to mAb treatments (or remdesivir for 72hrs) first, but monulpiravir will be better given its a pill for certain people. If you're in an area where you can't get sotrovimab, and omicron dominants, then you'll want to use more monu / paxoliv / remdes because they're unaffected. (Dr. Wolfe)

52. **With regards to effect modification of age on obesity risk - did you say that you plan to not offer BAM/ETE in obese children < 8 years old? If so, how did you decide on this age cut-off? Was it based on expert opinion, or do you happen to have a reference to share? We are struggling with deciding on what the age cut-off should be at our peds institution.**

    Yes, we will not offer it under 8 years for obesity. This is based on our own local data that showed a lower number of percentage hospitalized of obese children < 8 years, vs those over 8 years. This a rough estimate based on local data. (Dr. Patel)

53. At what percentage of circulating Omicron in a community would recommend to avoid Regeneron for COVID-19?

The HHS came out yesterday and suggested we use 20% as a guide to when we should switch to Sotrovimab, which they're going to start distributing (in small amounts) again soon. I think that's a good % to work from. Easier to think about this also when molnu or paxlovid is available, because then you can swing them over to that (assuming you don't have instantaneous variant strain visibility, which most of us don't have). (Dr. Wolfe)

54. Should we prioritize vaccinated solid organ transplant patients based on a detectable antibody titers of certain level?

Great question - remember there's data of reduced mortality even in those who didn't make antibodies, so there's clearly some cellular impact. We are going to prioritize SOTx patients who ALSO took b-cell / CD20 inhibitors or plasmaphoresis for mAb infusions though, to help their humoral defense, irrespective of what their cellular vaccine responsiveness is. (Dr. Wolfe)

55. How close is sotrovimab to EUA?

It is available, with EUA already, problem is supply. (Dr. Wolfe)

56. Do you have any guidelines or recommendations to the people who received other vaccine than mRNA, virus vectors for booster vaccination?

We at duke have extrapolated from J&J data, and European AZ data to give these folk mRNA boosters. There's not great data I'm aware of for other vaccines, but there's equally no signal in any of the studies so far for significant side effects. So, I think with Omicron coming /here, I'm trying to boost each of those patients with Pfizer/Moderna. (Dr. Wolfe)

57. Rapid testing for screening for gatherings is being recommended but it seems for asymptomatic individuals, it is so much less useful.

Totally agree - we have good data in our college and pro-league sports where the performance characteristics in asymptomatics was pretty mediocre. Doesn't take away the need to mask, as the Norwegian outbreak just talked about describes. (Dr. Wolfe)

58. I'm definitely seeing a higher false negative rate on my rapid testing in office here on Long Island NY. I use Quidel's Sofia, but I've heard similar report from colleagues using Binex. Schools here in NYS only require a negative rapid antigen result to return to school. Isn't that a concern?

Thanks for the information. For what it's worth, the manufacturers recommend making sure a good adequate specimen is collected and that the test is being performed as instructed and is also not past expiry. Assuming all that's in order, then it is worth both calling the manufacturer of the test being used and alerting local public health, which may be interested in helping review your data and documenting any problem so they can make informed recommendations about what test to use.

Attendee: I have called. They pretty much told me they have not begun studying it yet, are in the process of getting it together. I'm collecting the specimens the same way I have since the start. Have always backed up my rapid Ag with PCR and definitely seeing a higher false negative rate.

59. Since COVID-19 antigen testing is less sensitive in asymptomatic, should those individuals skip right to COVID-19 PCR testing for screening - for gatherings, etc.?

They shouldn't gather. Honestly, I can't see how to reliably trust any test right now. A rapid Ag with poor sensitivity vs a more reliable PCR that takes 3 days for result.

60. Do any of the panelists think there would be value in knowing whether any given lab does/doesn't or can/cannot report on SGTF, in case that turns out to be clinically useful for making treatment decisions (e.g., sotro or not)?

It is worth inquiring if the lab you use has that capacity. The FisherScientific TaqPath COVID-19 assay is the one that has this interesting characteristic about it.

61. Am I missing something? Can we use remdesivir in outpatient setting? I guess since it is no longer EUA and is Full FDA approved can do it off label?

See here for summary recommendations: https://www.covid19treatmentguidelines.nih.gov/management/clinical-management/clinical-management-summary. Remdesivir remains recommended only for inpatient setting.