CDC/IDSA COVID-19 Clinician Call

Omicron Updates Plus the Latest on Molnupiravir
December 4, 2021

Q&A

Below the Q&A transcript from the December 4, 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. **What do you do if an immunocompromised patient inadvertently was given 0.25mL of Moderna COVID vaccine instead of the 0.5mL dose?**

   Patients who meet the definition of moderately to severely immunocompromised and received a primary series of an mRNA vaccine are recommended to receive an additional full dose of the same vaccine at least 28 days after completion of the primary series. If inadvertently given a half dose of Moderna in that situation, they should be recalled and given a full dose (no minimum interval). If the error is identified immediately, the patient can be given an additional half dose on the same day to make a total of a full dose, but that only applies when this can be done on the same day. IC patients who have received an mRNA primary series and additional dose should also be given a booster dose 6 months after the additional dose.
   (Fox, Kimberley)

2. **Do any of the current rapid COVID-19 tests, including eMed, identify Omicron, or are they just generically + regardless of the specific type of COVID-19? If not, will rapid tests be quickly modified to include Omicron variant?**

   Current tests, including rapid antigen tests, are expected to detect omicron, but not distinguish it from other variants (Matthew Binnicker)

3. **Would you favor monoclonal antibodies over molnupiravir if both are available?**

   Ultimately CDC will defer that to NIH treatment guidelines (which we anticipate would follow an EUA approval within about a week) as well as clinician judgement on risk/benefits. (Amber Vasquez)

4. **Who is on the NIH guideline panel?**

   Here you go! https://www.covid19treatmentguidelines.nih.gov/about-the-guidelines/panel-roster/ (Amber Vasquez)

5. **When is Paxlovid being discussed as EUA? What about ADZ7442 (long acting monoclonal)?**

   It's expected that Paxlovid will go before ADAC by the end of December. I'm not sure about ADZ7442 but we can keep you updated when we hear more. (Amber Vasquez)

6. **Will a pregnancy test be required prior to dispensing Molnupiravir to pregnant/ women of childbearing age? How would health departments or prescribers ensure (both medically as well as medicolegally) that these women groups get the counseling they need regarding this, and that this is not inadvertently dispensed to these groups?**

   This is precisely what we were hoping to update you on today but unfortunately still need to wait on the specifics of the EUA to know details of things like a pregnancy test, HHS distribution plans, etc. But hopefully CDC or other HHS partners can update on the next call if the EUA is approved. (Amber Vasquez)

7. **Do you think the treatment changed between the first and second half? were other treatments received different? Do you think the treatment changed between the first and second half? were other treatments received different?**

   This was actually asked by a panelist at the ADAC meeting - could participants in the post-interim period have been taking concomitant COVID-19 therapies. It was a requirement of the trial that participants not take other therapies, but that is about all we know. (Amber Vasquez)

8. **What are the concerns for AEs for mulnupiravir and how is this being addressed given its unique mechanism of action?**

   The primary concerns addressed at the ADAC meeting were regarding mutagenicity potential given the drug's mechanism of action (incorporates into SARS-CoV-2 RNA template strand and introduces transition errors in the viral RNA that impairs replication and infectivity). There was in vitro concern for effect on human DNA that was not borne out on animal studies, so the concern for mutagenicity in adult human population is low. However, it will not be recommended for pregnant or lactating women, and its potential in pediatric populations are uncertain. The concern was also discussed regarding potential development of new VoC but this risk is unclear at this time. (Amber Vasquez)

9. **Participants were all unvaccinated, right?**

   That's correct. All unvaccinated though noted in the ADA meeting that participants were not tested for antibodies prior to enrollment. (Amber Vasquez)

10. **Could you comment on comparison with the Pfizer antiviral?**

    Efficacy for Paxlovid at preventing hospitalization and death appears to be higher based on interim analysis reported (89%). Notably Paxlovid will need to be given in conjunction with low dose ritonavir. More details here on the interim analysis of Paxlovid:

https://www.pfizer.com/news/press-release/press-release-detail/pfizers-novel-covid-19-oral-antiviral-treatment-candidate (Amber Vasquez)

Attendee reply: Paxlovid is the name of the combination drug. It already HAS ritonavir in the capsule. The drug that is new is PF-07321332.

That's correct thanks for clarifying! (Amber Vasquez)

11. **What % of participants in the mulnupiravir trial in the first half vs second half of the trial were infected with delta? Could this have affected the difference in outcome in the two time periods in the trial and argue against using the drug now?**

    Exact percentages weren't presented at the ADAC meeting but it was noted that it was greater in the second half than the first, though not identified as a single reason. (Amber Vasquez)

12. **Is there a comparison of molnupiravir vs monoclonal antibodies?**

    No direct comparisons that I know of at this time. (Amber Vasquez)

13. **Is the Omicron variant:**
    1. More contagious - Do patients who have had another COVID-19 variant experience breakthrough Omicron variant Infections?

    2. Are patients who have been vaccinated and contracting the omicron variant:
    a. With 2 of 2 Pfizer or Moderna vaccinations experience symptoms that leads to hospitalization? Or admission to ICUs? b. With 3 of 3 Pfizer or Moderna vaccinations experience symptoms that leads to hospitalization? Or admission to ICUs?

    Dr. Brooks will cover some of this in his slides. Other data on the interaction of primary or boosted vaccine responses vs omicron is being actively worked out in labs across the world in vitro and in epidemiologic studies. (Sanjat Kanjilal)

14. **How long does it take to sequence the variants? Does it take much longer than PCR testing to confirm the presence of the virus? I know that it's time consuming, but how much longer does it take? What are the barriers to sequence every positive sample?**

    Depending on where sequencing is done (i.e., at local lab or at a state health lab), results may be available in 1-7 days. If done locally, results may be available in as little as 24 hours. Currently, there is not capacity to perform sequencing on all positive samples but labs are working to increasing capacity. (Matthew Binnicker)

15. **The reported on NICD web page 22 Nov, not 23 Nov**

    Thanks! I'll amend the slide to note date of upload to GISAID. The key fact here is that three places picked up the new variant almost simultaneously. (John Brooks)

16. **Please discuss comparison between Molnupiravir and Paxlovid.**

    Paxlovid has a similar study population (confirmed mild-mod COVID in unvaccinated individuals at high risk of progression to severe disease). Paxlovid is also oral q12 for 5 days and intended to be given within 5 days of symptom onset. Unlike molnupiravir, Paxlovid (a protease inhibitor) is given in conjunction with low-dose ritonavir. Efficacy of Paxlovid in preventing hosp/death appears to be higher (89%) based on interim analysis. More details on the interim analysis of Paxlovid here: https://www.pfizer.com/news/press-release/press-release-detail/pfizers-novel-covid-19-oral-antiviral-treatment-candidate. (Amber Vasquez)

17. **Should patients without any risk factors be considered for molnupiravir? Is the list of risk factors for molnupiravir the same as the CDC list?**

    We are waiting for details of the EUA and subsequent NIH treatment guidelines Re: risk factors. Those included in the MOVe-OUT trial were: >60 years of age, active cancer, CKD, COPD, obesity (BMI ≥ 30), serious heart conditions (CAD, heart failure, cardiomyopathies), DM. (Amber Vasquez)

18. **Where was delta spike in hospital death in S. Africa?**

    The third surge primarily in Gauteng Province but occurred nationwide. (John Brooks)

19. **What is your take on this new data about recombination with common cold virus and potentially HIV?**

    There is a theoretical possibility for recombination in a CoV but the evidence in the recent preprint is based on a 3 amino acid sequence. This is too small to say that it is the result of recombination versus sequencing error. (Sanjat Kanjilal)

20. **Dr Brooks: Omicron being so different from previous known variants and with no clear recent predecessor, could it be considered a recent introduction into humans from whatever the natural host is (like HIV-1 vs HIV-2), independently of SARS-CoV-2 evolution (are we seeing SARS-CoV-3?)**

    There is phylogenetic link to older clade viruses likely derived from clade 20B see https://nextstrain.org/groups/neherlab/ncov/21K.Omicron?d=tree,entropy,frequencies&p=full (David Wentworth)

21. **Could failure of the ventilation system in the isolation hotel in Hong Kong be implicated in the two cases discussed?**

    Hong Kong is looking into it. Reminiscent of a similar story at a quarantine hotel in Australia. (John Brooks)

22. Discuss airborne transmission in setting of the Hong Kong cases. Presumably no other people in the Hong Kong quarantine area (e.g. staff) developed Covid-19. What was the air flow in the rooms?

I don't know yet the how the air handing system (both fresh air and filtration) was configured or functions and we're very interested. It certainly raises concerns that we need to encourage masking and assure indoor spaces ensure they had adequate air handing: both filtration and air turnover with fresh air intake. We have also asked the authors about contact tracing here. Other possibilities Omicron was already there in the hotel and both A. and B. were infected by that person somehow, they were infected in transit at the airport, or was some exposure through shared air or surfaces or other materials. (John Brooks)

23. Is the ventilation system common or individual to the room in the quarantine hotel where the 2 cases were? What about infant susceptibility?

I would be very surprised if the health authority in Hong Kong weren't looking at this given the Australian experience. (John Brooks)

24. Are home antigen tests reliable to pick up Omicron?

Currently, we anticipate that at-home antigen tests should detect omicron. (Matthew Binnicker)

25. It is my understanding that in Florida genomic surveillance is done on cases of vaccinated patients only. Is that the CDC recommendation?

I'm sorry but I don't know the answer but thanks for bringing it up; I'll ask. (John Brooks)

26. If a PCR assay just detects S gene, would the result be false negative for Omicron?

Potentially - but I'm not aware of a common molecular assay that targets only the S gene. (Matthew Binnicker)

27. Venky Soundararajan of Cambridge, Massachusetts-based data analytics firm inference is quoted by Reuters as stating in part regarding a mutation in Omicron as "...The same genetic sequence appears many times in one of the coronaviruses that causes colds in people - known as HCoV-229E - and in the human immunodeficiency virus (HIV)...". Are there data to show HIV genome sequence homology in Omicron?

Harold, very interesting hypothesis and concordant with the concept of evolving to be more transmissible but not more "dangerous". Unknown right now. I also bet you meant HCoV or did you mean HIV? It would be nice if this evolves to be like the common cold. (John Brooks)

28. We have had a slow increase in total cases? Relationship to undetected omicron?

Unlikely Omicron and more likely persistent circulation and infection with Delta. The same would be true for Europe where large surges are occurring. The US variant surveillance system is sufficiently sensitive to detect a new variants with </= 7 days at a prevalence of 0.1% of greater. Neither we in U.S. nor colleagues in Europe or Asia have seen this sequence before. (John Brooks)

29. For Rapid Antigen tests, what is the specificity and what effects does this have on false positive rates?

Fortunately, specificity of the rapid antigen tests (e.g., BinaxNOW) appears to be high. Several studies have shown specificity >95%. However, if large numbers of tests are done in an asymptomatic population, there is still the chance for false positive results. (Matthew Binnicker)

30. There is 10-15% false negative for rapid tests in infected individuals for delta and earlier positive SARS-CoV-2. What is it for omicron?

There is insufficient data to evaluate the performance of antigen tests versus omicron. However, the mutations in the antigen target (which is usually the nucleocapsid protein), are more modest than that seen in the spike protein. Therefore, a priori our concern for false negativity is a bit lower with rapid antigen tests. However, the issues around overall sensitivity remain. (Sanjat Kanjilal)

31. Does Covid vaccines affect Antigen test results? Such as possible false positive?

Vaccination does not impact antigen or molecular testing (i.e., should not cause a false-positive result). (Matthew Binnicker)

32. Comparing efficacy between paxlovid and molnupiravir, would paxlovid be considered a better medication than molnupiravir?

This would have to be done in a head-to-head study.
Agree we can't answer this with confidence at this time. However, if you'd like to read more about the Paxlovid interim analysis: https://www.pfizer.com/news/press-release/press-release-detail/pfizers-novel-covid-19-oral-antiviral-treatment-candidate. (Amber Vasquez)

33. Wonderful info always. PCR I understand would be feasible for at home test & would be more sensitive. Is there any company pursuing this important accurate method?

There are a few molecular at-home options. LuciraDx and Cue have received authorization for at-home testing using a molecular approach. (Matthew Binnicker)

34. Most home antigen tests include 2 tests meant to be used sequentially over 36-48 hours. How does this 2-test strategy then look in terms of sensitivity in symptomatic and asymptomatic patients?

That is correct. Serial testing over a 36-48hr time interval can help reduce the possibility of missing early infection, but there is not a lot of data showing this with real-world data. The difference in sensitivity for Ag tests between symptomatic and asymptomatic people is related to the fact because symptomatic people are more likely to present earlier in their illness and thus have a higher viral burden and be more easily detected. Asymptomatic people can present anywhere along their viral kinetic curve, which means they have a higher probability of having a viral burden below the limit of detection of an antigen-based assay. (Sanjat Kanjilal)

35. He said "...HCoV-229E - and in the human immunodeficiency virus (HIV)..."

Thanks! Got it. Interesting. (John Brooks)

36. A 5-year-old had COVID 19 on 11/9/2021. She had loss of taste and smell then. When should she receive her first COVID 19 vaccine? She has no problems now.

She can be vaccinated once she is completely well and has completed any required isolation.

37. Is it not true that if the person IS symptomatic and has a positive Ag test, that it should be believed and not discounted as a false positive? I agree that follow up PCR's are needed with negative test and high pre-test probability, or low pre-test positivity and positive result, however, getting the message right across to the public is essential to allow maximal effect of upcoming increased availability of at home tests in my humble opinion.

Agreed - a positive result in a symptomatic individual is likely a true positive. In these cases, having a lab-based. (Matthew Binnicker)

38. Do you advise booster for persons, who had been ill with Covid in 2020 and 2 doses of AstraZeneca vaccine in 2021 spring?

Yes. A booster dose is recommended for all persons 18 years and older. Prior infection does not change that recommendation. For those who received a primary series not authorized in the US such as AZ, a booster dose of Pfizer vaccine can be used under recently issued Emergency Use Instructions.

39. Molnupiravir studies in the unvaccinated? Theoretically efficacy in the unvaccinated might be higher. Worldwide many countries still with low vaccination rates. We have Immunocompromised, unvaccinated persons with medical exemptions.

Yes the MOVe-OUT trial was only in unvaccinated individuals. (Amber Vasquez)

40. When will boosters be available for 15-year-old and up?

Pfizer recently submitted paperwork to FDA requesting authorization for a booster dose for ages 16-17 years, so this is pending FDA action. There is no request yet from Pfizer for booster authorization for 12-15 years.

41. What is the CDC (or others) doing to educate physicians and consumers about interpretation of test results (rapid antigen and PCR) and what to do subsequently with each type of test result. In my opinion, there is an appalling lack of knowledge among physicians and consumers in this area.

Agreed - I'm aware of efforts at the national level to address this gap by putting together educational material on use and interpretation of testing, including at-home tests. (Matthew Binnicker)

42. Are there studies looking at combination molnupiravir + Paxlovid in early treatment?

Not that I know of at this time. (Amber Vasquez)

43. It has been two years since the emergence of SARS -CoV-2, why we do not have other of vaccine available for public? Isn't it a good idea to have another type of vaccine that do not just focus on spike protein?

You want to prevent the virus from even entering the target cell. SARS-CoV-2 enters the cell by attaching the ACE-2 receptor through the spike protein. So you WANT to target the spike protein. Getting to another target is also harder.

44. Difference in sensitivity and specificity between standard PCR and Rapid PCR

We have found that the sensitivity of rapid PCR tests, such as Roche Liat and Cue, are similar to standard PCR tests. (Matthew Binnicker)