CDC/IDSA Clinician Call:
Confronting BA.4/BA.5: What Clinicians Can Do
August 6, 2022
Q&A

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1. **Will the Monkey Pox public health emergency mean that we will have EUA tests we can use in hospitals? For example, Roche has a research use only test that could be used in many labs if EUA status is possible.**

   Dr. Wilkin: I don't know the answer. I think it frees up resources to help expand testing and treatment

   (Guest) EUA is generally issued when no alternative is available. Currently there are FDA-cleared CDC-developed MPX lesion PCR tests in use at commercial labs. Hospitals may verify RUOs in accordance with CLIA and provide as LDTs.

   (Guest) Covid had CDC test too. It's not enough. The CDC test is not as automated as commercially manufactured tests. If we have commercial EUA tests from Roche, Cepheid, Hologic etc. We could really ramp up testing and improve turnaround time.

   (Guest) No reason labs cannot verify and offer RUO assays now

2. **Can Tecovirimat be used for longer than 14 days if patient's lesions have not completely crusted over and/or proctitis unimproved (& provided other STIs excluded)? Thank you**

   Dr. Wilkin: We don't allow for that in the protocol. I don't think the CDC EA-IND allows for this. We need to understand more about the possibility of resistance to tecovirimat. This might be a situation to consider an alternative treatment such as brincidofovir. There are no data on this that I know of

   Correction: The CDC protocol does allow for prolonged treatment up to 90 days!!

3. **Given the discovery of replication-competent virus in the semen of two patients with HIV, is there concern that virus may linger persistently in testes (an immune privileged site) and thus may require eradication therapy to stop transmission?**

   Dr. Fischer: This is an important question that will be studied in this clinical trial

4. **Is presumptive Monkeypox disease for the study defined by symptoms or by a positive non-variola orthopoxvirus PCR?**

   Dr. Fischer: Presumptive disease is defined by symptoms and exposure

5. **Is there consideration of use of tecovirimat to accelerate the period in which patients may leave isolation given that it seems to rapidly and drastically reduce viral titers?**

   Dr. Fischer:: replication competent virus from samples will be included as an endpoint and this information could be used to inform guidelines

6. **Dear Tim: You may wish to also see if the pain decreases with the use of Tecovirimat (e.g., by decrease in lesion formation)**

   Dr. Zucker: Thank you for this question. Measuring pain is a secondary outcome in this study.

   Do you already have some cases of conjunctivitis?

   Dr. Wilkin: Yes, we have been treating patients with ocular symptoms in the EA-IND study. This requires topical antivirals as well

7. **We have noticed significant decrease in symptom duration and intensity with Tpoxx and it is plausible that shedding may be decreased as well. Why is the CDC not moving towards an EUA? By insisting on EA-IND, access to treatment and healthcare disparities are worsened in areas with fewer clinicians able/willing to go through the paperwork. Any paperwork is a deterrent, and it feels like CDC is putting data before public good. Thanks**.

   Dr. Fischer: Data from an RCT is critical to determining if this therapeutic is safe and effective.

   Guest Comment: Well, this is a public health emergency and perhaps the RCT can be done parallel with allowing access via EUA. They are not mutually exclusive. As you well know, it was studied for smallpox on a monkeypox model and Europe has granted EUA. I think there's enough data to move forward and the CDC needs to hear the voice of clinicians on the front lines.

   Dr. Fischer: Individuals who have evidence of severe disease, pregnant people, individuals <18 years of age, and those considered at high risk for severe disease will be able to enroll in an open label arm of the study which will increase access and also contribute important data on the use of this therapeutic and infection

   Dr. Wilkin, MD, MPH, FIDSA: It seems an EUA is not possible without efficacy data.

8. **If patients who receive TPOXX have complete resolution within a few days of treatment would shorter course than 14 days be considered in future?**

   Dr. Wilkin: Great question. once we establish efficacy, we can consider follow-up studies to refine length of treatment.

9. **Is there a disease severity score being developed?**
   Guest Comment: Yes, the disease severity scores likely need to be modified for mucosal routes of infection. (I know the older ones!)

   Dr. Fischer: This is such an important question and represents a current clinical gap. There have been two severity scores that I've seen reported one based on lesion number and functional status and another based on the number of symptoms. We are discussing how to contribute data towards the development of one.

10. **Can patients present with proctitis only without blistering lesions?**

    Dr. Zucker: Yes, some patients have presented with proctitis as the first symptom. While most have gone on to develop skin lesions some have not.

    (Guest): Yes, we had a patient here. Rectal swab positive. No skin lesions on presentation and only had perianal lesions develop on day 4

11. **Where geographically will be study sites for A5418?**

    Dr. Wilkin: The sites are being selected. ACTG sites are eligible, other DAIDS sites such as HIV prevention trials networks, vaccine sites etc. We also have sites participating in other DAIDS and DMID studies. We are aiming to cover the US broadly. Feel free to reach out if you have a particular concern.

12. **Once the trial starts will IND through CDC allow tpoxx to be available for institutions not part of trial?**

    Dr. Zucker: There is no plan to remove the current EA-IND that I am aware of.

13. **Once a patient is to be started on Tpoxx/ Tecovirimat, can you please outline what parameters need to be monitored at baseline, during and at treatment completion? Thank you!**

    Dr. Wilkin: At our institution, most of our patients are being followed remotely. We are mainly following symptoms, progression of lesions, and late onset of lesions. There is no obvious role for laboratory monitoring from what I can tell. After treatment, recrudescent lesions have been rarely reported. @Jason Zucker, anything to add?

    Dr. Zucker: That's consistent with what we are doing as well. We do baseline labs and then follow patients remotely only repeating labs if clinically indicated. We are doing follow-ups in person if clinically indicated (eye disease, severe bacterial superinfection, etc.).

14. **Is it known how long does Monkeypox stay infectious in inanimate surfaces/clothing?**

    Dr. Wilkin: I don't know the answer to this important question.

15. **Can we use 1 dose of Jynneos and wait 6-8 weeks for the second? How much protection is there after 1 dose?**

    Dr. Wilkin: We don't have any efficacy data yet. I think most people develop antibodies at 4weeks after the first dose. The second dose likely helps with immune memory and long-term protection. So, from a public health perspective, getting 1st doses into more people is likely important than getting 2nd doses administered according to schedule.

    (Guest) Jynneos is far less immunogenic than the 1st and 2nd generation vaccines. You NEED two doses as per all animal studies. Sánchez-Sampedro L, Perdiguero B, Mejías-Pérez E, García- Arriaza J, Di Pilato M, Esteban M. The evolution of poxvirus vaccines. Viruses. 2015 Apr 7;7(4):1726-803. doi: 10.3390/v7041726. PMID: 25853483; PMCID: PMC4411676. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4411676/

    (Guest) I've been at our county vaccination clinic last week. MOST of these men were surprised when we said they were NOT immune after 1 shot. I would say about 1/3rd of these men did NOT want change behavior/be more cautious between their 1st dose and 2 weeks after their second. We did 300 shots in 2 days.

16. **Monkeypox question in general: I haven't heard much about whether monkeypox lesions heal with scarring as does smallpox. Does it?**

    Dr. Zucker: Yes, clinically we are seeing scarring in some of our cases.

    Dr. Wilkin: Talk to dermatology for recommendations. They have recommended antibacterial ointments until healed and then scarguard thereafter to improve outcomes

    (Guest) Rob, You may wish to review the data in this report: Essbauer S, Meyer H, Porsch-Ozcürümez M, Pfeffer M. Long-lasting stability of vaccinia virus (orthopoxvirus) in food and environmental samples. Zoonoses Public Health. 2007;54(3-4):118-24. doi: 10.1111/j.1863-2378.2007.01035.x. PMID: 17456141.

17. **What fraction of cases are reported?**

    Dr. Wilkin: for HMPXV? I don't think we know yet. There is clearly asymptomatic or minimally symptomatic disease that will go undiagnosed.

18. **What is the intradermal protocol for monkey pox vaccine**

    Dr. Wilkin: PMID: 26143613 DOI: 10.1016/j.vaccine.2015.06.075

    It is a one fifth dose intradermally in this article. I assume it is similar to placing a PPD.

19. Is tecovirimat being used mostly in inpatient or is there heavy outpatient use in areas most affected?

Dr. Zucker: To date most patients have not required hospitalization. In NYC it's use has been primarily outpatient

20. What do we know about use of tecovirimat as PrEp and as PEP for MPX? Are RCTs planned?

Dr. Zucker: We do not currently know about tecovirimat for PEP and PrEP. The goal of this trial is to ensure that the drug demonstrates efficacy for treatment in a human trial.

(Guest) Thanks, Jason. I understand that this RCT is not focused on PrEP or PEP. However, particularly in the context of limited vaccine availability, rapidly evaluating tecovirimat use as PrEP and PEP could help in developing a combination strategy for control of the MPX pandemic.

21. Will the US NIH TPoxx trial evaluate oral fluid, oropharyngeal and/or saliva specimens for PCR MPX detection?

Dr. Zucker: Yes, there are plans to evaluate multiple compartments for HMPXV detection including with oral swabs.

22. Cidofovir, brincidofovir, and tecovirimat have proven activity against poxviruses in in vitro and animal studies. Why are we only hearing about tecovirimat (and rarely brincidovofivir)? And why is there so little discussion about the use of Trifluridine (Viroptic) for eye lesions in Monkeypox?

Dr. Wilkin: It seems that tecovirimat is the most potent in vitro. The toxicities of cidofovir would make the risk-benefit ratio unfavorable for this generally self-limited disease. Brincidofovir has been used. A small case series showed hepatitis with this drug. this is strange as hepatitis was not seen in other studies of brincidofovir. Maybe the LFT abnormalities were from HMPXV? Some people have advocated dual treatment for those with severe immunosuppression.

23. With the large scale mpox exposure in Illinois at a daycare, there was commentary that some of the children received Jynneos as PeP. Can you please comment on this recommendation and also that some public health dept are also recommending tecoviramat for PeP.

Dr. Zucker: This is a challenging question as there is limited data for both the vaccine and tecovirimat in children. The CDC does recommend vaccination for PEP (https://www.cdc.gov/poxvirus/monkeypox/considerations-for-monkeypox-vaccination.html) however Jynneos is only approved for age >18 but it is available for younger through an IND. Additionally, tecovirimat has limited pediatric data as well and per the EA-IND can be considered for PEP in a case-by-case basis in consultation with the CDC.

24. Are the new Covid variants more likely to give a negative result on home rapid antigen tests?

Dr. Logan: Antigen tests have been found to have sensitivity for the newer variants. These tests are still a good option for diagnosis.

25. **Would Paxlovid be recommended for children aged greater than 12 with mild asthma (on no chronic medications)?**

    Dr. Logan: Paxlovid is recommended for children 12 and older who have mild to moderate infection with risk for severe illness, so Paxlovid would be recommended for such a case.

26. **For patients who have had COVID-19 undergoing elective surgery, how long after symptoms have subsided should they be required to wait, and should they be retested?**

    Dr. Logan: Patients who have COVID-19 should wait to complete isolation and until they are no longer infectious before considering elective surgery. Each hospital or surgery center will have guidelines for how long after isolation for patients to wait before procedures. Retesting is not recommended for this purpose.

27. **What evidence is there so far about the clinical efficacy of Evusheld for currently circulating variants, including BA.5?**

    Dr. Giovanni: On July 14, 2022, AstraZeneca published "Update to Evusheld recommended dosage regimen for pre-exposure prophylaxis of COVID-19" (https://www.astrazeneca.com/media-centre/statements/2022/update-to-evusheld-recommended-dosage-regimen-for-pre-exposure-prophylaxis-of-covid-19.html). The update states that "multiple independent studies have shown that Evusheld retained neutralization activity against the highly transmissible Omicron BA.4 and BA.5 variants and retained potent neutralizing activity against BA.2...".

    Thank you. Is this clinical data as well as laboratory evidence?

    Dr. Giovanni: These are the cited references:
    Vector Engineering Lab et al. COVID CG. https://covidcg.org/ [Last accessed: July 2022]
    Tuekprakhon A, et al. Antibody Escape of SARS-CoV-2 Omicron BA.4 and BA.5 from Vaccine and BA.1 Serum. Cell. Published online July 7, 2022. doi:10.1016/J.CELL.2022.06.005

28. **All age group need booster dose in COVID?**

    Dr. Logan: All people 18 years and older are eligible for booster, and some younger age groups are also eligible. The schedule for boosters can be found on https://www.cdc.gov/coronavirus/2019-ncov/vaccines/stay-up-to-date.html

29. **I have noticed that there is what seems like a rebound phenomenon with this variant. Patients clinically improve their symptoms, and show a negative rapid test, and then begin again with symptoms and their test becomes positive again. This happens with patients who have taken, as well as those who have NOT taken Paxlovid. Have others noticed any of this happening?**

    Dr. Logan: COVID rebound (after Paxlovid and without Paxlovid treatment) has been reported by many providers. More information about this can be found at https://emergency.cdc.gov/han/2022/han00467.asp and at https://www.cdc.gov/mmwr/volumes/71/wr/pdfs/mm7125e2-H.pdf

30. **Will CDC update their level monitoring based on poor reliability of home-antigen test reporting and biased positivity results from reported results?**

    Dr. Butler: Although %+ is still reported for NAATs, it is not a particularly useful metric for the reasons you cite. It is not part of the estimation of COVID Community Levels.

31. **What's the blue variant between BA4 and BA5?**

    Dr. Butler: Thank you for calling that out! That is BA 4.6, now accounting for ~5% of sequences detected in the US.

32. **The theory is that we need new flu shots because of viral drift and shift, not because of loss of immunity. If there is not a lot of transmission, then logically there should have been less mutation. This logic would suggest that there is no reason to assume that we have "lost" immunity to influenza and that the use of normal public health protective measures including taking the annual flu should be enough. Do you agree?**

    Dr. Butler: I agree, at least in part--the same drifting that reduces the effectiveness of vaccines would also reduce any protection from natural infection. If there has been less exposure in recent years, there may be less protection among unvaccinated persons.

33. **Any comments about the characteristics of BA.2.75? Thank you!**

    Dr. Butler: Excellent question--A bit too early to say with any confidence.

34. **How would receipt of Evusheld after 4 doses of vaccine affect decision re timing of new booster? should someone with Evusheld in past 4 months wait for the new vaccine?**

    Dr Giovanni: Depending on the patient's type of immunocompromise, particularly those patients on anti-CD20 therapies, may not produce antibodies in response to vaccination. Evusheld provides the protection for these and similar patients.

35. **What do you think about cotreatment with Paxlovid and the new bebtelevomab to decrease the likelihood of rebound covid in patients that are high risk?**

    Dr Logan: At this time, we have no clinical trial data to support the treatment of COVID with combinations of antiviral medications or antiviral medications with monoclonal antibodies. Studies are ongoing though, and providers should continue review recommendations from the National Institutes of Health COVID-19 Treatment Guidelines. See https://www.covid19treatmentguidelines.nih.gov/

36. **Was Evusheld redosing recommended after 6 months?**

    Dr Logan: On June 29, 2022, FDA revised the Evusheld Fact Sheet for Healthcare Providers to recommend repeat dosing every six months with a dose of 300 mg of tixagevimab and 300 mg cilgavimab if patients need ongoing protection.

37. **Is the EVUSHELD dosing q6 months supposed to be indefinitely at present?**

    Dr Logan: on June 29, 2022, FDA revised the Evusheld Fact Sheet for Healthcare Providers to recommend repeat dosing every six months with a dose of 300 mg of tixagevimab and 300 mg cilgavimab if patients need ongoing protection.

38. **Why are some institutions requiring antibody titres before qualifying for evusheld?**

    We are unaware of reports of antibody titres used as a qualifier for Evusheld. Titers are not criteria for eligibility, as outlined in the Evusheld Emergency Use Authorization (https://aspr.hhs.gov/COVID-19/Therapeutics/Products/Evusheld/Pages/default.aspx).

39. **Do we tell patients to be quarantined after a rebound effect post Paxlovid treatment?**

    Dr Logan: When patients experience rebound after treatment with Paxlovid, they should isolate according to CDC guidelines. More information can be found at https://emergency.cdc.gov/han/2022/han00467.asp

40. **For inpatients who test covid positive and are at high risk for progression who do not require supplemental oxygen, which of Bebtelovimab or 3 days Remdesivir be recommended?**

    Dr Logan: For in-patients who test positive for COVID, remdesivir is a treatment option, but Bebtelovimab is a second-line treatment for outpatient treatment that should not be used, unless the first-line options (Paxlovid/remdesivir) are not available. Please see NIH COVID-19 treatment recommendations for hospitalized patients: https://www.covid19treatmentguidelines.nih.gov/management/clinical-management/hospitalized-adults--therapeutic-management/

41. **Can you please comment on an alternative dosing strategy for Paxlovid: bid x 2 d then qd for 6 d. 8 d total. to reduce rebound?**

    Dr Logan: In clinical trials, some persons who did not receive Paxlovid also experienced COVID-19 rebound. Trials have found that the recommended dosing of Paxlovid has been very effective as reducing the risk of severe illness. However, some patients who take Paxlovid (and some who do not) will experience rebound. At this time, there is not alternate dosing recommended to reduce the risk of rebound. Please find more information on rebound at: https://emergency.cdc.gov/han/2022/han00467.asp

42. **Where is the data on rebound with other ambulatory therapies or no therapy? Some pts now decline Paxlovid therapy because the rebound phenomenon extends the quarantine...something people are now more concerned about than small risk of hospitalization**

    Dr Logan: More information on the studies that identified rebound in patients who were treated with Paxlovid can be found on the National Institutes of Health Paxlovid webpage: https://www.covid19treatmentguidelines.nih.gov/therapies/antiviral-therapy/ritonavir-boosted-nirmatrelvir--paxlovid-/

43. Could dual antivirals or antiviral +mAb reduce risk of rebound?

Dr Logan: At this time, we have no clinical trial data to support the co-administration of antiviral medications or antiviral medications and monoclonal antibodies. Research is ongoing though. Clinicians are encouraged to continue to review COVID -19 Treatment Guidelines at: https://www.covid19treatmentguidelines.nih.gov/

44. If Evusheld is for immunocompromised "who likely would not respond to vaccination", how is this to be assessed? Is there some proxy for response that should be considered, such as SARS-CoV-2 spike antibody levels, or should providers assume that all such patients may not have responded and therefore should receive Evusheld?

Dr Giovanni: There are a number of case reports and case series that measured anti-SARS-CoV-2 antibody titers in moderate-to-severely immunocompromised patients with persistent infection. There are some reports of endogenous antibody production, but the responses were not robust.

45. Pharmacists are in short supply in some areas. Any thoughts about expanding access to Paxlovid by other means as people are being unable to get from PCPs who are over booked?

Dr Choi: Public health resources (in my state, MA) can offer other access points for Paxlovid. There is a free telehealth service for patients in my state.

46. Steroids - when to use - when to avoid? It's almost flu season: COVID vaccination is not in a vacuum - still need other vaccines - mpox, flu, and other schedule vaccines ….speak to combining delivery to increase uptake.

Dr Logan: COVID-19 vaccines may be administered without regard to timing of other vaccines. This includes simultaneous administration of COVID-19 vaccine and other vaccines on the same day. More information on administration of COVID-19 vaccines can be found at: https://www.cdc.gov/vaccines/covid-19/clinical-considerations/interim-considerations-us.html#timing-spacing-interchangeability

47. I really hope you will answer this question, especially with regards to severely immunocompromised patients. Can you explain RT-qPCR with cycle threshold testing, and when should it be implemented?

In clinical trials, some persons who did not receive Paxlovid also experienced COVID-19 rebound. Trials have found that the recommended dosing of Paxlovid has been very effective as reducing the risk of severe illness. However, some patients who take Paxlovid (and some who do not) will experience rebound. At this time, there is not alternate dosing recommended to reduce the risk of rebound. Please find more information on rebound at: https://emergency.cdc.gov/han/2022/han00467.asp

48. Did Paxlovid or any other treatments had decreased the incidence of long covid?

From clinical trial data, we know that Paxlovid decreases the risk of severe illness. Patients who have severe illness have been found to have greater risk of experiencing long COVID. Thus, Paxlovid could decrease the risk of long COVID. More information on Paxlovid can be found in the NIH COVID-19 Treatment Guidelines Paxlovid webpage: https://www.covid19treatmentguidelines.nih.gov/therapies/antiviral-therapy/ritonavir-boosted-nirmatrelvir--paxlovid-/.