CDC/IDSA Clinician Call:
Updates & Emerging Issues on COVID-19 and Monkeypox
September 24, 2022
Q&A

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1. **Is the current new booster ok for those seniors who have already had 2 boosters (>5mos ago)?**

   Attendee: The new booster is recommended regardless of previous boosters, as long as it has been at least two months since the last one. You no longer have to count the number of boosters, a good thing.

   Dr. Pragna Patel: Yes - it is recommended for seniors for protection against severe disease, hospitalizations, and death.

2. **Can you please have the CDC clarify the process of informed consent for TPOXX with CDC? after the initial diagnosis of MPX where a face-to-face evaluation has been done, for infection prevention reasons, we would prefer to do the treatment assessments for TPOXX via Telehealth. That does not lend itself well to a wet signature to document informed consent. We do have DocuSign available, but many of the patients we see are unable to use the DocuSign process. we are getting conflicting answers on if verbal consent is acceptable. our IRB says it's not. Could you please clarify?**

   Dr. Agam Rao: FDA tells us that their FDA IND regulations allow for oral consent, but they still require signature from the patient or legally authorized representative. This signature can be via wet or electronic signature and can occur after verbal consent has already been provided. While FDA has not waived the requirement for the TPOXX EA-IND, there are various ways for obtaining written documentation. Some health departments and providers have obtained wet signatures at the time of dispensing TPOXX to patients or have created an e-consent form using an electronic system to obtain e-consent, for example REDCap's Part 11 infrastructure. When the consent process is conducted remotely, the patient may print and sign the short form consent and can email a photo f the signed form to the provider or mail it. If printing the form is not possible, the patient can sign and date a blank piece of paper with a written statement that they agree to TPOXX treatment under EA-IND 116,039 (Protocol #6402) and send it to the provider.

   The witness should also sign and the date the Short Form consent and the witness and individual obtaining consent should sign and date the Written Summary. If a witness is not available, a

recording of the conversation can be made. All of this is per FDA's guidance and is what CDC has been messaging when asked this question.

Links to the forms I mentioned above: 1) https://www.cdc.gov/poxvirus/monkeypox/pdf/Short-Form-Instructions.pdf 2) https://www.cdc.gov/poxvirus/monkeypox/pdf/Written-Summary.pdf

a) **Like many other sites seeing these pts with MPX, after the initial diagnosis of MPX where a face-to-face evaluation has been done, for infection prevention reasons, we would prefer to do the treatment assessments for TPOXX via Telehealth. That does not lend itself well to a wet signature to document informed consent. We do have DocuSign available, but many of the patients we see are unable to use the DocuSign process.**

Dr. Yon Yu, Pharm.D., CDC: Yes, the FDA IND regulations allow for oral consent; however, the regulations still require documentation of oral consent that involves signature by the candidate patient for TPOXX treatment under the IND or their legally authorized representative (LAR), which can be a wet or electronic signature.

b) **I have heard of many organizations using verbal consent, and they say that their CDC contact said this was permissible. However, the persons contacted at CDC by our IRB implied that verbal consent was not acceptable and said that "those unwilling to sign the informed consent are ineligible for TPOXX". These patients with verbal consent are not unwilling to sign the consent form – they are giving verbal consent.**

Dr. Yon Yu, Pharm.D., CDC: While FDA has not waived the documentation of consent that still requires the candidate patient's/LAR's signature (whether the information is provided verbally (e.g., read to the patient/LAR) and the exchange of questions/answers take place via telehealth during which time the patient verbally indicates participation for Tpoxx treatment, or via written informed consent process), FDA has indicated the following as acceptable alternative ways for obtaining the documentation of oral consent:

1. When the oral consent process is conducted remotely, the patient may print and sign the Short Form consent and return the signed form to the provider by email, facsimile or take a photo the signed form and send by text message.
2. If the patient does not have means to receiving the Short Form electronically or printing the form to sign it, the patient can sign and date a blank piece of paper with a written statement that they agree to TPOXX treatment under EA-IND 116,039 (Protocol #6402) and send it to the provider by mail, bring it to a future, scheduled in-person visit, or take a photo of the signed form and send by text message.

c) **Could you give us a definitive answer on if verbal consent is acceptable for tpoxx via the EA-IND? Does it need to be witnessed? Verbal Consent would go a long way in securing access for our patients who are socioeconomically and educationally disadvantaged patients who sometimes cannot get transport to come in for an in-person wet signature**.

Dr. Yon Yu, Pharm.D., CDC: The FDA IND regulations require a witness attestation when oral consent is used. A signed and dated attestation by the witness should be obtained on the Short Form consent, and the witness and individual obtaining consent should sign and date the

Written Summary. If a witness is not available, a recording of the conversation can be an alternative per the FDA, provided that the recoding of the video call is done in a manner consistent with applicable state and local laws with all parties agree to being recorded.

3. **A lay person just insisted that, as she'd had COVID, she was immune to further infections for 100 days, and was not contagious during that time. Thoughts?**

   Dr. Pragna Patel: There is immunity conferred by SARS CoV2 infection. CDC recommends getting vaccinated approx. 3 months after infection as a result.

4. **Do recommend a wait period before vaccination, following resolution of a natural monkeypox infection?**

   Dr. Vivian Huang: For persons with natural MPXV infection, CDC currently doesn't recommend Jynneos vaccination. The thought is that natural infection at least offers short term immunity. The only caveat would be if the person was immunocompromised, then consideration to vaccinate is on a case by case basis.

5. **Since recent COVID vaccination or infection can impair response to a subsequent vaccination, would patients achieve a better immune response to bivalent vaccine by waiting 4-6 months after last vaccination or natural infection instead of 2 months as authorized by EUA?**

   Dr. Pragna Patel: Vaccination and infection do not impair response rather having a recent vaccination and infection offers some protection and thus waiting 2-3 months after infection is acceptable.

6. **With Biden declaring the pandemic "over", how on earth do we expect individuals of the lay public/general public to get booster shots?**

   Dr. Pragna Patel: Similar to the approach to influenza, the clinical community should recommend booster doses for protection against severe disease.

   Attendee: Thanks. Fair enough, but I'm uncertain as to the willingness to get a booster (not the recommendation) given that declaration. Could recommend it, sure. But who'd take up on that recommendation given that "it's over". Sigh.

7. **Any additional risk of more/severe mpx disease in patients that have underlying skin conditions with atopic dermatitis, psoriasis, other skin conditions?**

   Dr. Matthew Copeland: Yes, atopic dermatitis/eczema, psoriasis, severe acne, and other exfoliating skin disorders may all be risk factors for more severe MPOX infection

8. **A female patient developed hives for 6 months following her 3rd dose of COVID Moderna vaccine (not the bivalent). Has this been noted or experienced by anyone? appreciate any input, thank you!**

   Dr. Pragna Patel: Yes - allergic reactions have been noted

9. **Is there a recommendation for the application of two vaccines at the same time, for example, COVID-19 bivalent vaccine plus influenza vaccine or COVID-19 vaccine plus pneumococcal vaccine?**

   Dr. Pragna Patel: Two vaccines can be received at the same time - we recommend at they are administered in different arms.

10. **Do other already known coronaviruses also mutate as frequently as Sars-Cov2 and do those variants also get elderly hospitalized? thank you**

    Dr. Pragna Patel: Other coronaviruses have caused severe disease - SARS CoV1 and MER

11. **The bivalent booster had a better response in previously infected" but previously infected with which variants? - any? or other Omicron?**

    Dr. Pragna Patel: The authors do not report which variant patients were previously infected but persons with known SARS CoV2 within 3 months from screening were excluded

12. **What is romlusevimab?**

    Dr. Meghan Pennini: It's part of an antibody cocktail under development. PMID: 35997943 https://www.briibio.com/news-detail.php?id=1711#news

13. **Any input on recurrent/ necrotic lesions occurring in monkeypox patients already treated with tecovirimat? What are the circumstances under which an additional course of tecovirimat, or addition of cidofovir or other drugs would be considered? Thank you!**

    Dr. Agam Rao: These are the sorts of questions that you can consult the CDC MPX consult service about. We are available 24/7 to provide case specific advice about a patient. Unfortunately, it's not necessarily a one-size fits all guidance. We have not heard of recurrent lesions after a patient has fully recovered. But a protracted clinical course involving new lesions cropping up despite tecoviromat can occur, for example, in severely immunocompromised patients (e.g., very poorly controlled HIV).

    Dr. Matthew Copeland: There are also significant cases of bacterial superinfection of MPOX lesions, could consider that as well if a lesion appears necrotic/purulent or cellulitic

14. **How long does the protection from Evusheld last?**

    Dr. Meghan Pennini: Maintenance dosing is recommended every 6 months.

15. **Will you be able to share all these slides?**

    Dr. Dana Wollins: Yes. The slides will be posted at www.idsociety.org/cliniciancalls on Monday.

16. **Is AstraZeneca working on new monoclonal cocktails should new variants with resistance to Evusheld become dominant?**

    Dr. Meghan Pennini: While I can't speak to any individual program, I can say that there continues to be development of additional antibody products and these programs often work to ensure complementation to currently available products with regards to variant coverage.

17. **What is this group using as MPX indicators -1-to prolong TPOXX treatment beyond the 14 days? -2-to re-culture and send for sequencing?**

    Dr. Matthew Copeland: Would consider this in severe cases/immunocompromised with continued new lesions developing or signs of new disease sites after 14 days. Testing for resistance should be considered at that point as well.

    Dr. Agam Rao: If a patient has new lesions cropping up despite tecoviromat, clinicians may consider consulting CDC's monkeypox consultation service. One reason may be poor absorption of tecoviromat pills. IV tecoviromat may be a consideration. In addition, we have of severely immunocompromised persons continuing to develop lesions despite tecoviromat. We can facilitate consideration of VIGIV which might provide passive protection until a patient's immune system can clear the virus. We can also facilitate other testing including sequencing and laboratory testing to evaluate for resistance to the F13L gene (the viral target of tecoviromat).

18. **Thanks for putting "ample supply of all therapeutics—every eligible patient should have access" on a slide—it makes it easy to send to providers who are still rationing and refusing Evusheld and/or Bebtelovimab.**

    Attendee: I wish she didn't call treatment options widely available to those of us with patients less than 12 years and less than 40 kg though

    Dr. Meghan Pennini: Excellent point and thank you for highlighting! Currently, only Verklury/remdesivir is available to non-hospitalized patients less than 12. We continue to encourage development of additional treatments for that population.

19. **If an immunosuppressed has high titers of neutralizing antibodies to covid -19 why this patient need Evusheld?**

    Dr. Meghan Pennini: There is still not sufficient data to determine whether high titers in such a patient would translate to full protection.

20. **Where are the recent updated NIH guidelines re antibody testing and prophylaxis? Link, please?**

    Dr. Meghan Pennini: https://www.covid19treatmentguidelines.nih.gov/special-populations/immunocompromised/

21. **Patient is fully vaccinated (primary series, two boosters), has Covid in July. When to get the bivalent booster? Please address!**

    Dr. Vivian Huang: It is recommended that this patient receive the updated bivalent booster at least two months after the last dose.

22. **Is research leading to changes in Paxlovid dosing to help alleviate rebound illness?**

    Dr. Pragna Patel: There is a clinical trial underway to examine a longer course of treatment with Paxlovid.

23. **Define pandemic. What needs to occur to officially reclassify COVID-19 from pandemic to endemic?**

    That's a Million-dollar question.

24. **I have been giving ALL my patients bivalent booster, following guidelines- and getting my encounters denied by insurances who don't have the new codes updated. We need not to be hamstrung but the insurance industry when we are doing everything we can on the frontlines of patient care during this pandemic. can you help with this?**

    Dr. Dana Wollins: This is something IDSA and CDC can investigate further. Thank you for letting us know.

25. **Not a question, but there is very good data that sales of COVID home tests are a good proxy for the level of transmission in a community. Why does CDC not incorporate that data into its tracker?**

    Dr. Pragna Patel: Good thought - we are not certain that if a test is sold, it is used and the USG distributed a number of tests as well that may not have been used. We can discuss further and explore how these data may contribute to our understanding of testing and transmission. Thank you for the suggestion, Carlos.

26. **Any data on Molnupiravir vis a vis the new variants?**

    Dr. Meghan Pennini: There was a reference in the presentation which demonstrated molnupiravir activity against some of the current variants. As additional subvariants emerge, we continue to evaluate data for all the therapeutics including molnupiravir as they become available.

27. **Is the CDC working with USDA and Wildlife group in conducting surveillance in wildlife for monkeypox, and if so, what has been learned thus far...has our wildlife become infected?**

    Dr. Agam Rao: CDC's Poxvirus ecology experts have been working with USDA and other stakeholders. There is no evidence of wildlife infection at this time. They are evaluating household pets to understand if transmission is occurring in homes.

28. **Is failure to control pain with opioids an indication for tecovirimat?**

    Dr. Agam Rao: First other measures should be used for pain control: https://www.cdc.gov/poxvirus/monkeypox/clinicians/pain-management.html . If the lesions are in locations that put a patient at risk for concerning sequelae, tecoviromat should be considered. We have not heard of pain that severe in non mucosal areas so would be interested in hearing more.

29. **One case on longer tx: AIDS patient, started on TPOXX, >100 lesions, most lesions started improving on tx (similar to other patients) but many lesions grew in size and became increasingly painful and are very slow to resolve (pt still being followed) - any other similar observations in the wide difference in lesion evolution?**

    Dr. Agam Rao: You might consider swabbing new lesions to determine if these are indeed monkeypox or something else. You might also consider evaluation for resistant virus (testing at

CDC), ARVs, VIGIV, and consideration of other testing (e.g., serology). The CDC consultation service can be consulted through your health department for more specific guidance. These situations are hard to provide detailed guidance about without knowing all the details.

30. **How many patients had "severe infections "(Monkeypox)?**

    Dr. Agam Rao: We don't have surveillance specifically for severe infections. We only know of severe infections when our consultation service is consulted. We believe these likely comprise a small but important percentage of affected patients.

31. **Are you making any survey on asymptomatic patients for MKPV?**

    Dr. Agam Rao: CDC is looking into this. At this time, we are not aware of any asymptomatic cases.

32. **Please advise on recommended treatment for patient who received prophylactic MPXV and presents with a significant local inflammatory reaction at the site of his second vaccine dose?**

    Dr. Agam Rao: You may consider submitting a VAERS report about this patient but also, a CISA consult: https://www.cdc.gov/vaccinesafety/ensuringsafety/monitoring/cisa/index.html

33. **How many days does it take with TPOX treatment of Monkeypox for new lesions to stop appearing, and also for existing lesions to stop progressing?**

    Dr. Agam Rao: Use of tecoviromat in this outbreak is the first real world experience we have had. The RCTs that recently began will be the best source of information about this.

34. **Have there been any monkeypox cases transmitted in a health care setting? eg. to providers from infected patients?**

    Dr. Agam Rao: Worldwide, there have been a handful of cases reported among HCP exposed in the work place. From what we can tell, these have typically been due to sharps injuries (e.g., while attempting to unroof lesions or recap a syringe used to aspirate a lesion). To minimize these, CDC guidance is for lesions to NOT be unroofed. Rather, good specimens have been acquired through firm swabbing of a lesion alone.

35. **Any vaccine induced cases?**

    Dr. Agam Rao: Local reactions have been the most common adverse events reported to VAERS.

36. **Are new antivirals being developed? Although patients may not be hospitalized, many are sick for 4 to 8 weeks, severely impacting quality of life and ability to work.**

    I'm seeing prolonged illness in those who were diagnosed with mild infection too. Some still with long covid symptoms for more than 5 months who are vaccinated only one booster, not immunocompromised, and weren't hospitalized. Many lay people are arguing that they don't need another booster since they already had 1 booster or even 2 boosters and people are still getting infected.

37. **That link did not work**

    Dr. Agam Rao: https://stomptpoxx.org/main

38. **In your man with Monkeypox was the Hookah device tested for Monkeypox, could that have been the source of infection?**

    Dr. Robert Atmar: That's the thought - or possibly other contact with the friend

39. **Is CDC planning to conduct serosurveys for monkeypox? thank you!**

    Dr. Agam Rao: Yes these are in progress.

40. **Why wasn't TPOX started on admission?**

    Dr. Robert Atmar: It took time to get access to the drug at that point in the epidemic. It was started as quickly as we could

41. **Are there studies looking at effect of covid vaccine on long covid? Both from the perspective on existing long covid as well as preventing future long covid?**

    Attendee: There are. I am aware of at least one real-world data cohort study looking at this question. That study should be deposited as a preprint within a couple of weeks.

    Dr. Pragna Patel: Yes - there are. See link: https://www.thelancet.com/journals/eclinm/article/PIIS2589-5370(22)00354-6/fulltext#:~:text=Six%20studies%20(n%3D17%2C256%2C654%20individuals,more%20effective%20than%20one%20dose .

    Attendee: Thanks for answering the extremely important question, Dr Patel. We have yet to learn what the long term societal impacts long covid (possible permanent disability) will have on all of us.

42. **Is there a range of encephalomyelitis presentations? Are there mpx neurologic symptoms that do not necessitate hospitalization?**

    Dr. Matthew Copeland: I don't think we know this yet. Our case presented similar to an acute disseminated encephalomyelitis however I have also heard of cases that seemed more transverse myelitis as well.

43. **How effective is previous smallpox vaccine (decades ago) in preventing or minimizing monkeypox infection?**

    Dr. Agam Rao: During the 2003 U.S. monkeypox outbreak that occurred after exposure to infected prairie dogs, some cases occurred in people who had received the childhood smallpox vaccine. It is possible some protection is provided decades later but for the purposes of this outbreak, persons who received childhood smallpox vaccination who are eligible for PEP, PEP++, or PrEP vaccination should recieve the 2-dose JYNNEOS series.

44. **What is the recommendation for patients who develop mpox after receipt of first dose of vaccine? Should we only administer second dose to Immunocompromised patients? Thanks!**

    Dr. Agam Rao: We have been advising that persons who develop monkeypox do not need to be vaccinated. For immunocompromised persons, guidance may be on a case-by-case basis.

45. **Should all ocular monkeypox infections be treated with IV (as opposed to oral) tecovirimat?**

    Dr. Agam Rao: Experts from the Ophthalmology association are assisting CDC with providing more guidance about the management of eye infections including the question you asked. We hope that guidance will be on the CDC website in the 7-10 days or so.

46. **Trifluridine is not available nationally. Is there an alternative?**

    Dr. Agam Rao: Experts from the U.S. ophthalmology professional society are working with CDC to develop some general online guidance about management of MPX eye infections. I can take this question back to them in case they have advice.

47. **MPX eye involvement - tpoxx+topical antiviral; would the recommendation be to avoid steroid drops despite the extent of inflammation?**

    Dr. Agam Rao: Experts from the U.S. optho professional society are assisting with some general guidance about the management of eye infections. We will take this question to them. We hope a CDC website including this guidance will be viewable in less than 7-10 days.

48. **Does CDC have test for TPOXX resistance available?**

    CDC can test for resistance. CDC laboratorians have tested >600 specimens and no evidence of resistance at this time but they are continuing to regularly monitor. If you have a patient with persistent lesions despite tecoviromat, we would want to do that testing. You can reach CDC consultants through your health department.

49. **Would CDC please consider adding/hyperlinking to this MSM or similar guidance on STI/HIV testing recommendations (https://www.cdc.gov/std/treatment-guidelines/msm.htm) within CDC monkeypox clinical guidance, for timely and concurrent STI/HIV testing as indicated? I'm not able to locate mention of concurrent STI/HIV testing recommendations within monkeypox clinical guidance, particularly on the "Clinical Recognition" page. Thank you.**

    Absolutely. This is an opportunity to diagnose/ have a low suspicion for HIV in patients presenting and if uncontrolled HIV with low CD4 counts, the immune system is needed to clear the virus so ARVs are advised to be started. This is certainly an opportunity. I will speak with experts within the response.

50. **is it better to get the bivalent booster now, (healthy adult), or wait til later to "time it" for a possible winter surge? will it give at least a 3 month protection?**

    My understanding is that people should receive the bivalent booster as soon as they are eligible. At the last clinician call I think it was noted that based on the trends, it looks like we are going to have another surge late November (graph).

51. **Are any efforts underway to develop an antiviral with similar effectiveness to Paxlovid but with reduced (or at least different) drug-drug interactions that would enable some vulnerable groups to benefit from them with less risk, including those on immunosuppression such as tacrolimus?**

    Ensitrelvir (S-217622) may be equally active in vitro. A phase 2/3 trial is underway (PMID: 36098519).