

CDC/IDSA COVID-19 Clinician Call: Antibody Therapy & Second Boosters: Updates and Perspectives on Protecting Our Most Vulnerable

May 7, 2022

Q&A

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- 1. Evusheld seems to be still limited in distribution - we need more post exposure prophylaxis options. Which are the best candidates in the pipeline?**

Dr. Eisnor: You are correct, we need to work on better access. No new PrEP products in the near term.

Attendee: I am personally aware of one heart transplant patient [in situ for ~ 10 years] who was denied Evusheld because it was being 'saved' for newer transplant recipients.

Attendee: I have a patient that was denied because of minor angina. Is this a problem with Evusheld?

Dr. Kotton: I am not worried about cardiac issues with Evusheld. The population studied was at higher risk. And the NIH guidelines suggest focus on more recent transplants if there are supply issues.

- 2. When do you think the guidance for the second round of Evusheld will be forthcoming?**

Soon. AZ and FDA are currently deliberating. (Dr. Eisnor)

- 3. Can you please discuss cardiac considerations /concerns with Evusheld?**

I am not worried about cardiac issues with Evusheld. The population studied was at higher risk. And the NIH guidelines suggest focus on more recent transplants if there are supply issues. (Dr. Kotton)

- 4. Do you foresee a time when people might be able to get a course of Paxlovid that they could keep on hand to use if they develop symptomatic? Covid with a positive home test?**

Good question. The EUA does not currently allow this. (Dr. Eisnor)

That would be nice, when possible, especially for travel medicine. Not possible under EUA. I also worry about drug interactions, especially if delayed use of drug (in case new meds are started). (Dr. Kotton)

- 5. What about tacrolimus and Paxlovid?**

We do not co-administer due to safety concerns. We always try to use mAb in transplant patients. I think tacrolimus may not have made it in to the top 100 drugs for the IDSA website (Dr. Kotton)

Remember the list in the IDSA Resource is for the "Top 100" most prescribed drugs. Tacrolimus is not one of them! If your drug is not on the list we recommend using other resources like the Liverpool drug interaction one. <https://www.covid19-druginteractions.org/checker> (Dr. del Rio)

6. EUA still limits Paxlovid use to patients with risk factors- yes?

Yes but a broad category considering obesity for example, BMI>30 almost 1 in 3 adult Americans. (Dr. Eisnor)

7. What is available for patients with CrCl<30?

Everything minus RDV and Paxlovid. (Dr. Eisnor)

8. Can Paxlovid be used in patients who catch Covid in hospitals while admitted for another reason?

yes. (Dr. Eisnor)

9. Recommended booster dosing timeline after Evusheld?

I would give fairly soon if they are due - not clear there is an interaction and I'm worried about relying too much on Evusheld. (Dr. Kotton)

10. Many centers are drawing antibody levels before offering Evusheld. Is this what should be happening?

Serology testing has not been validated to a clinical outcome or endpoint, thus unable to provide guidance until this data becomes available. (Dr. Eisnor)

11. The PROVENT study only had 195 patients who AZ classified as immunocompromised. Is anyone collecting data on how efficacious Evusheld is proving to be in the immunocompromised population? Who is gathering this data?

Yes and in regard to Omicron variants, but data not available yet. (Dr. Eisnor)

12. Can you please discuss Paxlovid for prevention - considering recent data on this did not pan out - is this planned to continue to be pursued or studied- considering this would be a convenient option if it works out?

The study of Paxlovid for prevention was a negative one and I am not aware of others but to me what we need is rapid start once infected. (Dr. del Rio)

13. If evusheld successfully prevents infection, are the evusheld antibodies used up when they bind to the virus? If so, would this account for the severe drop off of antibodies seen in the weeks after evusheld?

Difficult to say. We know the Fc portion is engineered to resist phagocytosis. We do not have data that reflects a drop in protection in this setting. (Dr. Eisnor)

14. What is the status on use of serology to determine use of monoclonals in COVID inpatients?

Serology is not recommended to guide use of monoclonals (Dr. Razonable)

15. Likelihood Paxlovid dosage will change from 5 to 10 days with increase of rebound cases, particularly immunocompromised?

At this point I am not aware that the FDA is not planning to increase the recommendation from 5 to 10 days (Dr. del Rio)

16. Is Paxlovid still indicated in immunocompromised patients who have recently received Evusheld, if they test positive for infection?

yes. options for the patient will be Paxlovid, remdesivir or bebtelovimab. (Dr. Razonable)

17. Paxlovid rebound: What is the data for replication competence or genomic sequencing in Paxlovid rebound cases? Was replication competence performed during any of the initial clinical trials? Results?

There appears to be no evidence of resistance in those cases. (Dr. del Rio)

18. When immune reconstitution occurs in an aids pt who has gotten evusheld when can you revaccinate with Pfizer vaccine?

Yes, you can revaccinate immunocompromised patients - I use this a lot, "On a case-by-case basis, providers caring for moderately or severely immunocompromised patients may administer mRNA COVID-19 vaccines outside of the FDA and CDC dosing intervals based on clinical judgment when the benefits of vaccination are deemed to outweigh the potential and unknown risks for the recipient. However, providers should not routinely administer doses of COVID-19 vaccine beyond those recommended in this guidance."

<https://www.cdc.gov/vaccines/covid-19/clinical-considerations/interim-considerations-us.html#immunocompromised> (Dr. Kotton)

19. Is there any data on immunosuppressed renal transplant patients who have had four mRNA vaccines (boosters included) and evusheld and still got breakthrough infections?

yes, we have had few patients like this. (Dr. Razonable)

Yes, those are the cases I described in my talk, and I have heard of many more. We are not out of the woods yet with this vulnerable population. (Dr. Kotton)

20. Can you comment on Mab and Paxlovid given together to stem cell transplant recipients?

Possible, but due to supply issue with mabs, and high demand, one treatment is what is recommended (Dr. Razonable)

21. Dr. Kotton, you are recommending immunocompromised continue to wear masks, but where is that in the CDC guidelines.?

<https://www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/people-with-medical-conditions.html> This has not changed for high-risk patients (Dr. Kotton)

22. How long AFTER Evusheld shall a patient get the next booster?

At least 2 weeks after Evusheld. (Dr. Razonable)

23. What information is available about COVID-19 rebound after Paxlovid therapy? Have studies been initiated (by Pfizer or others) and, if so, where?

The best information I have seen is what Paul Sax has written on his blog in the past two weeks. Link is here: <https://blogs.jwatch.org/hiv-id-observations/index.php/more-on-relapses-after-paxlovid-treatment-for-covid-19/2022/05/04/> (Dr. del Rio)

24. What is the reasoning for the 4th dose of the vaccine first rather than Evusheld first then 4th dose of the vaccine (without having to wait 2 weeks)?

Vaccine preferred over mAb, given broader response, plus cellular and humoral immunity. There is no formal guidance on time after Evusheld before vaccine (just the opposite, b/c in EUA for Evusheld). I don't wait (much). (Dr. Kotton)

25. For immunosuppressed patients (B cell suppression therapy) who have already received Evusheld, when should they receive their 2nd vaccine booster? (No measurable antibodies pre-Evusheld, but post- 2 + 1 doses of vaccine)

Probably best if they get mAb 2-4 weeks before their next dose of anti B cell tx. They need 3 doses as their primary series, plus 2 boosters. (Dr. Kotton)

26. Are expiration dates a problem with Evusheld?

One lot approaching in June, some in July and August. AZ is working on shelf-life extensions. (Dr. Eisnor)

27. Have administration fees equalized yet? eg some locations charging no fees vs very high fees if administered in hospital setting?

We are looking into (with our state partners) and continue to receive reports of high fees from concierge services for at home Evusheld administration. It is a considerable administrative lift on both sides but reflects how evaluation of selected distribution sites is not a 'one and done'. (Dr. Eisnor)

28. Is there a difference in a transplant patient who was vaccinated pretransplant vs post transplant?

Yes, pre-transplant works much better c/w post-transplant. Hard to correct that, in hindsight. It's why we very strongly encourage and even mandate (40-50% of programs) pre-transplant vaccine. True for all vaccines. (Dr. Kotton)

29. Are you giving mAb (bebtelovimab) to SOT pts admitted with COVID?

Yes, if they have mild to moderate disease and within 7 days of symptom onset. and they have to be admitted for non-covid reasons. (Dr. Razonable)

30. Why is there no enforcement of daily reporting requirements for evusheld and paxlovid?

Good question. There is much debate in USG on this. The same conversation with vaccines. The concern was the potential to limit product. (Dr. Eisnor)

31. The EUA for Paxlovid references the CDC site for list of medical conditions associated with progression to severe COVID diseases. That list is extremely broad, for example including even persons with learning disabilities. Will this list be refined or is the suggestion that almost everyone who develops COVID should be offered treatment, even though it seems that many might not actually be at high risk for disease progression? The data supporting the benefits for the use of this drug (Epic HR study) was in a more limited group of "high risk" patients.

Agreed. This requires an in depth risk/benefit discussion between HCP and their patient. We still do not know the NNT to prevent hospitalization in vaccinated individuals. (Dr. Eisnor)

32. Should all immunosuppressed SOT recipients receive Evusheld, regardless of their response to the COVID-19 vaccines as measured by spike antibody tests? Or is there some level of spike antibodies above which Evusheld would not be expected to have any benefit?

Recommended for all regardless of antibody titers. titers are not routinely recommended for use. (Dr. Razonable)

33. How do we increase/encourage greater utilization of Evusheld?

Attendee response: We sent out an email to our nephrologists to make them aware of the availability of Evusheld for the renal transplant patients who may have poor immune response to vaccination.

Dr. Eisnor: That is the key question. Better access, better awareness and reimbursement support to all HCPs providing these services.

Dr. Kotton: We are struggling with short staffing, busy clinics, etc. In the State of Massachusetts, we have outsourced to Gothams, a Texas-based emergency management company w/ experience supporting commercial, federal, & state facilities in COVID-19 emergency response. It's very efficient for patients to go there.

34. When can we expect guidance on Evusheld "booster"

Soon. FDA and AZ are currently deliberating. (Dr. Eisnor)

35. What is per patient cost of Evusheld?

Product is free. Administration fees depend on insurance status. No costs for CMS patients. HRSA clinics provide sliding scale evaluations. (Dr. Eisnor)

Can't be given at vaccine centers that are fully funded with federal funds for COVID-19 vaccines. Centers with hybrid funding might be able to supply information i.e. through a call center regarding where to get access to monoclonal antibodies for pre-exposure prophylaxis. (Dr. Kotton)

36. Is there any newer data about Evusheld for those with cardiac issues?

Apologies, not that I am aware of, but definitely a key area of surveillance with this product. (Dr. Eisnor)

37. Please comment on the use of bebtelovimab versus Evusheld

Evusheld is for prophylaxis. bebtelovimab is for treatment of active mild to moderate covid-19. (Dr. Razonable)

38. What should be considered a reasonable patient cost-sharing amount on evusheld for a) covid test, b) provider consultation, c) administration fee. Should a patient be responsible for the entire amount if they have not completed their deductible?

Perhaps biased but I look to CMS rates. <https://www.cms.gov/medicare/medicare-part-b-drug-average-sales-price/covid-19-vaccines-and-monoclonal-antibodies> (Dr. Eisnor)

39. What data supports 1 hour observation period vs 15 minutes vs 30 minutes?

From the P3 clinical study, but there are discussions on the possibility of reducing this. (Dr. Eisnor)

- 40. Has HHS developed a plan to deal with using the unused boxes on the shelves that are due to expire in July? Is there any discussion about beginning to dispense the next doses in June to make sure that no vials would need to be thrown out?**

We are hoping there is more uptake and use - <5% of immunocompromised patients have gotten Evusheld. Would focus on first dose. Will have to see impact of BA.4/5. (Dr. Kotton)

Also, AZ is working on shelf life extensions. (Dr. Eisnor)

- 41. If initially after getting Evusheld, antibody numbers increase, but after a month or two, antibody numbers decrease. What could account for this decrease? What can be done about it?**

We expect decline/decay of antibody - this happens with all mAbs. Would not trend. (Dr. Kotton)

- 42. Is it OK to have the patient be observed in a waiting room versus in a clinic room under observation in case there is an allergic reaction? This is after Evusheld.**

In our experience Julie, we had patients wait in the clinic room for the first 15 minutes for any immediate concerns (ex. anaphylaxis) and the remaining 45 minutes they would wait in the waiting room where nurses were asked to monitor those patients closely. Hope this helps. (Dr. Thomas)

- 43. We have received calls from patients receiving care from Kaiser Southern California (a very very large provider in our area, especially to older patients) who do not have access to Paxlovid because their outpatient services and pharmacies claim to be unable to offer Paxlovid because they are overwhelmed (too busy) with new acute COVID-19 infections either in the ER or inpatient (staff are being shifted to newly re-opening COVID inpatient units). Any thoughts?**

If other options retail pharmacy (Test-to-treat) sites are not available, USG is happy to support (FEMA) a state managed T2T site in any areas of high need. (Dr. Eisnor)

- 44. Can you comment on bebtelovimab versus Paxlovid? Can you comment on the difference in side effects with these treatments?**

Paxlovid use is supported by RCT. Bebtelovimab appears to be effective based on limited clinical data and retrospective analysis. Both are effective. (Dr. Razonable)

- 45. How is Paxlovid distribution being handled (by pharmacies like CVS, our largest pharmacy in So Cal and also health care systems) in terms of infected patients who are at home (and within 5 day period) and family members or friends who bring in patient's test results requesting Paxlovid for the infected patient. This is a core issue and creating lots of confusion and inaction.**

CVS one of the largest participants in the federal pharmacy partners T2T program, continues to augment these services particularly with telehealth options for those with positive home tests. (Dr. Eisnor)

46. Is there a way to track VA facilities for available therapies? They do not appear to be on the distribution website.

These sites should be listed on the product locator. Do you have a specific example I can take back to my IT team? (Dr. Eisnor)

Attendee Response: Atlanta VA

47. Does anyone have any piece of good or hopeful news for us that are SOTRs? Is there a reason to keep living at all?

Recently, most of my SOTRs are doing well with all of this. Vaccine + mAb, tx if ill. It's MUCH better than it was. I do understand how hard it is. Summer is a good time to be outside and socialize. (Dr. Kotton)

48. Another practical question. ER doctors are denying Paxlovid for infected patients (e.g., over 65, DM and within 5 day period) in the following manner: they do an extensive clinical and lab work up in the ER and say that the patient is not getting worse and do not need Paxlovid. Some ER physicians are saying that the initial data on Paxlovid is not holding up and is not efficacious. Your thoughts about this scenario and addressing the issues raised in the scenario.

Very frustrating to hear this, especially from my own specialty. (Dr. Eisnor)

49. anyone over 50 is eligible for a booster. no?

Yes, anyone >50yo or immunocompromised. (Dr. Kotton)

50. So, if a 30-year-old medical resident wants to receive a second booster, do we administer the second booster?

Unless they are immunocompromised, that is beyond the EUA. They should have robust immunity/protection against severe disease from their primary series. (Dr. Kotton)

51. What is the expected time of protection against actual circulating variants when receiving the 2nd booster? Speaking in neutralizing abs terms

The short answer is we don't know yet. Studies on the 2nd booster are fairly recent. A study from Israel in the older age group showed protection didn't last very long for infection (waned a little more than a month after) but duration against severe illness remained throughout the end of the study. We don't have additional follow-up data on waning since the study. (Dr. Hall)

52. Is F/U data on second booster available? Israel data very short duration and waning might be a problem. How many people needed to vaccinate to prevent one case of severe disease?

Israel may have more data on this. You are right, large number to vaccinate to prevent each case. That's why the ACIP agreed that people "may" (not "should") get a second booster. (Dr. Kotton)

53. Would you recommend that a woman planning to become pregnant get a second booster?

Thanks, if they are <50 then that is beyond the EUA. Does not seem they need it. Robust protection vs severe infection from primary series plus booster. (Dr. Kotton)

54. Can anyone comment on Mab plus Paxlovid or remdesivir in the profoundly immunocompromised hosts such as those with severe GVHD, are we violating EUA if done (when supply permits)?

i do not believe the EUA prohibits. it is being discussed, but i do not think it has been done. (Dr. Razonable)

55. Not high risk

Not that I have heard of - probably just for this fall. Might be bivalent vaccines, ancestral strain plus another one. we have excellent protection against severe disease from primary series plus booster. (Dr. Kotton)

56. Is moderate obesity considered as a severity risk factor for Covid in order to receive second booster dose?

It's tricky, but not if they are <50yo or not immunocompromised. (I asked the CDC myself.) They are at risk but primary series plus booster should be enough. (Dr. Kotton)

57. What is the likelihood that FDA&CDC will approve Moderna's Spikevax for children 6 months to 17 years of age?

We need to see what the trials show. We will make decisions based on the science. Hoping we see that soon. (I am an ACIP member.) (Dr. Kotton)

58. What is the number of sequencings now that the rate is much lower? Is it the same as when the rate was much higher? how were BA4 and BA5 found? how do we know if any new variant emerges?

I would defer to my CDC colleagues, but surveillance also increases when we are seeing changes or new variants/subvariants. (Dr. Eisnor)

59. Camille, Thank you. At this point Moderna hasn't given you any data, or they haven't given you all the data?

It goes to the FDA first and then to the CDC/ACIP. It goes very quickly. (Dr. Kotton)

60. What is the definition of "second booster"? 4th dose or 5th dose?

Depends if IC'd or not - 5 doses for IC'd, 4 for non-IC'd (IC=immunocompromised). (Dr. Kotton)

61. How long after recovering from Mild case of COVID 19 should someone wait before getting a second Booster shot? First booster was in October. Covid illness was in February

People who recently had SARS-CoV-2 infection may consider delaying their first or second COVID-19 vaccine booster dose by 3 months from symptom onset or positive test (if infection was asymptomatic). Studies have shown that increased time between infection and vaccination may result in an improved immune response to vaccination. Also, a low risk of reinfection has been observed in the weeks to months following infection. (Dr. Hall)

62. Can you talk more about if a booster after getting Evusheld would have an adverse effect on the efficacy of Evusheld?

No it should not have an impact on Evusheld efficacy. (Dr. Kotton)

63. I wish the specialty offices (rheum, transplant, oncology) in Boston were promoting Evusheld more

We are trying - it's overwhelming. I use Gothams program in Mass quite often, very well organized. (Dr. Kotton)

64. Please can you comment on adenovirus vector vaccines and the global pediatric hepatitis outbreak which is being linked to adenovirus?

Those would be unrelated given the changes in the vaccine backbone.

65. For a 42 y.o. immunocompromised female on biologics for sjrogens disease complicated with moderate rheumatoid arthritis, currently on day 5 of Paxlovid for moderate covid-19 infection, she has had 2 Pfizer vaccines and 1 booster, what should come next: Evusheld or the 2nd Pfizer booster, and when is the ideal timing for each of them?

The new rec for a 2nd booster suggest waiting 3 months after infection, but that's not for IC'd. I might wait 2 months or so. Depends on biologic, details, etc. (Dr. Kotton)

66. Dr. Kotton, did you say that fully federally funded clinics are prohibited from administering evusheld? Why?

They need to give vaccines, per funding, not mAb (not my idea!) (Dr. Kotton)

67. Any comparative data on immunocompromised in these clinics who get were not able to get evusheld

Not that I know of.

68. This is the worst of all timing problems....more attention needed for Evusheld and Paxlovid while at the same time, increased admissions and ER care are demanding resources and attention. Your thoughts about this specific problem?

ED staffing companies have been cutting staffing (nurses too) since the first summer of the pandemic. Private institutions do not function in the best interest of public health. I would like to see an overhaul to our entire facility/hospital reimbursement scheme. (Dr. Eisnor)

69. If a patient with Rituximab, who after getting Evusheld, has finally had detectable antibodies after having no B-cells, and not having any antibodies after 3 vaccines, would you recommend that they get another vaccine or wait until another dose of Evusheld becomes available?

Good question - right now can't get more evusheld under the EUA. You are just measuring the Evusheld mAb.

70. Should all transplant patients get evusheld?

Yes, probably - some need more than others. Those on single drug might not need it.

71. Should bebetelovid replace Evusheld now?

Beb is for treatment, Evusheld for prevention. We would need trial of beb for pre-exposure prophylaxis.

72. Did Dr. Kotton say that locations giving Evusheld cannot also give COVID vaccines/boosters? That they have to be separate locations?

Only if fully federal funded - so just specific clinics. (Dr. Kotton)

73. Doctor Kotton, do you sometimes recommend a full Moderna dose for the 4th, 5th, etc. dose? What are your thoughts on that? If you do, do you consider that revaccination?

When I want them to have full dose, I go with Pfizer - I tend to follow the rules. (Dr. Kotton)

74. Will someone comment for those of us who have generated zero antibodies after 4 vaccines...there are A LOT of us.

Thanks, it's unlikely that a 5th dose will result in Ab. You may have a cellular response. I do rec that you get mAb like Evusheld.