

CDC/IDSA COVID-19 Clinician Call

Updates in COVID-19 Treatment and Antibody-Based Prevention

November 20, 2021

Q&A

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1. Do you use Methylprednisolone for Covid treatment? When? How?

In general, I don't recommend corticosteroids for outpatients with COVID-19 unless there is another indication. For inpatients, we use dexamethasone, as per NIH guidelines "If dexamethasone is not available, alternative glucocorticoids (e.g., prednisone, methylprednisolone, hydrocortisone) can be used." Thanks for your question! (Kim, Arthur)

2. Is there any clinical evidence (not just changing antibody levels) of benefit of covid boosters in preventing asymptomatic or mild covid infection? I also have not seen evidence that there is an increase in serious endpoints such as hospitalization and death in fully-vaccinated patients who were immunized earlier eg. December 2020 or January 2021.

I was unable to attend the ACIP meeting live, but my understanding is that data were presented there. Eric Topol has a twitter thread re the RCT from Pfizer for symptomatic infection. <https://twitter.com/EricTopol/status/1461786768131465219> (Kim, Arthur)

3. Are there any studies regarding kidney damage with use of remdesivir in COVID patients?

In general, it is tough to sort out remdesivir exposure from the kidney injury that occurs with severe COVID-19 itself from observational studies. The concern with short-term exposure of the SBECD is similar to IV voriconazole - probably safe in those with reduced eGFR. There is a RCT (Gilead-funded) for hospitalized patients with reduced eGFR that would provide more definitive evidence. Right now, we discuss use of remdesivir with nephrology, or enroll into that trial which is active at our site. (Kim, Arthur)

4. When should we treat the COVID patient with corticotherapy?

Hi Dr. Heng, we use dexamethasone for hospitalized patients with severe COVID-19 on Oxygen during the inflammatory phase of infection. This would include patients on hi-flow / mechanical ventilation. Generally studies would suggest that earlier use would be not beneficial or theoretically harmful if it delays beneficial immune responses. (Kim, Arthur)

5. Can Molnupiravir induce DNA mutations?

In one study in CHO cells exposed to MOV for 32 days, there was evidence for mutagenicity. In in vivo animal studies, no evidence for mutagenicity. this will be discussed further, I'm sure, by FDA. (Gandhi, Rajesh)

6. What about Favipiravir in Covid-19 treatment?

There was a recent negative phase 3 study evaluating favipiravir (below). at this point, it is not recommended by NIH nor IDSA guidelines.

<https://www.appilitherapeutics.com/newsfeed/Appili-Therapeutics-Provides-Update-on-Phase-3-PRESECO-Clinical-Trial-Evaluating-Avigan%C2%AE%2FReeqonus%E2%84%A2> (Luetkemeyer, Annie)

7. After 3 doses of COVID vaccination by AstraZeneca, the dosage antibodies in the blood were negative, should we give the 4th dose of vaccination? What is the next management?

This drug looks less potent given the high EC50- i think the emerging oral antivirals will likely be more effective. (Luetkemeyer, Annie)

8. What about a young man with Bruton syndrome? Do you recommend vaccination, even if not very useful...or it should be better wait for approval of monoclonal in prophylaxis?

I still recommend vaccination, as it is unlikely to cause harm and it is widely available. I do believe the severely immunocompromised will be candidates for PREP. There are studies in process that I am aware of for both cas/imd and sotrovimab, if available in your area. (Kim, Arthur)

9. Do you expect to see a negative pregnancy tests for reproductive age women in the FDA recommendations?

This is not known yet. Draft distribution guidance I have seen suggest possible need for pregnancy test. For clarity this would only be for molnupiravir, if required, and not '322. (Luetkemeyer, Annie)

10. How worrying is the evidence of mutagenicity in mammalian cells for Molnupiravir? Even if after prolonged use?

I think mutagenicity is going to be discussed at the Nov 30 FDA meeting. See my answer to a previous participant who asked similar question. (Gandhi, Rajesh)

11. Any data on using Molnupiravir in hospitalized patients?

I will talk about this briefly in my talk- the MOVE-IN study, which was stopped early due to lack of efficacy. (Luetkemeyer, Annie)

12. Can you please comment on the effect modification of vaccination status and/or serostatus on outcomes with monoclonal antibody treatment?

Doesn't quite answer your exact question but I'll be reviewing (briefly) this recent report from the Mayo Group <https://academic.oup.com/jid/advance-article/doi/10.1093/infdis/jiab570/6429422> (Kim, Arthur)

13. Any reason provided for not "boosting" '332 with cobicistat instead of RTV?

Makes sense but hasn't been studied as far as I know. (Gandhi, Rajesh)

14. How does PF-07321332 differ from ritonavir (some early press said they were the same)?

Ritonavir is a booster used to raise levels of '322 - it is not the same drug as '322. (Luetkemeyer, Annie)

15. Can this new Pfizer med be used in pregnant women or childbearing age?

Great question -- they were excluded in the clinical trial. Not sure yet what the FDA will decide. (Gandhi, Rajesh)

16. Are there published reports (in vitro and/or clinical trial studies) on pre-existing or emergence of viral resistance to Molnupiravir or Paxlovid ("332" drug) so far?

I have not seen viral resistance data for '332 yet. There was a poster at ID Week showing that despite the mutagenic mechanism of action, that MOL did not select specifically for MOL resistance mutations- the mutations were distributed throughout the virus. But we will need more data in those who have persistent viral shedding after MOL or '332 treatment to understand if clinically relevant emergent viral resistance. (Luetkemeyer, Annie)

17. Any thoughts about how Paxlovid (332) will be dosed among PWH who already are taking a regimen with RTV or cobi?

My assumption is that if already on RTV 100 mg BID that added RTV will not be needed. However, we will need data on drug drug interactions for ART including PI's with '332. (Luetkemeyer, Annie)

18. In Monkeys best if given before infection in PNAS study?

Yes, RDV was given very early in the animal study. (Gandhi, Rajesh)

19. The anti-inflammatory action of Fluvoxamine has been attributed to blocking Calcium entry into cytosol, can you please comment on this?

There are multiple putative mechanisms for fluvoxamine activity including as a sigma 1 agonist and interfering with lysosomal trafficking. See

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8094534/> for a nice review of possible mechanisms. (Luetkemeyer, Annie)

20. Are severely immunocompromised patients less likely than immunocompetent patients to develop inflammation? What about hyper coagulation

We have not observed a lower rate - in fact many progress readily into the inflammatory phase and have suffered from thrombotic complications. (Kim, Arthur)

21. How about using convalescent plasma in hospitalized immunocompromised patients?

Great question. This is a group that I think should be studied with CP. (Gandhi, Rajesh)

22. Any comments on use of interferons type I for COVID-19 Dr Gandhi?

Systemic interferon beta in a large trial did not show benefit. There are still trials of inhaled interferon and of other interferons (lambda, alpha). Would await clinical trials results before using. (Gandhi, Rajesh)

23. Can you comment on IDSA update basically recommending consideration of baricitinib in all patient with severe disease (not just rapidly progressing)?

I think the data (COV BARRIER) for baricitinib in terms of mortality is strongest for people on high flow oxygen. my own approach is to give a person with progressive disease dex + either toci or bari. (Gandhi, Rajesh)

24. Using post exposure Monoclonal antibodies is easy in Florida but may be harder in other states. Please address these differences.

Absolutely there is wide variation in access to these therapies. Many do not have capacity for PEP, just for treatment. Some systems have tried to overcome with home visits. SC administration helps! (Kim, Arthur)

25. Is there any benefit of therapeutics and incidence of PAS-C? Any data?

See answer to previous participant who asked similar question. no data yet and important to study. (Gandhi, Rajesh)

26. Do we truly know the level of antibody is required for protective immunity? We don't check antibodies in transplant recipients for that reason.

Agree. (Gandhi, Rajesh)

27. Did you observe a difference of immune response between pediatric and adult post-transplant patients of the same solid organ?

Hi the Hopkins group has done pediatric studies in parallel with their adult studies - indeed the young have better Ab responses. As I grow older, I completely get that my immune system isn't what it once was. Notably I was touching base with a pediatric ID doc at a major center who has NOT seen respiratory failure in a pediatric patient who was fully vaccinated. (Kim, Arthur)

28. Can you give both remdesivir and Monoclonal Ab?

We don't have studies of that combination but we have done that through expanded access casi/imdev in hospitalized patients on low flow oxygen and who are on remdesivir. (Gandhi, Rajesh)

29. Is there data on a 4th vaccine for immunocompromised patients?

I guess there are likely measurements somewhere in the literature but not systematic studies to my knowledge.

30. Will we have data on combination antiviral therapy (MAb + small molecules or multiple small molecules)?

I think combination therapy would theoretically most helpful for immunosuppressed patients who can have prolonged viral replication. I would love to see combination therapy studies in those patients. (Gandhi, Rajesh)

31. Our hospital is not administering the Monoclonal antibody therapies in the ED. Are any hospitals doing that? Some patients will not call our office but rather present to the ED. I feel like this may be a stop gap to reduce readmission especially if the PCP is notified day 7 it is often less likely we will be able to get them the infusion same day (though has happened a few times 😊)?

The ED has been a very effective location for our hospital to administer mAbs, in addition to an outpatient mAb program (Luetkemeyer, Annie)

Additional Question/Comment: We have asked our ED director, but we're told the monitoring was an institutional hurdle I suspect due to staffing issues. Anything we could do to help our hospitals to do this? They will do it for those who get admitted at home. Our office has been unable to do so because of our own staffing issues.

If they are admitted for a reason other than Covid, then they can receive antibodies if they otherwise meet EUA criteria. (Gandhi, Rajesh)

32. Are studies underway using COVID vaccination as an antibody booster in early infection? Particularly in persons who have remote dosing. Similar to rabies vaccine as a boost without RIG in previously vaccinated persons.?

Intriguing hypothesis! I worry that the incubation time of SARS-CoV-2 is too short for this approach, as compared to rabies or hepatitis A which have weeks of incubation. I will have to go to clinicaltrials.gov to look to see if there are studies. Thanks (Kim, Arthur)

33. We administer MAb in the ED (weekend and after hours) as well as in an infusion room adjacent (M-F). Average about 40-50 infusions per week. Really need to do this to get them in as early as possible.

Agree with you. (Gandhi, Rajesh)

34. Raj: What are your thoughts about giving monoclonal antibodies to those with mild COVID-19 but have been vaccinated several months earlier IN REGARDS to having a significant boost to their immune response. Does the monoclonal dampen the natural boost response to infection?

Key question. If the person is at high risk for progression, I would favor using mAb despite theoretic considerations about effect on natural boost. (Gandhi, Rajesh)

35. Can you give both remdesivir and Monoclonal Ab?

I think that's a key question. Many studies to date only go out to 29 or 60 days and haven't focused on late complications. We need longer term data from treatment studies. (Gandhi, Rajesh)

36. When should patient receive 3rd dose? After recovering from infection?

Hi there isn't exact guidance: I have been saying at least 1 month - Dr. Luetkemeyer in her response thought 2-3 months - I think these are reasonable timeframes. (Kim, Arthur)

37. any data on antiviral treatment and the impact on long covid (any decrease in risk of long covid)?

Not yet for antiviral treatment but I did see this preprint today showing inpatient dexamethasone was associated with lower Long-COVID.

<https://www.medrxiv.org/content/10.1101/2021.11.17.21266392v1> Generally avoiding severe illness should be helpful to avoid long-COVID. (Kim, Arthur)

38. What is the Turn around time to obtain the compassionate use of the MAB?

Kami Kim messaged me to remind me to mention - it does take 1-2 days and sometimes the supply has to come from non-hospital. (Kim, Arthur)

39. How do you define low titer of antibodies?

Depends on the assay! Many have cutoffs while Positive that would be below the threshold where neutralizing antibodies are detected. (Kim, Arthur)

40. Raj: Do you think there is a dose response to monoclonal antibodies? Initial trials used 8 gm doses, but current dosing is no more than 1.2 gms.?

In outpatient studies, based on viral load decay, I think the higher dose didn't seem to confer benefit. (Gandhi, Rajesh)

41. Is anyone looking at combining Molnupiravir and Paxlovid?

It's a great idea. I haven't seen any announcement of that study. I'd like to see it done in immunocompromised hosts. (Gandhi, Rajesh)

42. Do you use online risk calculator for Covid progression?

On occasion. I do know our mAb program if we don't have enough slots have sometimes used calculators to prioritize cases. Note the calculators were made pre-vaccine era and generally do not account for risk after vaccination. (Kim, Arthur)

43. Any thoughts on immediate, post-exposure vaccination of a previously unvaccinated person?

With high-risk features (older patient with comorbidities) this would be a prioritized patient in our system, but only if capacity allows beyond patients who have already developed COVID.

44. What therapeutical options do we have for children under 12?

RDV can be given on weight-based basis under EUA.

45. What is the 3-2-2 rule?

Paxlovid. (Luetkemeyer, Annie)

46. How about combination of both Monulpiravir and Paxlovid 332? would it add benefit? reduce chance of resistance?

Great question -- see reply to participant who asked similar question. (Gandhi, Rajesh)

47. What about oral agents for post exposure prophylaxis such as Tamiflu?

Studies of paxlovid and molnupiravir will look at PEP.

48. Can pregnant women get vaccinated with viral vector vaccines?

Yes, fine for pregnant women to get vector vaccine (they're not replication competent).

49. Patients can get Tamiflu without a positive flu test. Will patients be required to have a positive SARS-CoV-2 test to receive oral antivirals?

More to come, I do believe most systems are likely to require a positive test.

50. For preexposure prophylaxis how often will you give monoclonals?

The AZD combination appears to last 9-12 months based on PK.