

CDC/IDSA COVID-19 Clinician Call

All About Paxlovid: Plus Variants Update

April 9, 2022

Q&A

Below the Q&A transcript from the April 9, 2022 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 are the current recommendations for pregnant patients with covid disease? BEB IV (with limited clinical efficacy data), Paxlovid (with no clinical data in pregnancy)?

Paxlovid is not currently recommended because of, as you noted, a paucity of data. My clinical opinion is that it's tough to give a blanket recommendation. It depends on how far along the pregnancy is and if there are other high-risk features. (E.g., very different if at 6 weeks vs 39 weeks, how did prior pregnancies go if any). A monoclonal antibody is more likely to have difficult to anticipate off-target effects than Paxlovid (protease inhibitor but targets a protease very unique to SARSCOV2).

2. What is the current epidemiologic findings about LENGTH OF TIME OMICRON Illness can protect against new covid illnesses? can B A1 infected become symptomatic from BA2? is that happening?

<https://www.medrxiv.org/content/10.1101/2022.02.19.22271112v1> . Reinfections with BA.2 after BA.1 appear to be rare, at least in the short-term. This study in Denmark is useful. Most infections were mild and occurred primarily in unvaccinated individuals.

3. Please comment on the use of Plaxlovid for those patients taking tacrolimus?

Here is the link to the Lange et al. manuscript with the tacrolimus/cyclosporine algorithm:
<https://onlinelibrary.wiley.com/doi/10.1111/ajt.16955>

Paxlovid contains ritonavir, which inhibits 3A4. Might need to decrease tacro levels. I would start by checking levels more frequently and looking for signs of toxicity (e.g. decreased urine rising Cr, tremors, headaches).

4. Thank you, can you address the X subvariants (XD, XE, XF, XG, etc); and in particular XE that WHO has stated has a 10% advantage compared to BA.2?

XD and XF variants are Delta/Omicron BA.1 recombinants and so far have limited spread. Please see: <https://www.biorxiv.org/content/10.1101/2022.03.19.484981v1> for a preprint publication from CDC describing first 9 cases of XD identified in U.S. Most were from mid-Atlantic region. XE recombinants are Omicron BA.1/BA.2, first identified in UK in January 2022 and about 600 sequences have been confirmed. Early data suggest a possible 10% transmission advantage over BA.2 but this requires confirmation. Recombination among coronaviruses is very common so these will likely continue to be identified and we need to continue monitoring for any evidence of increased transmissibility, immune evasion, virulence, etc.

5. I realize that boosters are not on today's agenda, but I would appreciate any comments by the panel regarding the available data on the utility of someone over the age of 65 or 70 receiving the second booster, and also whether there is any downside of receiving the booster at this particular time.

Data from Israel (<https://www.nejm.org/doi/full/10.1056/NEJMoa2201570>) suggest protection against severe disease for at least 6 weeks (during the study period) from a second booster, although protection against infection is relatively short-lived and began waning after 4 weeks. Please see CDC's interim clinical considerations for COVID19 vaccines for additional information: <https://www.cdc.gov/vaccines/covid-19/clinical-considerations/interim-considerations-us.html# covid-vaccines>

6. Do you think our estimates are still accurate - as most positive cases are by home testing thus not officially recorded anywhere?

Thanks for your questions. Please see <https://www.cdc.gov/mmwr/volumes/71/wr/mm7113e1.htm> for more discussion on this topic. An excerpt from the MMWR: With variable access to timely, medically administered tests (e.g., NAATs), coupled with pandemic fatigue, U.S. residents might increasingly rely on at-home tests if such tests are readily available (2,5). These self-administered at-home tests have a high specificity and moderate sensitivity, which peaks during viral shedding and symptomatic illness. At-home tests can provide valuable information related to community infection incidence and prevalence, even among asymptomatic persons (2,3). Official COVID-19 surveillance systems aim to capture a comprehensive count of infections. Thus, measuring at-home test use can help quantify the proportion of SARS-CoV-2 infections that might be missed by these systems. These data can also be used to understand reasons for using at-home tests, which were different from those for using tests administered in other settings.

- 7. The known protection that BA.1 infection confers against BA.2 infection plus the % of vaccinated persons may help explain why BA.2 has not seemed to cause a significant increase in BA.2 in USA; however I am concerned that since immunity from natural infection (and vaccine immunity) seems to fade, I can't help to wonder about what will happen when the NEXT variant hits sometime after immunity drops. Please let me know your thoughts on this.**

Thanks for your question. As immunity from infection and vaccination wane, there is the possibility of future waves with current circulating variants or future emerging variants. So far, modeling scenarios suggest that, in the current environment, waves in the near future are not likely to be as severe as previous waves. These models do not necessarily account for additional boosters, new vaccines, or new variants. Emergence of new variants is being closely monitored through genomic surveillance in the U.S. and other countries.

- 8. Could you please expand on why the second boosting for J&J vaccine recipients is only recommended after a J&J first booster and not mRNA first booster? What is the strength of that recommendation?**

People ages 18–49 years who received Janssen COVID-19 Vaccine as both their primary series dose and booster dose may receive an mRNA COVID-19 booster dose at least 4 months after the Janssen booster dose. People ages 50 years and older may choose to receive a second booster dose if it has been at least 4 months after the first booster dose. Please see <https://www.cdc.gov/vaccines/covid-19/clinical-considerations/interim-considerations-us.html# covid-vaccines> for more information.

- 9. Can we talk about herd immunity now? It's not been mentioned for some time.**

I'll share this topic back to the planning group for consideration of a future call. Thank you!

- 10. Please discuss vaccine-associated tinnitus and vestibular problems?**

Although not the topic for today's call, please find this resource that might be helpful: <https://www.sciencedirect.com/science/article/pii/S204908012200053X>

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. Do we anticipate vaccines to be updated based on circulating variant?**

<https://thehill.com/news/3012274-biontech-begins-production-on-omicron-specific-vaccine-to-publish-data/> and <https://pharmaphorum.com/news/moderna-starts-dosing-patients-with-its-omicron-covid-jab/>

- 12. Thank you for that answer. I am not familiar with that data - so is the risk highest early in pregnancy or later? I suppose it also depends whether we are considering direct viral effects vs risk of severe disease (impact of hypoxia) and the potential impact of vaccine efficacy and whether pt has high baseline BMI and/or dm before pregnancy.?**

My point about when in pregnancy is not referencing new data, just a general tox and OB/GYN principle that drug effects vary across gestation (spontaneous abortion early on, neurocognitive issues in later on). Yes, I would be more aggressive in treating a woman with sleep apnea and gestational diabetes at 6 weeks than in a woman with an uneventful pregnancy and no symptoms at 39 weeks.

- 13. Why is there no data on dose adjusting Paxlovid in patients with renal clearance <30 ml/min? Seems like we might be able to get away with a single dose or 2 in this group but would be nice to at least have safety data.?**

Evaluation of the safety and PK of paxlovid in patients with severe renal impairment, including patients on dialysis, was a condition of authorization for the EUA. This was recommended due to results of a Phase I renal impairment study with Paxlovid where more adverse events were noted in subjects with severe renal impairment. This study may provide more information for the appropriate dose in this population.

- 14. It is not so easy to find information on drug interactions with OTC/herbal products. Lots of patients are taking these. Is there a good resource for this?**

Case by case basis. Call Poison Control. Not trying to be glib, but each of these herbal medications has a unique history. Kratom isn't banana leaf, isn't ginseng. The actual ingredients are different as are the usual contaminants. Easier to talk it through with someone who deals with it more frequently.

Good suggestion re: poison control. Offering only my experience with RTV during chronic use for HIV, St. John's Wort is my only hard stop because it could compromise the HIV - or here Covid - therapy. For other herbals, I be sure I know what they are, and monitor for adverse events.

So what do I do when I find my patient is on TUDCA or St John's wort, etc.?

Sorry, wrong click. This is challenging for a few reasons. The herbal products are not regulated so we don't know what's in them. Good rule of thumb is assume they are all hepatotoxic.

St. John's wort is one key example covered in the DDI resources and is contraindicated because of enzyme induction which will decrease Paxlovid.

TUDCA is relatively benign. In some reports (a while ago) it decreased (not increased) transaminases and GGT. Once I looked at the formulation, I'd probably not be insistent over it.

15. What does the drug fact sheet say about use of Pax with atorvastatin? Also, is this high risk patient the type of person you want to hold atorvastatin in?

IMO, you could switch to pravastatin (no 3A4 interaction, yes not as effective for lowering LDL but it's only for a short time). Or just monitor LFTs, CK more closely.

16. Had any of the transplant patients received Evusheld in the study done at Columbia?

At the time of the study, Evusheld use was just starting at CUMC, so I don't believe any of the included participants had received it. Evusheld is now routinely used in our patients for primary prevention, but I don't know the local data on efficacy at our center.

17. Per the EUA for paxlovid, symptom duration has to be less than or equal to 5 days when prescribing paxlovid. Does that not apply to immunocompromised patients? I have not seen anything in the EUA addressing this.

Hi Michelle, at our center we generally adhere to that same timeline although individual transplant physicians sometimes make exceptions. As with most other populations (and other drugs), the earlier the treatment is given is better.

18. If holding Tacro is risky i.e., renal transplant requiring significant immunosuppression prevent rejection then would you still recommend using Paxlovid which requires withholding Tacro

Hi Hasan, if risky bc of individual patient factors, I think you would consider other therapies (short course RDV or monoclonal ab), if available. If those aren't possible and pt is at risk for COVID complications, you could still consider Paxlovid, although you'd want to monitor levels very closely with pharmDs and transplant team. Thanks

19. Our rural hospital lab sends out for tacrolimus levels, and it takes several days for the results. Would you recommend that the patient stay in a more urban area with better testing capacity (post treatment) if Paxlovid is the drug of choice?

Hi Susan, I think it could be problematic to not have results in a timely fashion. For patients with low risk of rejection/toxicity (i.e., remote transplant, no previous rejection) it may be okay to do local monitoring, but I think close monitoring may be better for new transplants or those with a complex rejection history. Thanks

20. Given the risk with NR and SOTR why not go direct to 3 days remdesivir?

Hi Richard. RDV is certainly compelling in that context, esp. in patients with RFs for rejection/toxicity. In NYC, we have struggled with the logistics of giving IV therapies to outpatients in a timely fashion, so that sometimes pushes us to paxlovid. Thanks.

21. Remdesivir? Paxlovid any help?

Hi Winnie. I think it often depends on the logistics. Both have good data. RDV has less drug interactions so that can be compelling, but it can be hard to get in a timely fashion for outpatients given its IV administration. We often give it for inpatients. Paxlovid is often easier for outpatients, at least in our region.

22. if paxlovid is contraindicated in a SOTR, which is preferable, if both are available: bebtelovimab, outpatient remdesivir, or a combination of both?

Hi Laura, I think either would be viable options and the decision on which one to use would likely depend on logistics and availability in your local area. In general, we don't do combinations because of lack of data to support that.