

CDC/IDSA COVID-19 Clinician Call

Outpatient COVID-19 Treatment Strategies for High-Risk Populations

January 22, 2022

Q&A

Below the Q&A transcript from the January 22, 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. Any hope for alternative formulations of remdesivir such as subcutaneous, oral or inhaled options?

Yes, recent exciting publications for SQ remdesivir, as well as inhaled, in non-human primate model. Oral formulation development ongoing.

2. Can the panelist address the differences in the drug interaction lists for the paxlovid EUA vs the NIH treatment guidelines, referring to both is time consuming and sometimes contradictory; the Liverpool COVID drug interaction site is not user friendly?

The ritonavir drug interactions are EXTENSIVE, to say the least. It is a major substrate and inhibitor of CYP3A4, which drives most of the clinically significant interactions. It is also a minor inhibitor and substrate of several other enzymes (CYP1A2 is an underappreciated one), and an inducer of CYP1A2, 2B6, and C19. With this level of complexity, it's difficult to write every single interaction that can occur. We also struggle with this when developing decision support in the electronic health record—to many alerts causes alert fatigue and “clicking thru” the alerts whereas not enough may miss a very important interaction. So, the discrepancies in references is bodies of experts doing their best to be concise and comprehensive.

There will be some disagreements amongst clinicians about severity of interaction and best approach. The best example of this is how to handle the tacrolimus interaction. We see an immediate elevation of tacrolimus levels, and this can last for up to a week of ritonavir is discontinued. Ideally, a pharmacist would be involved in every patient receiving Paxlovid to do a medication reconciliation and navigate the interactions as best as possible. If mAbs were widely available, we would prefer mAb in a patient with a significant interacting drug. (Dr. McCreary)

3. What & when to do it (booster) after an infection with COVID? Also, when to do first vaccine of primary series after COVID-19 infection?

You can receive a COVID-19 vaccine after recovery from acute illness and when your institution's criteria to discontinue isolation precautions has been achieved. This may vary by institution. For severely immunocompromised patients, my institution requires at least 20 days from test positive with two negative PCRs, a week apart, before we discontinue precautions. (Dr. McCreary)

4. Any data coming out of Cuba re: pediatric vaccine efficacy and safety for children under 5 years old?

Thank you for the question, Suzanne. The data from Cuba is still very preliminary. The clinical trials done in US on infants 6 mo. to 2 years actually showed that the very low dose Pfizer vaccine at 3 ug generated a very robust immune response. However, this was not seen in the 2-to-5-year age group after 2 doses. Clinical trials are ongoing looking at giving a 3rd dose of the vaccine to this age group to see if it significantly boost the immune response. (Dr. Tan)

5. Could you please address the recommendation for an immunocompromised host who got 2 doses of Moderna primary series followed by a half dose booster instead of full dose 3? Do you recommend another full dose 5 months after the 1/2 dose booster?

Unfortunately, there is a bit of data vacuum, here, because the third Moderna dose should have been 100 mcg. it is not very likely that pharmacies will dispense 100 mcg as a fourth dose, so 50 mcg would usually be given and that may be OK. Pfizer 30 mcg is also an option if desired. (Dr. Werbel)

6. Use monoclonals or antiviral for early COVID (in those expected to progress)?

Right now, we recommend sotrovimab OR paxlovid in qualifying patients. Due to the extreme scarcity of both meds and the small subgroup in the Paxlovid EUA where there seemed to be no additional benefit with mAb, we do not recommend both for any patient, but all high-risk patients should seek one or the other. Patients with renal dysfunction should get mAbs. Patients with contraindicated drug interactions should get mAbs. (Dr. McCreary)

7. What would the reasons be for advising parents of 13-year-old male with Down syndrome not to get COVID-19 vaccine? He had multiple drug reactions in his 8-week NICU stay with his lungs being biggest problem?

There is no contraindication to receiving a COVID-19 vaccine outside of anaphylaxis to a previous mRNA vaccine. Patients with severe allergic reactions to other medications should be monitored very closely when getting vaccinated, but it is not a contraindication to vaccination

8. Any hope for subcutaneous option for sotrovimab?

There are studies of intramuscular sotrovimab that have shown good results, so would anticipate this would be the next route of administration to be authorized. (Dr. Werbel).

9. Can you share any efficacy and safety data on IM sotrovimab?

COMET TAIL Phase 3 data has demonstrated that IM sotrovimab demonstrated non-inferior efficacy to IV sotrovimab in the treatment of outpatients with early COVID and risk factors for progression. Vir has submitted a request on January 13th to amend their EUA to include IM. (Dr. Weld)

10. 70 yo with mild comorbidities who 2-3 weeks after first dose Pfizer vaccine developed thrombocytopenia and leg DVT. Told to avoid repeat vaccination. Given Evusheld. Any advice about completing vaccine series?

This is a challenging case without knowing everything else about the patient, to know if truly caused by vaccine. Would recommend consultation with patients primary providers along with an allergy specialist to determine best path forward for that patient. (Dr. McCreary)

11. Despite the EUA requirements for the use of Monoclonal antibodies, how should one approach those compromised patients like CLL or solid organ transplants who are hospitalized with moderate or severe disease? is empiric monoclonal antibody therapy appropriate consideration given the inability to truly assess patient immune and antibody response

This gets tricky. If patients are hospitalized with COVID-19, they don't qualify for mAbs under the EUA, and we cannot use mAbs outside of the EUA (you can't use a drug off-label when there isn't a label). However, if patients are hospitalized for non-COVID-19 (i.e., they have AKI but only mild-moderate COVID-19 symptoms) and are within 10 days of symptom onset, we will give mAbs inpatient because the physical location shouldn't dictate optional treatment based on clinical status. But if they progress beyond mild-moderate, there is no mAb option—to my knowledge GSK doesn't have a compassionate use program. We were sometimes filing for compassionate use REGN in the Delta era. (Dr. McCreary)

12. What is the role for fluvoxamine like agents for outpatient therapy?

NIH says neither for nor against: Fluvoxamine | COVID-19 Treatment Guidelines (nih.gov)

IDSA rec 26 says only in a clinical trial: IDSA Guidelines on the Treatment and Management of Patients with COVID-19 (idsociety.org)

Ontario says it may be considered: Clinical Practice Guideline Summary: Recommended Drugs and Biologics in Adult Patients with COVID-19 - Ontario COVID-19 Science Advisory Table (covid19-sciencetable.ca)

My institution says paxlovid or mAb; if you cannot get either, can consider molnupiravir OR fluvoxamine. (Dr. McCreary)

13. Will the panelists be discussing immunocompromised individuals on immunosuppressants? If so, when might they qualify for getting Evusheld?

Yes, this will be a focus of a couple of the questions moving forward. (Dr. Werbel)

14. Despite the EUA requirements for the use of Monoclonal antibodies, how should one approach those compromised patients like CLL or solid organ transplants who are hospitalized with moderate or severe disease? is empiric monoclonal antibody therapy appropriate consideration given the inability to truly assess patient immune and antibody response?

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15. Any timeline for when Paxlovid may be more readily available?

Not that I know of (Dr. McCreary)

- 16. Pregnant patients- much more experience with safety of Remdesivir. Sotrovimab is newer, less actual experience, though experience with mAb class with REGEN-COV. Preference between the two? Risk assessment between vaccinated and unvaccinated pregnant patient in offering Tx if meds were available?**

mAb if it was my friend who was pregnant. mAbs consistently show benefit and outpatient remdesivir is logistically difficult-- we have ongoing discussions with our W&C hospital ongoing about standing up remdesivir if/when we run out of sotrovimab, but fortunate to have enough sotrovimab right now for tier 1 risk patients, so continuing to only use sotrovimab in pregnancy. If we run out of sotrovimab, we will offer outpatient RDV to pregnant patients. (Dr. McCreary)

- 17. if you have a severely immunocompromised patient who received Evusheld (i.e., SOT, HSCT etc.), would you exclude them for receipt of sotrovimab? this is in the setting of knowing our predominant strains are omicron?**

- **Dr. Werbel:** A great question, we are not considering having received evusheld to be a contraindication to receipt or referral for sotrovimab. particularly if the patient has a very high-risk phenotype (which given scarcity guides allocation, a bit).
- **Dr. McCreary:** We also allow sotrovimab if patients have a breakthrough case, regardless of timing to evusheld. if prevention fails, we still treat.

- 18. In the USA, we are now seeing cases of Omicron BA.2 (a variant of Omicron now identified in multiple countries, and which seems to have overtaken the original Omicron in Denmark). Omicron BA.2 is harder to distinguish from other SARS-CoV-2 variants because it lacks the S-Target drop-out seen in the original Omicron. If this subtype of Omicron gains dominance in the USA, how will it affect patient risk and management?**

it was originally recommended in our state to consider SGTF as a marker to distinguish delta vs omicron, but I do not use this anymore due to dominance of omicron. our center does whole genome sequencing on a subset of positives, so we are tracking the changing landscape, but I am not aware of omicron sub lineage dictating major changes in therapeutic strategies. there are sotrovimab-resistant variants in the community, but I don't have access to a mechanism to distinguish these. (Dr. Werbel)

- 19. Timing of Evusheld In postpost-transplant patients and subsequent vaccination post 100 days from transplantation? should we wait 3 months or 6 months post Evusheld to revaccinate those patients?**

We proposed giving Evusheld on POD1 and then starting vaccination series at D90+ like usual. Agree to not delay vaccination for Evusheld. (Dr. McCreary)

- 20. If person takes Astra Zeneca mAb – and then wishes to get vaccinated – how long would they have to wait to take the vaccine?**

We currently say 30 days, but I don't think the answer to this question is known currently. (Dr. McCreary)

21. How do you respond to those individuals who still are asking/demanding ivermectin? Is there any new data on this medication? We have restricted it at our institution.

We do not allow ivermectin at our institutions. We have support from legal, ethics, and senior leadership to say no to these patients. We developed a patient-facing one-pager to describe, in a 7th grade reading level, why we only offer certain therapies. Happy to share if you email me (mccrearye3@upmc.edu) (Dr. McCreary)

22. The NIH has listed the priority on the OP antivirals based on the primary outcome rates as Paxlovid>sotrovimab>Remdesivir and molnupiravir. But looking at the raw data submitted to the FDA for the EUA the MOVE-OUT had 74% obese patients and the EPIC-HR only about 30%-does anyone know why this significant difference? Could it have affected the outcome rates of 88% vs 30% and how do we adjust for this-I know there is no peer reviewed data but would love to know what the panel thinks?

Molnupiravir does have a greater Vd and less protein binding, but obesity impact would be hypothesis only at this point. (Dr. McCreary)

23. Are there settings where use of both Sotrovimab and Paxlovid would be considered for an individual patient (if supply allows)?

I would personally be comfortable using this combination (or substituting molnupiravir, remdesivir) in high-risk persons without contraindication to nirma/ritonavir if supply permitted. (Dr. Werbel)

24. What about congenital immunodeficiency? where would that fall on the risk scale?

Severe primary immunodeficiencies are Tier 1. (Dr. McCreary)

25. Any recommendations on immunocompromised patients who fail Evusheld and now require treatment for active COVID (Sotrovimab? paxlovid? remdesivir? or a combo?)

Treat them the same. If prevention fails and they get infection, they move into the infection algorithm and therapy shouldn't be altered compared to someone who did not get Evusheld.

26. For your framework, how do you fit in former Covid infection?

A great question. persons who have had prior COVID and then get vaccinated generally have quite augmented immune response. *very* crudely, it is akin to one additional dose of vaccine. prior infection, alone, in the omicron era does not protect much against reinfection though there is a signal for protection against severe disease likely owing to a degree of T cell memory. assessing prior infection is reasonable to include as part of the risk assessment (particularly if recent), but with variable immune response especially =following mild infection and in persons with immunocompromise, it is not always a reliable factor (Dr. Werbel)

27. Any recommendations on immunocompromised patients who fail Evusheld and now require treatment for active COVID (Sotrovimab? paxlovid? remdesivir? or a combo?)

Treat them the same. If prevention fails and they get infection, they move into the infection algorithm and therapy shouldn't be altered compared to someone who did not get Evusheld. (Dr. McCreary)

28. Any thoughts on the optimal timing of booster vaccination in an immunocompromised patient who has already received evusheld? wait 90 days? 30 days? especially when community incidence of omicron is high and knowing omicron coverage may be inadequate with evusheld.

We currently say wait 30 days from Evusheld to COVID-19 vaccination, but honestly, we don't know the right answer. If patients are considering their booster vs Evusheld we say go, get your booster and we'll schedule your Evusheld appointment in ~2 weeks. At this point we'd prioritize vaccination over Evusheld and with the scarcity of Evusheld, it's difficult to plan timing of both (especially when we're allocating Evusheld in a lottery). (Dr. McCreary)

29. Let's please make sure clinicians are aware of <https://covid-19-therapeutics-locator-dhhs.hub.arcgis.com/> Looking at my Zip Code right now there are 45 doses of Paxlovid immediately available at local pharmacy?

Thank you! States may also send out local guidance-- PA has online resources to track which pharmacies have paxlovid and molnupiravir. (Dr. McCreary)

30. Have you seen patients suffering from long COVID being reinfected with Sars-CoV-2? Do they experience worse symptoms than in the prior infection? How do you categorize these patients? Are there data on this?

We definitely see patients who get COVID-19 twice; the patients who are Tier 1 for Evusheld are likely to have multiple lifetime infections. Symptoms can be better, same, or worse-- this hasn't really been fully described. We treat each infection as we would treat a first infection. Anecdotally though patients with persistent COVID (immunocompromised patients can shed live virus for months) do poorly; if not from COVID, if from the fact that their other healthcare (chemo, etc.) has to be delayed. (Dr. McCreary)

31. On the slide with covid 19 risk framework where would place pregnant women?

Truthfully, the exact location on this continuum can be debated, but pregnancy is a serious risk factor for many viral illnesses including COVID-19 particularly if pregnant person is unvaccinated.

32. Would you give MAB or remdesivir on a pregnant woman UpToDate with vaccine or hold off?

Ideally give mAb in pregnant women with COVID-19, regardless of vaccine status. New Mayo pre-print showing mAb efficacy even in vaccinated patients, and a small case series from the same group about safety in pregnancy.

33. Any suggestions about if a person has recovered from covid, with or without receipt of monoclonals for treatment – and are eager to receive Evusheld for prophylaxis- when can they receive Evusheld?

We allow Evusheld as soon as they meet criteria to discontinue precautions so for this profoundly immunocompromised group, it's a negative PCR at day 20 and another on day 27. So ~1 month (Dr. McCreary)

34. Any thoughts facilitating the use of high titer convalescent plasma or even IVIG as early outpatient (or even early inpatient in certain patients) as an option given lack of supply of other options. Recent data showing 54% RRR in hospitalization?

We have not re-explored plasma as we're not sure if this pans out in an Omicron world and logistically, this isn't available. (Dr. McCreary)

35. Is a person with chronic use of Hydroxychloroquine for rheumatological condition considered to have any degree of immune suppression?

Answers will vary here, we place these patients in the last group to receive Evusheld based on having an autoimmune disease but not on highly immunosuppressive therapy, so low down the priority list. Many of these patients respond adequately to vaccination. (Dr. McCreary)

36. As a large patient population in the US how are HIV providers to “look” at their HIV/AIDS patients who are well controlled for years with good CD4 cells (>350 or so, w or w/o prior low t-cells/OIs), vaccinated and doing well with regards to their immunosuppression status on this continuum?

These patients respond quite well to vaccination and are lower priority for Evusheld (<https://www.medrxiv.org/content/10.1101/2021.06.28.21259576v1>) (Dr. McCreary)

37. Could you please address the timing of booster after Evusheld? My county has a mandatory booster requirement for healthcare workers. If an immunocompromised HCW received Evusheld, when can they take the booster? Dr. David Weber at last week's Shea call stated booster can be received as early as needed after RegenCOV, no need to wait 90 days because that drug has no efficacy against omicron. would you say the same for Evusheld?

We currently say 30 days but there's no good answer here. Ideally would get booster prior to Evusheld. (Dr. McCreary)

38. Bill, when can we start to see routine testing for antibody response and/or cellular immunity for solid organ transplants?

Hello! This is still hotly debated for some of the reasons that Mike and I discussed. We would need some guidance from FDA/CDC as well as transplant societies on how best to use these kinds of assays before wide adoption. Right now, it is case by case. The clinical T cell assays are not particularly helpful, right now. There are research assays similar to quantiferons but their association with clinical outcomes is very uncertain. antibody testing has more evidence, but mostly indirect. (Dr. Werbel)

39. For transplant patients - should they be getting a 4th dose of mRNA vaccine? with the first 3 doses be considered the primary series and the 4th dose as a booster?

Yes, it is recommended that transplant patients get a 4th mRNA dose 5 months after completing the 3-dose primary series that was authorized in August. so, many patients will be eligible this month. (Dr. Werbel)

40. Would you consider stopping interacting meds for a short time in case 1 setting so that paxlovid could be given? If available that is.?

Possibly-- it really is a case-by-case basis. Paxlovid has such a narrow window to start treatment and with current testing limitations, it may not be possible (or in the best interest of the COVID-19 infection) to stop medications before starting Paxlovid. Really have to look at each individual patient's comorbidities, COVID-19, and medication list and make the best decision for that patient (Dr. McCreary)

41. Are solid transplant organ recipients advised to receive 4 doses (3 doses then booster?) for most up to date vaccination recs?

Correct - 3 doses and then a booster 5 months after.

<https://www.cdc.gov/coronavirus/2019-ncov/vaccines/recommendations/immuno.html> (Dr. Ison)

42. Do you know how long after the Evusheld was administered that the breakthrough occurred?

For our patient it was 4 days after infusion. (Dr. Ison)

43. Can you comment on why there is so little concern about using Paxlovid in a patient with HIV on a boosted ARV regimen?

If they're already on a booster-containing ARV regimen, then only giving Nirmatrelvir part of paxlovid can be given without the ritonavir in the paxlovid. Granted they fit all the other criteria and no contraindications.

44. What is an appropriate antibody level for protection?

We don't have reliable targets that predict protection for the entire 6-month period after measuring for Omicron. (Dr. Ison)

45. Will there be some centralized way to see what therapies are available? For the orals I can call pharmacy chains and ask. mAb has been by asking colleagues around town, unfortunately.

For the US, you can use the HHS website below. Filter to your state and drug of interest. The data is updated once per day. https://healthdata.gov/widgets/rxn6-qnx8?mobile_redirect=true (Dr. Ison)

Attendee: You can also go to this link - <https://covid-19-therapeutics-locator-dhhs.hub.arcgis.com>

46. How much data does sotrovimab have with Omicron? especially in the real world.

I am not familiar with any extensive published real-world sotrovimab effectiveness data vs omicron, yet. in vitro data are encouraging. can share our clinical experience in transplant patients has been very good (albeit in vaccinated persons). (Dr. Werbel)

47. Being a rather small program, we have used Pax in a handful of kidney transplant recipients on Tacro during mAb shortage. Many covid+ pts has high CNI levels to begin with. The most reasonable approach, I think, is to hold Tac the moment it is started and re-introduce it 2-3 days after Pax completion but with close follow-up of levels, since the inhibition can last for 1 wk or longer. But even then, the levels are quite unpredictable, and some labs have restrictions for COVID+ patients (also time of the day being important for trough measurement). Our pts eventually did clinically well but with a lot of effort on both ends (patient and transplant team), so the feasibility of Pax+CNI co-administration on a larger scale is questionable

Thanks, I have seen most groups recommending holding tacro for a week or so and restarting and I think this is reasonable if one can get the tacro level and renal function is stable etc. we would all benefit from groups publishing their experience with daily or every other day level trending to get a sense of the actual drug exposure in the setting of coadministration with ritonavir. is tricky as you note in those who are acutely ill. (Dr. Werbel)

48. How about strovimab plus Paxlovid?

The EUA for Paxlovid shows that was the only subgroup that didn't have a significant benefit (<https://www.fda.gov/media/155050/download>). With the scarcity of both medications as well, we recommend one or the other but not both. (Dr. McCreary)

49. Persons born with IgA deficiency (this deficiency seems to play a part in asthma and allergies, and autoimmune health problems) and a Japanese study shows a strong positive correlation between the frequency of selective IgA deficiency and the COVID-19 infection rate per population (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7533856/>). Has anyone on the panel seen this correlation? I ask this question in the setting of the cancer patient with decreased IgA, but also curious as an overall issue for COVID-19. Should I consider my IgA deficient patients at increased risk for more severe COVID-19?

I have not but we just had our pediatric group review this and they determined IgA deficiency should be group 2, not group 1, for Evusheld prioritization. (Dr. McCreary)

50. And is paxlovid appropriate for multiple myeloma patients?

Yes, it can be used as long as no drug drug interactions, studies excluded patients with cancer, however. (Dr. Berg)

51. Should spike-protein antibody levels be considered when allocating Evusheld?

This is quite controversial but currently not required and not considered in prioritization because 1) antibody tests vary, 2) there is no clinical correlation between any result and severity of COVID-19 and 3) it isn't widely available for every patient when trying to make ethical allocation decisions. (Dr. McCreary)

52. What would be the priority level for Evusheld for a patient >75, chronic liver disease, and on Mycophenolate mofetil?

Priority 3 for my health system. This may vary. Any patient aged 65 and older who ALSO has loss of 2 or more activities of daily living is priority 1 for us, since these patients do not respond to vaccination compared to healthier patients of advanced age. Mycophenolate alone doesn't seem to correlate to severely diminished vaccine response but is a factor when you have cumulative medications. (Dr. McCreary)

53. For 68 yr. old breast cancer female patient, completed 4 med ChemoTx and 6 wk. RadTx, currently on 2 med infusions (Herceptin&Kadcyla) to complete 1 yr., also w/ typ2 DM, obesity, and CKD3: is Sotrovimab best option? if in case still progresses despite Sotrovimab, can you still give Remdesivir?

At this time Sotrovimab seems to be the best option in terms of minimal interactions with current chemotherapy and drug-drug interactions with the oral covid therapy; I would agree if they progress with symptoms on Sotrovimab, Remdesivir is a good option. (Dr. Berg)

54. Please comment on cancer patients infected with omicron puci symptomatic and with increased transaminases when sotrovimab is not available... would you consider treating this patient?

It would be challenging to give the oral treatment with liver dysfunction, but one can consider outpatient remdesivir. (Dr. Berg)

55. Using ritonavir for 5 days only, can we adjust for these 5 days to be able to use all these high-risk patients?

RTV inhibition likely lasts beyond when RTV is stopped (<https://pubmed.ncbi.nlm.nih.gov/21937987/>). We are saying hold tacrolimus for at least 5 days, maybe up to 7, ideally check levels if possible. (Dr. McCreary)

56. Have you ever used remdesivir in patient with ESKD + AST/ALT 1500?

We do not use RDV in patients with ALT/AST > 10x ULN per the package insert and previously per the EUA. We do use RDV in patients with renal dysfunction since cyclodextrin accumulation isn't clinically relevant (<https://pubmed.ncbi.nlm.nih.gov/33229428/>). (Dr. McCreary)

57. If a patient with RA, 1 yr. post Rituxan infusion, was infected with COVID, when would they be eligible to get Evusheld? Would they need to test for antibody levels?

This isn't clearly outlined in the NIH guidelines but are including anyone who has received a B-cell depleting therapy within the past year as tier 1. (Dr. McCreary)

58. Can a transplant patient that takes mycophenolate and tacrolimus that gets >2500 antibodies to the neutralization point, still get T and B cells?

Generally speaking, persons who mount high levels of binding anti-spike antibody responses have greater virus neutralization capacity as well as B and helper T cell function. but there is variation depending on the type of immunosuppression, so this is a highly individualized assessment. (Dr. Werbel)

59. Are there any options for Post Exposure prophylaxis for immunocompromised patients who do not yet qualify for Evusheld?

EUA excluded pills from use as pre-exposure prophylaxis and sotrovimab does not have an authorization for this indication. (Dr. Ison)

60. Ritonavir and Flonase are a category X drug interaction with risk of iatrogenic Cushings - with Flonase being OTC and used for nasal symptoms, should we be making sure our patients are warned, or is 5 days likely not an issue? This is long enough to cause high plasma levels of fluticasone, but not sure about clinical significance?

I think patients should absolutely be warned. This is one of the big concerns about this medication widely in the community. (Dr. McCreary)

61. What to do if start iv remdesivir for nonhypoxic patient with risk for progression that is covid + on admit but hospitalized for something apart from covid and is ready for discharge before the 3rd dose?

We do not recommend prolonging hospitalization to complete a course of remdesivir if otherwise ready for discharge; oral dex can continue outpatient (if indicated), but okay to cut the remdesivir course short based on current practice approaches (and to be mindful of hospital capacity etc.). (Dr. Hill)

62. Follow-up with Dr Josh's discussion: he mentioned to give antiviral early to high-risk patients now that remdesivir is available outpatient: do you mean give/prefer remdesivir over sotrovimab? (i.e., for BreastCA patient on Chemo, with mild symptoms and ok O2 sat)?

I don't think there is a preference for remdesivir over sotrovimab. But this patient would not currently meet our institutions criteria for sotrovimab given not in the highest risk categories and we have limited supply. (Dr. Hill)

63. What is the first line treatment Remdesivir or dexamethasone in the case?

Remdesivir alone if within 7 days of symptoms and no oxygen requirement. dex typically not given concomitantly unless patient has oxygen requirement. (Dr. Hill)

64. For high-risk patients admitted to the hospital for reasons unrelated to acute COVID19 and are found to be positive, would you use 3 days of remdesivir to prevent progression of their infection even though they're inpatient?

Yes, agree. (Dr. Hill)

65. Are facilities using Remdesivir for patients who are asymptomatic but have multiple risk factors for disease?

No - we do not use any treatment for asymptomatic patients. (Dr. McCreary)

66. For case 2: would you give dex + Tocilizumab if the patient is getting worse or admitted to the ICU? any concern for « triple » suppression? (MM-treatment + dexta. + toci)?

Toci has fallen out of favor for treatment but can be considered and would even consider a longer course of Remdesivir as well if worsening. (Dr. Berg)

67. Because of the extreme supply shortages of Paxlovid and sotrovimab, would you consider at this time still consider giving REGEN-COV® (casirivimab and imdevimab) despite the in-vitro data suggesting its limited activity against Omicron?

Given that the IC50 and IC90 are well in excess of what is clinically achievable, I would not. We suspended use systemwide when we got above 20% Omicron. (Dr. Ison)

68. Have use regen-cov under comp use many times, have not looked into the GSK process.

GSK has a compassionate use section of the website but to my knowledge, there isn't a process for compassionate use sotrovimab. If I am wrong and anyone has successfully received compassionate use sotrovimab for a moderate-severe inpatient, please let me know!! (Dr. McCreary)

69. While I appreciate and certainly agree with antimicrobial stewardship, (and one report that only 15% of Pts have co-infection with Covid), I noted that Pts who passed away from Covid while on the ventilator not infrequently had (untreated) gram negative ventilator-associated pneumonia upon autopsy - Pseudomonas, Klebsiella, Acinetobacter. The presence of these infections was consistent with the number of days on the ventilator and remained unaddressed by some of the ICU teams. So role of VAP upon Covid remains to be defined?

- **Dr. Berg:** Agree, I think it is a clinical decision and with sick ICU patients appropriate to treat.
- **Dr. Hill:** Agree.
- **Dr. McCreary:** Agree, after ~5 days admitted likelihood of bacterial co-infection increases and these patients should be treated.

70. What is the higher dose of dexamethasone in pregnant woman?

6mg IM every 12hrs x 48 hrs. followed by up to a total of 10 days of 6mg po or IV. (Dr. Badell)

71. Any issues with a booster dose in pregnancy?

We DO recommend Booster dose in pregnancy (5 months after Pfizer/Moderna 2 months after J&J. (Dr. Badell)

72. To follow a previous question, how do you consider the use of sotrovimab in patients with mild-mod COVID who are hospitalized not due to severe COVID, but because of a complication that would (reasonably) not have occurred if the patient did not have COVID? i.e., acute coronary syndrome, AKI.?

We have fairly restrictive use protocols for scarce resources that generally align with FDA EUA, but for persons with “incidental” or “nosocomial/early” (eg vr), we recommend if able to give sotrovimab inpatient. (Dr. Werbel)

73. Can provide language to lay to rest fears of risk to fetus from COVID 19 vaccines?

https://s3.amazonaws.com/cdn.smfm.org/media/3290/Provider_Considerations_for_Engaging_in_COVID_Vaccination_Considerations_1-11-22_%28final%29_KS.pdf (Dr. Badell)

74. Asthma is a risk factor?

Mild persistent asthma has not generally shaken out as a risk factor for severe COVID-19. persons with severe asthma or other lung disease, yes. there is equipoise about whether inhaled corticosteroids at baseline help mitigate COVID severity (given there is some evidence for its use as an outpatient therapy, but a little mixed). (Dr. Werbel)

75. Can any of the monoclonals be given off label to high-risk pediatric patients who are <40 kg or younger than 12 years?

They are under EUA; no off-label use. (Attendee)

76. Why can't the 13yo get paxlovid?

Age 12 and older allowed per EUA, as long as 40kg. (Dr. McCreary)

77. Do HIV patients on antiretrovirals do better?

Patients with well controlled HIV and adequate CD4 response respond to vaccination (<https://www.medrxiv.org/content/10.1101/2021.06.28.21259576v1>). (Dr. McCreary)

78. How soon after recovering from mild to moderate COVID-19 can a severely immunosuppressed individual receive Evusheld?

Here's the language we tell patients:

If you have recently had a COVID-19 infection, you can receive Evusheld 20 or more days after you were diagnosed and are fully recovered.

So that we can plan for infection prevention measures at our clinic, we will ask you to have a PCR test for COVID-19 on day 20 or more after you were diagnosed, and then another PCR test 7 days later. If both are negative, you can come to the clinic wearing a mask. If you are fully recovered but one or both of the PCR tests are positive, or you are completely asymptomatic and unable to get PCR testing, we will talk with you about what additional infection prevention measures we may need to use to keep you and all safe.

Discuss with your provider about the best time to receive Evusheld. (Dr. McCreary)

79. Do you have to wait to give Evusheld 3 months after Mab? Regen? Sotrovimab? Does it make a difference in answer?

We don't have a wait time between treatment mAb and Evusheld; they just have to have been fully recovered from COVID-19 and out of precautions per those guidelines (at least 20 days). (Dr. McCreary)

80. We just spent 45 minutes in cancer/transplant and 5 minutes in pregnancy and 5 minutes in children. Are our priorities correct (patient-wise and society-wise); should the Society (IDSA) advocate for a different approach or are we OK with priorities? Please, poll the audience!

Ya, seemed that way. but i think that these cancer/ICH have the toughest situations b/c they have the most drug options, being Tier 1/2. that's where the scarcity/prioritization balance falls and the toughest decisions. From my lens anyway

81. Lung transplant vs rituximab recipient? Who gets evusheld first priority of these 2?

This is a difficult clinical scenario, I think just receiving anti-CD20 dose pose one at risk for severe covid19 but are they also a cancer patient with lymphopenia?

82. Would you consider Evusheld for a 68yr old breast CA Female, currently on 2 med chemo (herceptin&kadzela) recently completed 6 wks. RadTx and 6sessions of 4 med CTx with typ2DM, obesity, CKD3?

HEr2 targeted therapy typically doesn't cause as much immunosuppression as other chemotherapies thus I would recommend this patient to get a full series of COVID vaccinations and one can use Evusheld if she were exposed etc. per EUA approval. Vaccines take priority. (Dr. Berg)

83. Since pregnancy not in NIH prioritization tiers or MASS score, how are others prioritizing them with limited therapeutics?

Tier 1 for us

84. Am puzzled by recommendation to give ritonavir twice in the HIV patient. The pills in Paxlovid are separate, so the ritonavir could be omitted. Is the concern they might leave out the wrong pills?

Indeed, I believe the concern is too many pills, too much room for confusion, and nirmatrelvir might not end up getting appropriately boosted, and the harm of 300mg of ritonavir a day is well characterized and not large for 5 days of use. Also, it is already complex as the nirmatrelvir is co-packaged (two 150mg pills of nirmatrelvir and one 100 mg pill of ritonavir, twice a day) rather than co-formulated. Easier just to say: take what's in the package and also take your HIV meds as prescribed. You are correct, however, that their usual ritonavir would be adequate technically to boost the nirmatrelvir. (Dr. Weld)

85. Any contraindication between paxlovid and sotrovimab?

No, they could be given together in theory, we just don't currently for reasons described (Paxlovid EUA subgroup and scarcity of resources)

86. How long is Evusheld effective?

PROVENT looks at 6 months; to be determined in the real world and with Omicron

87. For patients already on monthly IVIG, how much anti-SARSCOV2 antibodies do you think they are already getting?

That's a really interesting question and unsure if this has been examined in any studies monitoring antibody response etc.

Not much data, but probably not enough to be relevant. Also, very little if any data that IVIG reduces risk for majority of viral infections.

88. Is anyone using Sotrovimab IM now?

Not yet-- pending full data set and EUA updates (if they approve). We only have press release at this point and know that they've submitted for EUA update.

Not yet but anticipate transitioning rapidly once EUA is updated considering findings from COMET-TAIL.