CDC/IDSA COVID-19 Clinician Call:

COVID-19 Treatment Updates

September 11, 2021

Q&A

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1. **Please discuss the risk/benefits ratio of the use of anti-SARS-CoV-2, particularly in Monoclonal antibody field centers.**

   The products are very safe. Increasingly people are giving them at home settings. (Dr. Shoham)

2. **We up to date info. - not just what is established. We are one step BEHIND the patients!**

   This has been a problem since the beginning. Challenge of offering evidence-based therapy in a rapidly evolving situation (Dr. Shoham)

3. **Update on mu variant and when HCWs vaccinated early will be up for third vaccine dose?**

   Thank you for your question. We will keep it on file and address it during our next vaccine-focused call. (Dr. Wollins)

4. **Can you please comment on use of monoclonal antibodies in children below 12 yrs of age? Are there any ongoing pediatric studies for monoclonals in less than 12 yrs of age?**

   We have some nice parent handouts on www.healthychildren.org about masks and are working on one which addresses this issue more directly. In short, we are not seeing this, especially if the adults keep a positive attitude. (Dr. Edwards)

5. **Hoping to hear any news on the 9/17 FDA mtg to review data for booster vaccine doses- will both Pfizer and Moderna data be reviewed?**

   It is my understanding that the meeting will focus on Pfizer booster data. This should be a very informative meeting and one that individuals can watch real time via live stream. This meeting should provide data to make decisions about boosters. (Dr. Edwards)

6. **Use of COVID Mab in hospitalized patients admitted for other reasons Like Ileus or social reasons?**

   FDA Emergency Use Authorization recommends mAb's in such situations providing the patient meets criteria for having received it were they outpatients. (Dr. Shoham)

7. **Calling Ivermectin a deworming medicine for livestock, is not representative of the use of Ivermectin, nor of the fact that it is helpful in many specific human infections e.g., onchocerciasis. While I agree that the data is NOT supportive of the use of ivermectin for SARS-CoV-2 infection, shouldn't the presentation of the use of ivermectin have been more honest?**

   It is incumbent upon us as physician scientists to be as accurate as we can in our communication. The temptation to make dramatic statements, even if the goal is positive, should be avoided. We gain trust in drops and lose it in buckets. (Dr. Shoham)

8. **Could you please discuss what is the current situation with encephalitis / ADEM cases in pediatrics? We are seeing these patients quite frequently here in Florida and treatment appears to be not be well defined. Could you please provide some insight?**

   Are you asking about encephalitis and ADEM after COVID? I am aware that this has been reported but was not aware that it appeared to be more common in an outbreak in Florida. (Dr. Edwards)

9. **The NNT with mAbs are you asking about encephalitis and ADEM after COVID? I am aware that this has been reported but was not aware that it appeared to be more common in an outbreak in Florida. To truly impact volume of hospitalizations is relatively unfavorable, ie during a surge the resources needed to administer mAbs at scale is unavailable due to the acute care needs. This has severely impacted the applicability of mAbs in this pandemic situation. Please comment with suggestions to how to overcome this paradox.**

   Patient selection is key. Biggest impact in people at high risk for complications of COVID-19. (Dr. Shoham)

10. **When can we expect manufacture of these antibody cocktails to meet the current need? Most are in very short supply.**

    At many places in the US, problem is not supply of product, but infrastructure and human resources to administer them. (Dr. Shoham)

11. **Can you comment on data from recovery trial showing mortality benefit among inpatients given mAb who didn't have spike antibody? Has there been discussion on authorizing mAb for subgroups of inpatients?**

    This is being covered in the presentation by Dr Gandhi. (Dr. Shoham)

12. **Are other mAbs suggested in case of lack of availability to these mAbs?**

    Currently, only the 3 anti SARS CoV-2 mAbs that I mentioned are authorized in the US. (Dr. Gandhi)

13. **For individuals administered monoclonal antibody therapy (either as treatment for COVID-19, or post-exposure prophylaxis), the subsequent required delay in vaccination after the treatment poses a challenge for vaccination - what are your thoughts on this?**

    As you say, the current recommendation is to wait 90 days from time of mAb administration to vaccination because of concern that the mAbs may interfere with vaccine induced immune responses. For people who have had Covid (and received mAbs for treatment), they are at low risk for reinfection for at least 3 months so I think the current recommendation is reasonable but happy to discuss. (Dr. Shoham)

14. **Are Monoclonal Antibodies available outside the US?**

    Increasingly yes. Examples are some EU countries and Israel who are utilizing this. (Dr. Shoham)

15. **I am surprised that only 7.8% of household contacts acquired COVID. (The placebo group) What is the usual % of household contacts that get COVID?**

    There is a broad range of attack rates, between 5-25%. Of note, the study I mentioned was done in the pre-delta era. (Dr. Gandhi)

16. **Would mAb be justified in immune suppressed patients hospitalized with CPVID-19?**

    Depends. If hospitalized for non-COVID-19 condition- then generally yes. If hospitalized for COVID-19 this could be done as part of an investigational IND (usually single patient). At my institution we have had some B cell impaired patients that were persistently infected for weeks to months and mAb was effective in stemming infection (given with remdesivir). (Dr. Shoham)

17. **What are the practical aspects of subcutaneous casi/imdev that we should know? Need 4 injections of 2.5ml per injection site - Please speak to local reactions, pain, sequelae, etc.**

    Local reactions were reported but generally appeared to be mild and well tolerated. No frequent complaints of pain or long term sequelae. (Dr. Edwards)

18. **Can you share the data re: what is the max time after PEP that casirivimab/imdevimab is still effective (there is no within X time after exposure provided in the EUA); in trial was received within 96h of + in the index case?**

    Excellent question. As you say, the EUA doesn't specify. The clinical trial enrolled household contacts within 96 hours of exposure. The NIH guidelines suggest using with 7 days of exposure. (Dr. Gandhi)

19. **Why does authorization of mAb in inpatients rely on development of a rapid serology test—and how rapid is necessary? Is one being developed? This would be a game changer among our immunocompromised patients.**

    the study under the RECOVERY platform in UK, showed efficacy with inpatient mAb only for that group. Those that were already + had no impact. Please note, dose of Regeneron product was much higher than what we use in US (8 grams). (Dr. Shoham)

20. **Does respiratory conditions include asthma?**

    I think people with asthma who have COVID should be treated with mAb early on in course. (Dr. Shoham)

21. **Public Health England has sent a negative anti-spike antibody test as an essential criteria for dual mab therapy in high risk individuals with h/o exposure. Is the same criteria used in US?**

    Not formally. (Dr. Shoham)

22. **Any insight on safety of vaccination after MIS-C or MIS-A?**

    At this time patients who have fully recovered from MISC and MISA and are 90 days post administration of IVIG can receive COVID vaccine. We have been recommending it in unimmunized patients. (Dr. Edwards)

23. **Is there written guidelines available to address the safe administration of mRNA vaccines interchangeability for 3rd dosing? Lack thereof is resulting in refusals and hesitancy.**

    At the current time the recommendations are that you receive the same vaccine for the primary vaccination, unless there are situations where there has been a severe allergic reaction to one vaccine, then another type can be recommended. The data on interchangeability of the primary series has been published from the UK. Data are currently being compiled from a study in the US.

    Data on the use of the boosters in the non-immunocompromised will be outlined once they are approved by the FDA. More information will be coming in the weeks ahead. (Dr. Edwards)

24. **Should asplenia be considered as one of the high risk conditions for monoclonal ab therapy?**

    I would consider it a high risk condition. (Dr. Shoham)

25. **'@Dr Shoham, please discuss risk/benefits of use of anti-SARS-CoV-2 compared to vaccination. Specific data we can use to increase % of the population vaccinated.**

    They are different products for different indications. Vaccination is for pre-exposure prophylaxis. It will prevent infection from happening in the first place. mAb is for post exposure prophylaxis or for early treatment. Risks of waiting until one gets an infection is that they may get "long covid", might pass it on to others and may not get to therapy (or post exposure prophylaxis) in a timely manner. One does not substitute for the other. (Dr. Shoham)

26. **Are there any in-vitro data on mAbs against the mu variant"?**

    I was look for such data last night but didn't find any. The data I've seen with Mu are decreased susceptibility to convalescent plasma and to vaccine induced antibodies. (Dr. Gandhi)

27. **Any benefit of giving monoclonals beyond the approved 10 days after symptom onset?**

    Generally, in immunocompetent people, probably no benefit this far out. (Dr. Shoham)

28. **I am referring to the NNT when the high risk criteria in the EUA are being used. Are you suggesting further refining patient selection criteria rather than using the EUA?**

    Depends on availability of resources. If there is a good supply of product and people to give it, I would make threshold to give it as low as feasible. (Dr. Shoham)

29. **Is melatonin being studied?**

    It is/has been studied. Still preliminary. (Dr. Shoham)

30. **Can we use Prozac instead of fluvoxamine? In our hospital it is non formulary and not available.**

    The drugs are not the same and are actually from slightly different classes. Not sure that they are interchangeable for this use. (Dr. Shoham)

31. **Why fluvoxamine need a week to work?**

    It is available as a generic medication so cost should be manageable. (Dr. Shoham)

32. **Is there a weight limit for monoclonal in kids?**

    The children must be > 12 years of age and weigh > 40 kg according to the EUA. (Dr. Edwards)

33. **Can the sub cutaneous dose be given with no post injection observation?**

    No, the EUA still calls for post-injection observation after sc.

34. **Where does splenectomy fit in MAB treatment and 3 dose of vaccine?**

    I would give mAb to someone with splenectomy and infection even if thrice vaccinated.

35. **But do we need to vaccinate those who have had COVID?**

    We do recommend that people who have had COVID get vaccinated. The immune response after COVID infection is variable and generally does not equal the immune response to a primary series of vaccination with COVID vaccine. Reinfection is more common in people who have had covid infection than in those who have been fully immunized.

36. **If the data for fluvoxamine appears positive (way more evidence than ivermectin!), how has it not made it's way into more treatment guidelines? because ID docs don't do anti-depressants?**

    Fluvoxamine is showing promising data. It is out of the comfort zone of many physicians who do not typically prescribe such medications. (Dr. Shoham)

37. **Please elaborate if fluvoxamine helps with hypoxia in hospitalized patients or if more studies needed?**

    The work has been done in the outpatient space. (Dr. Shoham)

38. **When will we get an EUA for fluvoxamine? Not everybody at high risk agrees to mABs….**

    Please note that fluvoxamine is an FDA approved medication for other indications. In the US, a clinician can prescribe it off label, with all the usual provisos about off label medication prescribing. (Dr. Shoham)

39. **Any anticipated timeline or update on oral antivirals/therapeutics?**

    Several promising drugs in trials -- I hope we'll have more data this year. I agree this is a very high priority. (Dr. Shoham)

40. **Is there any supporting information in RCTs for the use of other mAbs, esp., tocilizumab and anti-TNF in COVID-19?**

    There are RCTs on tocilizumab that the IDSA and NIH guidelines summarize. (Dr. Shoham)

41. **Has fluvoxamine been used in adolescents?**

    It is commonly used in adolescents for psychiatric indications. (Dr. Shoham)

42. **What is the current breakdown of who is vaccinated by race/ethnicity?**

    The CDC website provides this breakdown as well as the breakdown regarding the states and regions. It is a great website and very user friendly.

43. **Unvaccinated patients seem to end up hospitalized. Shouldn't even those who may not be considered high risk but are unvaccinated be prioritized for monoclonal antibody therapy?**

    Too many variables to generalized. An unvaccinated 23 year old triathlete may not have much benefit from mAb, whereas a thrice vaccinated person with B cell dysfunction due to CLL may really need it. (Dr. Shoham)

44. Should a pregnant woman who was fully vaccinated just prior to getting pregnant receive a third shot of mRNA vaccine?

The data and recommendations on the timing of booster doses will be forthcoming with the FDA meeting this Friday and the ACIP recommendations after the FDA approval. These should be coming very soon. At this time, I cannot comment on what the recommendations will be. (Dr. Edwards)

45. Is Latinx ethnicity and/or non-white race alone (without other risk factors) an indications for MAbs for adults and/or children?

The EUAs include these as potential indications.

46. What is the data that subQ is effective in treatment rather than prophylaxis?

For PEP, study was done with sc injections. For treatment, there are supportive PK and virologic data but more limited clinical outcomes data. that being said, sc is reasonable if iv will introduce delays in treating. (Dr. Gandhi)

47. I thought subcutaneous administration of monoclonal antibodies was only authorized for PEP, not treatment. Is that incorrect?

Authorized for treatment providing there is a barrier to getting it by IV. (Dr. Shoham)

48. We had patient with monoclonal ab infusion that had hypoxia and mild anaphylaxis with iv monoclonal. Is the risk for anaphylaxis same with subcutaneous?

If the patient had anaphylaxis, I'd be worried about using subcutaneous antibody.

49. SQ is it equally efficacious?

For treatment FDA recommends IV as preferential, but if cannot get someone IV in an expeditious manner- SQ is recommended. (Dr. Shoham)

50. Any actual data on subcutaneous injections?

For PEP, study was done with sc injections. For treatment, there are supportive PK and virologic data but more limited clinical outcomes data. that being said, sc is reasonable if iv will introduce delays in treating. (Dr. Gandhi)

51. Fluvoxamine is the most poten SSRI with respect to sigma-1 receptor agonism.

Yes. I believe that is why the investigators went after it as a possible therapeutic. Really amazing work on their part. (Dr. Shoham)