CDC/IDSA COVID-19 Clinician Call

January 30

Monoclonal Antibodies Update Q&A

Below are the written responses provided by panel members during the call. This is the Q&A transcript from the Zoom webinar, formatted and edited for spelling and grammar only. There are an additional two questions at the end of this document that were answered via email by the presenters following the 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.

Monoclonal Antibodies

1. **What are the criteria for monoclonal antibody therapy? High viral load and belong to a risk group - Prevention?**

   For treatment, the EUA criteria are high risk outpatients (criteria in the EUA) who have mild to moderate COVID-19 within 10 days of symptom onset. In the trials, the median duration of symptoms was about 3-4 days.

2. **Early use of monoclonal antibodies - pulmonary infiltrate + low oxygen therapy, less than 5 days of disease?**

   Earlier is essential. I know of no data after pneumonia is present. As Raj said, Regeneron is still studying this question.

3. **Isn't the monoclonal antibody indicated first 5-7 days of symptoms, so it is difficult if you are following patients? What is the latest you can give it?**

   The indication allows a long window (10 days), and the ACTV-2 trials are using that. For prevention we used 4 days after exposure. EARLIER IS BETTER. Reduce VL in nose as quickly as possible in high-risk people.

4. **How long does the effect of monoclonal antibody therapy last?**

   The half-life of several of the antibodies we discuss is about 3-4 weeks. Some other antibodies have even longer half-lives.

5. **Do these monoclonal antibodies have any immunomodulatory effects (outside of neutralizing COVID-19)?**

   No except some may help with T cell immunity. But they DO NOT have the side effects of the anti-cancer, skin, and rheumatology monoclonal antibodies so widely advertised on TV.

6. **Our obstetricians want to use the monoclonals for pregnant women who have no other indications. We have not allowed this. Is this correct?**

   I do not believe pregnant women are excluded. See EUA.

7. **Do you have information about monoclonal antibodies in the pediatric population?**

   Regeneron is enrolling children in some of their studies. No data yet.

8. **Your thoughts about use of the monoclonal antibodies in pediatric patients ages 12-18? Is there interest in collecting blood samples from patients who had COVID, received monoclonal antibodies and the vaccine?**

This issue is being studied.

9. **Are monoclonal antibodies being studied in post-transplant or immunocompromised patients? Any contraindication to use them in this patient population?**

   Studies planned. No contraindication.

10. **What do we know about efficacy of monoclonal antibodies with variant strains?**

    We have a great deal of "test tube" results and no clinical data. Some combinations remain robust.

11. **Will the antibodies be effective against the resistant or mutant strains?**

    Yes, but new monoclonal antibody cocktails may be required.

12. **Getting questions about efficacy of monoclonal antibodies in the B117 and the South African or other variants.**

    Data on the effect of variants on the antibodies we discussed is still coming out. So far, it appears that he B.1.351 variant has a greater effect on several of the antibodies than the B.117. More data to come.

13. **Can you share the links to some of these test tube results on monoclonal antibodies against B117 and B135?**

    Study published in Science by Starr et al on 25 Jan. Biorxiv preprint by Wang/Liu/Luo (senior author David Ho).

14. **Any data on efficacy of monoclonal antibodies against the South African and Brazilian strains?**

    Yes. See publication of Wang and Ho in bioarchives.

15. **Can patients who have received the monoclonal antibodies receive the vaccine? Do they have to wait a certain time period after receiving the antibody infusion?**

    Currently 90 days is recommended but this is being studied and may differ among products.

16. **Can patients who have had the COVID-19 vaccine receive monoclonal antibody therapy?**

    For now, would decide on a case-by-case basis depending on the person's risk.

    Yes. But if you think vaccine will be sufficient to prevent morbidity and mortality the monoclonal antibody is superfluous. But there is no contraindication EXCEPT you may compromise vaccine response, a question we ARE studying.

17. **If patient gets first dose of Moderna then later in week tests positive for COVID-19 and is able to get Bamlanivimab should they get their follow-up Moderna dose in 2 weeks to complete series or wait the full 90 days as is recommended after monoclonal antibody therapy.**

    For now, I would wait at least 90 days between Bamlanivimab and the next vaccine dose (because of concern about antibodies affecting vaccine induced immune responses). This is an area of active investigation so may change in the future.

18. **Is there any data on patients who have been vaccinated? Should they get monoclonal antibodies?**

    This is a research question. But I would treat a sick patient.

19. **My patient had COVID after first dose of vaccine hospitalized and received convalescent plasma. Recommendation regarding timing of second dose of vaccine?**

CDC recommends waiting for at least 90 days between mAb or CCP and 2nd dose of vaccine. Studies of this issue are ongoing.

20. **Sounds like there is little role for convalescent plasma.**

    This is an ongoing discussion. Certainly, only titered plasma should be used, but we don't know the minimal beneficial neutralizing titer. Early use of high titered plasma is best, like mAb.

21. **Why is there discrepancy in the recommendations? While a person can receive the SARS-Cov-2 vaccine after one month of being infected with the virus, he or she has to wait for three months from receiving monoclonal antibody treatment.**

    Two different issues.

22. **Given vaccination roll-out in high-risk facilities, what is the likely benefit of monoclonal antibodies in those vaccinated?**

    We have no firm idea how well vaccines will work across the aged population. Vaccination is of course preferred. Monoclonal antibodies are a safety valve.

23. **How realistic is to get infusion monoclonal antibodies for treatment or prevention to those who need it? How? Timing matters.**

    Agree with you. Would be helpful to have easier delivery systems (e.g., SC) or more rapid infusions in terms of the logistics. And I think it's likely that the antibodies will have their largest effect when used early.

24. **What are costs for monoclonal antibodies?**

    The US government bought them. There may be an administration charge but currently NO drug cost under EUA.

    Currently free as Lily and Regeneron donated supplies. Infusion charges apply, though. Free except for administration cost currently.

25. **Monoclonal antibody infusion has serious equity issues at present because of logistic of infusion, limited sites where this can be done and referral process to these centers.**

    I completely agree with you -- and we need to keep this front of mind and make sure we address it as we move forward.

26. **The dose of Bamlanivimab in BLAZE-2 was 2400 mg. Will this be the dose for the prophylaxis EUA?**

    Good question. Not sure exactly what Lilly will request.

27. **How is the Vir antibody different from the Lilly antibody?**

    They are directed at different parts of the RBD.

28. **Do you think monoclonals will continue to have a role for PEP/treatment for antibody-deficient people in the future (like VZIG, etc.)?**

    Yes.

29. **Are there other pharma companies making SARS-CoV-2 monoclonal antibodies that I can approach for an IND? I have a patient with essentially no immune system who has lingering COVID since November 2020. He received 5 days of Remdesivir and then again 10 days of Remdesivir + Decadron. Both times he did well. Now he is on high flow oxygen with worsening cycle threshold and CT Chest. He has not developed a**

SARS-cov-2 antibody response at days 65 post symptom onset. He would benefit from something with a high neutralizing potential. He does not fit the criteria for Regeneron or Eli Lily monoclonal antibodies.

https://www.regeneron.com/sites/default/files/Regeneron-Compassionate-Use-Request.pdf

Compassionate Use requests will be considered for the following individuals who test positive for SARS-cov-2: - Patient-facing healthcare workers, including individuals who may not be at high risk for poor outcomes or otherwise do not meet the current EUA criteria - Individuals at high risk for poor outcomes who do not meet the conditions for treatment under the EUA. Email: compassionateuse_Requests@regeneron.com

This would be directed to compassionate use for Lilly or Regeneron. This question has come up in people with malignancy treatment. Go to company website for info.

COVID-19 Vaccines

1. **If you had COVID, and you are going to be vaccinated, do you need two doses or one shot only?**

   You can find information addressing this question on the COVID Real-Time Learning Network's Frequently Asked Questions page: https://www.idsociety.org/covid-19-real-time-learning-network/vaccines/vaccines-information--faq/

2. **How would you advise a patient who had Covid19 six months ago, recovered, received the 1st vaccine 3 weeks ago and is again symptomatic and COVID-19 positive? Should she receive the second dose on schedule?**

   You can find information addressing this question on the COVID Real-Time Learning Network's Frequently Asked Questions page: https://www.idsociety.org/covid-19-real-time-learning-network/vaccines/vaccines-information--faq/.

3. **Hearing the possibility of NSAIDS and aspirin decreasing the effectiveness of the vaccine if you take it before your dose?**

   Our local ID expert is recommending avoiding NSAIDS before and after vaccine due to concerns about decreasing B cell response to vaccine.

   You can find information addressing this question on the COVID Real-Time Learning Network's Frequently Asked Questions page: https://www.idsociety.org/covid-19-real-time-learning-network/vaccines/vaccines-information--faq/

4. **Can patients with COVID on IVIG supplementation take the mRNA vaccines?**

   There is some guidance on the CDC's Interim Clinical Considerations page:

   “For persons receiving antibody therapies not specific to COVID-19 treatment (e.g., intravenous immunoglobulin, RhoGAM), administration of mRNA COVID-19 vaccines either simultaneously with or at any interval before or after receipt of an antibody-containing product is unlikely to substantially impair development of a protective antibody response. Thus, there is no recommended minimum interval between other antibody therapies (i.e., those that are not specific to COVID-19 treatment) and mRNA COVID-19 vaccination. I hope that helps."

5. **Post vaccination, do you think recommendations for quarantine after close contact exposure will be changing?**

We are trying to study this question.

6. **Is there a role for post vaccination antibody measurement to assess response, at least in high-risk population e.g., HCW?**

   Currently CDC does not recommend post vaccine serology. If serology is done, important to do test that detects antibodies against spike protein (some serologic tests detect antibodies against nucleocapsid).

7. **Is there contraindication to COVID-19 vaccine, if there was shellfish allergy?**

   You can find information addressing this question on the COVID Real-Time Learning Network's Frequently Asked Questions page: https://www.idsociety.org/covid-19-real-time-learning-network/vaccines/vaccines-information--faq/.

8. **If the Ab are checked after vaccination what means being negative? No protection?**

   It's not currently recommended to check antibody after vaccination to assess protection (unlike for hepatitis B vaccine).

9. **The vaccines don't protect asymptomatic infection?**

   This is not known.

10. **Is there a way to explain increased transmissibility [of SARS-CoV-2 variants], and therefore what to do about it, to the general population: redefining close contact as a larger distance or shorter time?**

    Increased transmissibility has been argued to represent VL in nose and affinity of the variant for the ACE 2 receptor but there could be MORE explanation.