CDC/IDSA COVID-19 Clinician Call

COVID-19 Treatment Updates: Focus on Monoclonal Antibodies and Tocilizumab – Plus Extended Time for COVID-19 Vaccine Q&A

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1. **What are your thoughts on using tocilizumab in patients who are already immunosuppressed (such as solid organ transplant recipients)?**

   The cohort studies to date looking at this haven't yielded a clear answer; Pereira et al. reported a study demonstrating no clear benefit or harm, while some of the studies looking at the kidney transplant subpopulation have been more variable. It looks like it may be reasonable to consider, but given the already immune suppressed state, may be less likely to yield benefits to as many of these patients.

2. **Can IL6 level help in deciding the use of toci?**

   It can help to identify the clinical phenotype of a patient in the inflammatory phase. However, CRP is the only such marker where the trials give clearer cutoffs on how to use them (>75 mg/dL). It can have a role as a particular metric in context for the clinical pictures.

3. **What are the panel's thoughts on 'off label' use of mAb infusions in those with underlying conditions but who don't technically reach 'high risk' criteria (e.g., BMI 30-35, Pre-DM, Age 64, etc.)?**

   We established the high-risk definition in the EUA based on the most persuasive clinical trial I/E criteria. FDA may revisit as additional positive trials are reviewed.

4. **Any role for/likely benefits for use of monoclonal antibodies in moderate to severe COVID (actually admitted for COVID) if severely immunocompromised?**

   Maybe, but that's not covered by the EUA. It's plausible based on the convalescent plasma experience with immune compromised patients, and that remains an option for admitted patients who are immune compromised- but data on specific monoclonal formulations in this setting is lacking.

5. **Corporate Internal Debate ongoing: Do we now order etesevimab and add to BAM, or just give BAM. We have only native strain and b.117 in Michigan, not others.**

   Some sites have been able to order etesevimab to give with bamlanivimab. This is a rapidly evolving area. At Mass General, we are giving the combination if we have it available.

6. **How do monoclonals work in post exp prophylaxis?**

There are data emerging on monoclonals for prevention in long term care facilities and in house-hold contacts. These data have not yet been published (some data have been presented) but are eagerly awaited.

7. **So, FDA allows under EUA to give Bam or RGN to pts admitted for reasons unrelated to COVID?**

   Yes, if they meet the other EUA criteria. This issue is addressed in the FAQ documents that accompany the EUAs.

8. **Are monoclonal antibodies indicated for fully vaccinated (post 2 weeks of completing the 2 doses) individuals who are symptomatic and are at high risk of disease progression?**

   Benefit unknown, but that would fall within the authorized use as the Fact Sheets currently read.

9. **In case mAb not available would you use instead convalescent plasma?**

   Right now, these are really available in non-overlapping populations (per EUA). Monoclonals are for outpatients, CP is for inpatients (ignoring ongoing studies, compassionate use cases, and some other site-specific nuance). CP probably has the most benefit given early in the course, and a patient who may have missed the window for mAb and got admitted would likely benefit from CP, but it's not a 1:1 substitution.

10. **@Dr Farley, can you provide some details about the nature of the REGEN-CoV that result in a much better response to variants than the other monoclonals?**

    Likely related to difference in sites within the RBD for each of the mAbs.

11. **Wasn't Bamlaminivab recommended to not be used alone by CDPH?**

    The most recent guidance on this from CDPH I'm familiar with says "both bamlanivimab as monotherapy and casirivimab/imdevimab are readily available from CDPH. Contact your county's Medical and Health Operational Area Coordinator (MHOAC) to request either of these products from CDPH."

    It's very plausible that state and local public health guidance will change with variant monitoring, however, and this is subject to change.

12. **Can the reduced susceptibility to the monoclonal antibodies in the variants be overcome by increased dose? Is there any data?**

    No data that I am aware of. For the pseudo virus models with very high reduced susceptibility, it is unlikely that increasing the dose would be sufficient to overcome.

13. **There is confusing role of MAB in LTC. Do patients need to be symptomatic or is there EUA for asymptomatic infected patients?**

    All patients in the clinical trials had at least mild symptoms.

14. **Besides worsening hypoxia along with rising or high CRP, ferritin as indicators, if IL-6 levels are available with same day turnaround time, should they be used in addition.**

    Agreed; this is about coming up with a phenotype to stratify the patient's overall picture. It would be nice to hang our hats on a specific lab value, but the current evidence isn't really strong enough to do that.

15. **Do you recommend given tocilizumab alone without steroids? I see some practitioners believe in it.**

    The data supports using tocilizumab in people who are receiving steroids. In RECOVERY, there did not appear to be a benefit in people who were not on steroids.

16. **And procalcitonin to rule out infection?**

    Procalcitonin's role is unclear here. Pulmonary inflammation from a variety of sources can cause this to be elevated, and I would not rely on it as a rule in or rule out for co-infections with ARDS patients.

17. **Can you please comment on any theoretical risk of vaccine and mAbs antagonist or no difference anticipated? And for the timing of second dose, is there no need to wait?**

    For mRNA vaccines, if someone diagnosed with COVID after 1st dose, CDC recommends waiting at least 90 days before giving 2nd dose.

18. **Toci single vs second doses?**

    No great answer here; I can say my own practice is to give one dose, wait 24 hours, and if patient is the same or improved, give a second dose, but that's my own practice and I can't say that there's good guidance on when to give a second dose right now.

19. **Can mAb be used in pregnancy?**

    We have negative fetal tissue cross-reactivity studies for each, but no interpretable data on pregnant women in clinical trials. Risk benefit individual decision at this point.

20. **Can someone comment on sickle cell patients with COVID19 and use monoclonal AB data if any? Thanks.**

    Sickle cell disease is included as a high-risk condition for ages 12-17 years in the EUA criteria.

21. **Please send the slide with the references; that was just barely flashes.**

    We will show that again. I also sent links in chat and will be posted https://www.idsociety.org/cliniciancalls.

22. **Is there any reason to check antibody to spike protein in an immunocompromised patient following vaccination to see if they produced an antibody response? If so, how do you act on the info?**

    Last time I checked, the CDC did not recommend checking serology after receiving vaccine as the clinical implications are not yet known.