CDC/IDSA COVID-19 Clinician Call

February 6, 2021

COVID-19 Treatment Updates & More Vaccine Q&A

Q&A Transcript

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Treatment

1. **Role of plasma in treatment? If it is still treatment option; can you give plasma from vaccine recipients?**

   I believe we will re-address this with high-titer plasma soon. Give it soon, and high titer. Vaccine recipients should generate some nice antibodies.

2. **Do monoclonal antibodies prevent for going on to more serious disease in all groups?**

   The press release data which is not in pre-print or peer reviewed publications looks promising in reducing mortality and severe disease which we did not see in the published pilot studies, but I think the key is using it early mild disease. The data from a trial in hospitalized patients showed futility so was stopped early. Hope the press release data is peer reviewed and published soon for us to critically appraise.

3. **Should we be monitoring cytokine serum levels and viral loads to guide therapy? - Dave Gilbert**

   We wish biomarkers like viral loads (exact quantitative titers than using CT's across platforms) and inflammatory phenotypes as part of inclusion criteria in trials and as response markers and surrogate markers to clinically meaningful outcomes. They have been done in Hepatitis C trials and HIV trials, but we haven't seen standardization and use of that in COVID-19 trials. With the limited data we have, viral loads have not translated into clinical outcomes, but there are several limitations in the studies that precludes any conclusions on their utility.

4. **Is there a dose response with tocilizumab? Remap-cap used higher doses up to 800 mg.**

   That has been the dose limit in many studies. Repeat doses have been used in many of them if response isn't seen. I don't know anything about dose-response besides that.

5. **Please address new data of value of Monoclonal antibodies on persons infected with variants that include the E484K mutation (e.g., South Africa, Brazil, and most recently some versions of the UK variant).**

   To the best of my knowledge, we don't have clinical studies to answer this question, especially if these mutations have meaningful clinical impact despite in vitro studies. There should be clinical data on that soon.

6. **Given the Convalescent plasma might not have uniformly high titer, is there a link between convalescent plasm and development of various SARS-COV2 variants?**

   I don't think there is any data. Plasma harvested from patients infected with those variants could be useful in treating or preventing them.

7. **Any thought on using mAb for prophylaxis including PEP?**

   There is data coming for this. A press release came out from Regeneron showing efficacy in household contacts. Even better, it was given SubQ!

8. **We have seen in-vitro data before hydroxychloroquine.**

Indeed. I'm cautious about all of the in-vitro data on its own, especially when the PK doesn't look favorable.

9. **Can ivermectin be used for post exposure prophylaxis? What is the optimal treatment dose regimen?**

   There are no good RCT's for prophylaxis, but studies going on, which we should wait for before routine use.

10. **Colchicine for treatment of COVID-19?**

    I want to see this publication. The preprint showed a large NNT of about 71. Also, I'm wary of treating for 30 days.

11. **When will expect potential specific guidance on using Tocilizumab? It seems to me there is more evidence based on REMAP-CAP. More potential benefit than Baricitinib which got FDA EUA.**

    NIH just updated, and we have discussed also. It is a really tough one IMO, probably the toughest of the agents.

    Baricitinib had one well-designed study with no other data (that I'm aware of) to contradict it. The study was larger than any of the toci ones.

    The question to me is if REMAP-CAP is proof or an outlier. I can't argue with someone wanting to treat patients similar to those in the study. Toci may be useful for preventing progression to mechanical vents.

12. **When does IDSA plan to do a proper randomized controlled trial with ivermectin? It looks better than Remdesivir which is currently licensed, based on some of the same outcomes as ivermectin.**

    Do agree Remdesivir has a modest clinical effect but no mortality benefit at best, but ACCT-1 is a well-designed placebo controlled well blinded RCT. Ivermectin studies are small and highly methodologically limited as we have presented and don't think we have the same amount of certainty.

13. **How does your idea of biologic time differ from ordinal scale?**

    I have to give Adarsh credit for his idea. But we need something to tell us where the patient is in his/her course instead of relying on clinical interventions by clinicians, or on chronological time. It could be as simple as viral load (though that doesn't seem so useful), or another biomarker. I'd like to see rapid serology to judge of mAbs or plasma would be useful.

    The ordinal scales are based on clinical response (going on supplemental O2 without a measure of hypoxemia) or being in a hospital or discharge. Also, time of admission to the hospital and transfer to the ICU are very subjective depend on the patient, provider, institution surge capacity and other non-biologic variables. Biologic time measurement should be based on symptom onset and clinical deterioration onset with clearly defined parameters. It is not easy and has some subjectivity, but defining it and standardizing them across studies will make it more useful than the way we are using composite outcomes or movement on existing ordinal scales.

14. **Any data to use Remdesivir in CKD or HD pt.?**

    There are some small case series that have been published. My personal approach is to give it if indicated, since the cyclodextrin is the same one as in IV voriconazole. Also, the duration of treatment is short.

15. **What is the role of Bamlanivimab?**

    Personally, I'm coming around from being a skeptic to a believer. It is probably not the winner of the 3 agents (bam + etes, cas + imdev) but still useful. Health systems are figuring it out - we need to spread successful models.

    Many other mAbs in the pipeline.

16. **Do you think giving steroids in the outpatient setting (not on oxygen) could be increasing the risk of viral variants by increasing duration of viral shedding?**

    I think that is quite possible. The Recovery trial suggested possible harm in patients not on O2, and this is my concern as for the reason.

It also makes me wonder if the Remdesivir + steroid combo frequently used in the hospital is particularly good one - could see steroids prolonging shedding and Remdesivir addressing that. Just my personal thought though.

17. **Any evidence regarding colchicine in preventing progression and or treatment of covid-19**

    Please see other answer. COLCORONA is available as a preprint.

    Warning- “My Sharona” may get stuck in your head when you read it.

18. **Given possible autoantibodies/autoimmune related to pathophysiology of COVID-19 or MIS-A, would there be any role for IVIG or other treatment in adults as in MIS-C?**

    Great question and makes pathophysiologic sense, but I am not aware of any data on this. Also, given the rarity of MIS-A we probably have to rely on observational or registry studies than RCT's.

Vaccines

19. **Can you speak on pre-medication prior to COVID vaccine? Does taking Acetaminophen or NSAID prior to taking the vaccine interfere with the effectiveness of the vaccine?**

    There is some evidence (mostly from the pediatric literature) that prophylactic use can blunt the immunogenicity of vaccines. However, it is unclear how clinically significant this is. There was a study published recently in mice that demonstrates that this may be of concern with the mRNA vaccines, but we do not have any data. Therefore, CDC does not recommend prophylactic use of NSAIDS or acetaminophen before mRNA vaccination. As an aside, there is some data for the AstraZeneca/Oxford vaccines that shows no difference in people with prophylactic use; the UK guidelines permit use of these medications before AZ vaccination.

20. **Is there new information on the vaccines in patients with organ transplants and other immunocompromised conditions?**

    We do not have safety or efficacy data on transplant or other immunocompromised patients. Persons with stable HIV were included in the clinical trials, but no data have been reported yet in this group. CDC recommends that immunocompromised persons can receive COVID-19 vaccines.

21. **Have any deaths been noted r/t to the vaccines? Thank you!**

    Deaths after vaccination are required to be reported to VAERS. CDC and FDA review all deaths reported after vaccination. Findings were presented recently at the January ACIP meeting: https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2021-01/06-COVID-Shimabukuro.pdf.

    The conclusions so far are that there are no concerning safety signals related to deaths have been identified.

22. **Could you comment on rate of severe reaction (e.g., anaphylaxis) after 1st vs 2nd dose? Rate seems really low and wonder if it changes with 2nd dose...**

    The most recent rates are reported in the safety update presented at the January ACIP meeting: https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2021-01/06-COVID-Shimabukuro.pdf

    Most of the reactions so far have occurred after the 1st dose. However, this may be related to the fact that there has been more time for people to get the 1st dose vs. the 2nd dose. This will continue to be followed closely."

23. **I did not hear the answer to my question regarding post-vaccination quarantining and travel recommendations. Can you please answer in writing?**

    We'll make sure to get to the question about post-vaccination quarantining.

24. **How do physicians recommend nonprofits work with clients who are fearful of receiving the vaccine?**

CDC has a toolkit related to strengthening vaccine confidence that has a lot of good resources: https://www.cdc.gov/vaccines/covid-19/health-systems-communication-toolkit.html

These tools can be adapted to various settings, including nonprofits.

25. **Any recs regarding if we need to wait a certain time period after giving mAb before vaccinating the individual?**

    CDC has given recommendations for this - to wait 90 days. I think the time period is just a guestimate, but since you're giving them to people with COVID-19 and the antibodies have a long half-life themselves, there is some logic.

26. **Can persons who receive the COVID-19 vaccine donate convalescent plasma?**

    FDA is developing guidance around this issue. I do not see that it has been posted, I will follow-up on it and if there is anything to share, I will send it to the IDSA organizers for dissemination.

27. **Have there been any reports of severe side effects from the COVID Vaccine?**

    The most recent update of safety data was presented at the January 27 ACIP meeting: https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2021-01/06-COVID-Shimabukuro.pdf.

    Anaphylaxis has been reported, though is rare. There have been no unexpected safety signals identified so far. Robust post-authorization safety monitoring will continue to be conducted.

28. **Several patients who received Moderna vaccine have developed hard lumps surrounded by large circular areas of swelling and redness. With administration of OTC antihistamines (Zyrtec, Benadryl) and topical hydrocortisone cream, the swelling and redness was reduced and dissipated. However, after 8 days following vaccine administration the redness and swelling re-emerged. How typical are these reactions to the Moderna vaccine? What are the recommendations to help this reaction subside? Should a patient with such a reaction take Benadryl before the administration of the 2nd dose of the Moderna vaccine?**

    Delayed, local injection-site reactions have been reported following vaccination. These do not appear uncommon, though we don't have an exact rate of how often they are reported. It is not known whether persons who experienced a delayed-onset injection site reaction after the first dose will experience a similar reaction after the second dose. However, these delayed-onset local reactions are not felt to represent a risk for anaphylaxis upon receipt of the second dose. Thus, individuals with such delayed injection site reactions after the first mRNA COVID-19 vaccine dose should receive the second dose using the same vaccine product as the first dose and at the recommended interval, and preferably in the opposite arm. We do not recommend Benadryl pre-treatment prior to vaccination.

29. **When do you expect vaccines to be available for children?**

    Pfizer's clinical trial in adolescents is fully enrolled, and trials are planned for early 2021 in younger children. Thus, vaccination for children is on the horizon but not immediately. Here is the link for a recent update on pediatric vaccination trials: https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2021-01/04-COVID-Erbelding.pdf

30. **Should aspirin or Plavix be held temporarily prior to taking vaccine**

    Plavix should not matter- it is not an NSAID. Just my opinion, but I wouldn't hold ASA for someone using it for a cardiovascular indication based on an unproven concern on vaccine efficacy.

31. **If you get the vaccine, both doses, and then get COVID-19 infection within a week of getting the 2nd dose should you get one of the monoclonal antibodies?**

    I think that question won't be in a trial and doesn't have a straightforward answer. Personally, I'd treat someone at high risk. I've been asked this about patients after the 1st dose a few times.