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AAMC Discusses Monoclonal Antibody Therapeutics for SARS-CoV-2 Infection

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On Friday evening, January 15, 2021, Drs David Skorton, President of the Association of American Medical Colleges (AAMC), Anthony Fauci, the National Institute of Allergy and Infectious Diseases Director, and Francis Collins, the National Institutes of Health Director, convened a live conference call entitled "A Discussion of COVID Therapeutics and Other Matters" to provide an update to the AAMC Leadership Team and AAMC constituent leaders on the latest in coronavirus disease 2019 (COVID) therapeutics and related matters. The discussion opened with Dr Collins summarizing data on the use of anti–severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) monoclonal antibodies produced by Eli Lilly and Regeneron, published in the *New England Journal of Medicine* in October 2020[1] and distributed for human use under US Food and Drug Administration Emergency Use Authorization. Dr Collins reported the modest effects that were reported. The percentage of patients who had a COVID-19–related hospitalization or visit to an emergency department was 1.6% in the antibody group and 6.3% in the placebo group. Dr Collins speculated that further subanalysis of additional covariates/risk factors may reveal risk populations for whom these therapeutics have a more pronounced efficacy. The "push" to the academic medical community is justified by the recent spike of new SARS-CoV-2 infections, overcrowding our emergency rooms and our intensive care units. Both monoclonal therapeutics (casirivimab and imdevimab cocktail, bamlanivimab) have been purchased in bulk by the US government, were distributed under the US government initiative Operation Warp Speed, and can be easily reordered by contacting aspr.mcop@hhs.gov or Dr John T. Redd directly. There is no charge for the therapeutics themselves since they have already been paid for by the US taxpayers; infusion is reimbursed at the Centers for Medicare and Medicaid Services (CMS.gov) rate of $310. So why are these potentially lifesaving therapeutics underutilized? Both therapeutics require reconstitution by an intravenous pharmacy and a 1-hour infusion at an intravenous infusion facility.

The audience, composed of leaders from academic medical institutions and academic societies, provided insightful comments and suggestions but not all were addressed by the discussants:

1. The goal is to decrease hospitalization of patients with COVID-19 by preemptive treatment with monoclonal antibodies. The impact of the infusions may vary depending on the patient population.
2. The data are "lukewarm" at best, and further analysis is needed, including subsetting SARS-CoV-2–positive patients based on body mass index, age, and other known risk factors.
3. The effective titers of these therapeutic monoclonal antibodies need to be determined.
4. These agents should be administered to patients in high-risk groups early in the infection, when viral load is low and patients may be asymptomatic. This approach requires expanded SARS-CoV-2 testing.
5. The Food and Drug Administration's Emergency Use Authorization criteria for use are too restrictive; the access should be expanded to patients with risk factors such as high body mass index but ≥40 years of age.
6. Federally qualified health centers and other sites such as Med Express could be included and converted into infusion centers with minimal infrastructure changes, making use of innovations

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such as elastomeric intravenous pumps. These pumps are designed for in-home infusions, do not require specialized training, and can deliver therapeutics over a 30- to 90-minutes period. The YouTube instructional video (https://www.youtube.com/watch?v = plP-fU3cqCU) demonstrates the ease of use.

7. The efficacy of each monoclonal antibody to recognize and neutralize developing strains must be determined, especially given that Centers for Disease Control and Prevention modeling suggesting that the highly contagious SARS-CoV-2 B.1.1.7 lineage is emerging as a dominant strain in the United States. This approach would presumably favor antibody cocktails over single monoclonal antibodies.
8. A dedicated investment in developing antivirals is needed.
9. A program that provides monoclonal antibody infusions in combination with remdesivir/antiviral therapy needs to be established.
10. Data should be collected to determine whether vaccinated individuals can be infected asymptomatically, and if so, whether they contribute to viral spread or are less likely to transmit the virus due to lower viral load, and to determine at what point fully vaccinated individuals associating together can consider eliminating mask use.
11. The development, commercialization, and distribution of other COVID-19 vaccines based on more conventional vaccine platforms should be supported, but the more mRNA vaccines are used, the more difficult it will be to conduct clinical trials of other technologies. Since placebo-controlled trials would be unethical, would new trials measure vaccine equivalency, as suggested in this teleconference by Dr. Fauci? Federal regulatory review of alternative vaccines should be expedited, since vaccine availability will be critical to generating herd immunity in the US population.
12. Do we need a vaccine mandate to achieve herd immunity?
13. Is the mRNA vaccine platform the only vaccine platform capable of rapid adjustments for SARS-CoV-2 mutants, or are more conventual vaccine platforms such as killed virus as nimble?

Because a transcription of this discussion will not be openly available for a while, it is of paramount importance that we, the ACCP membership, immediately engage in a discussion of these critical pharmacotherapeutic issues. Discussion can be initiated by contacting Dr John Redd, the chief medical officer for the Office of the Assistant Secretary for Preparedness and Response within Health and Human Services.

Reference

1. Chen P, Nirula A, Heller B, et al. SARS-CoV-2 neutralizing antibody LY-CoV555 in outpatients with Covid-19. *N Engl J Med*. 2020;384:229-237.