MARAC Advisory Statement About Monoclonal Antibodies Against SARS-CoV-2

Executive Summary for Health Care Providers and Health Policy Makers
MARAC recommends that people with sickle cell disease should have access to monoclonal antibody (mAbs) treatment according to established guidelines, to prevent mild COVID from progressing to severe disease.

Criteria for treatment in sickle cell disease (SCD) are stated in the Emergency Use Authorizations (EUA) and NIH guidelines: COVID symptoms but not hospitalized due to COVID or requiring oxygen therapy due to COVID, 12y and older, body weight at least 40 kg, and direct SARS-CoV-2 viral test positive (PCR test or antigen test). Optimal timing is soon after COVID diagnosis, not waiting until patients get sicker.

- MARAC notes that SCD patients with baseline hypoxia might be treated if they are simply at baseline.
- MARAC suggests that patients treated for pain in a SCD day hospital or infusion unit are eligible for mAbs as outpatients.
- Decisions to treat with mAbs are individualized.

Information for patients:
When a person's immune system is not prepared with antibodies to attack the invading virus, monoclonal antibodies (mAbs) are laboratory-produced molecules that serve as substitute antibodies. The mAbs are designed to block viral attachment and entry into human cells, thus neutralizing the virus. Studies of people at high risk for severe COVID disease progression showed that the groups that received mAbs had less hospitalizations and emergency room visits compared to the groups that did not get mAbs. Single or pairs of mAbs are administered together, given as one-time infusion into a vein or in the skin.

- Consult with your doctor or healthcare team about whether your personal medical condition causes an exception to this general recommendation.
- Do not relax your precautions right after receiving mAbs. You might still get infected in the few weeks after infusion. You could still transmit infection to those around you. Continue to wear a mask covering your nose and mouth. Wash your hands often. Maintain physical distance. Avoid crowds and people who are ill.

Q: What mAbs are available?
A: Two mAbs treatments are available as of 8-31-2021:
- Casirivimab and Imdevimab (Regeneron) given together
- Sotrovimab (Glaxo Smith Kline / Vir)
Each showed an estimated 70% reduction in hospitalization for COVID-19. Not needing hospitalization means the people recovered from COVID at home and did not die.

Q. Are there side effects (adverse events) of mAbs?
A. There is a potential for serious hypersensitivity reactions, including a life-threatening pattern called anaphylaxis, with administration of mAbs. If a clinically significant hypersensitivity reaction or anaphylaxis occurs, the medical team will stop the infusion and give appropriate medications and/or supportive care.

Other side effects have been reported with observed infusion of these mAbs. If these infusion-related reactions occur, the medical team will also consider slowing or stopping the infusion and giving appropriate medications and/or supportive care.
Signs and symptoms of infusion-related reactions to Casirivimab and Imdevimab may include:
• fever, chills, nausea, headache, tight airway (bronchospasm), low blood pressure (hypotension), allergic swelling (angioedema), throat irritation, rash including hives (urticaria), itch (pruritus), muscle aches (myalgia), or dizziness.

Signs and symptoms of infusion-related reactions to Sotrovimab may include:
• fever; difficulty breathing; low oxygen level in your blood; chills; tiredness; fast or slow heart rate; chest discomfort or pain; weakness; confusion; nausea; headache; shortness of breath; low or high blood pressure; wheezing; swelling of your lips, face, or throat; rash including hives; itching; muscle aches; dizziness; feeling faint; and sweating.

Signs and symptoms of infusion-related reactions to Bamlanivimab and Etesevimab may include:
• fever, difficulty breathing, low oxygen (reduced oxygen saturation), chills, fatigue, abnormal heart rhythm (e.g., atrial fibrillation, sinus tachycardia, bradycardia), chest pain or discomfort, weakness, altered mental status, nausea, headache, bronchospasm, hypotension, hypertension, allergic swelling (angioedema), throat irritation, rash including hives (urticaria), itch (pruritus), muscle aches (myalgia), dizziness and abnormal sweating (diaphoresis).

These are not all the possible side effects of mAbs, as not a lot of people have received mAbs treatments. Serious and unexpected side effects may happen. mAbs are still being studied, so it is possible that all the risks are not known at this time.

Q. What are the differences between the three monoclonal antibody preparations?
A. • Regeneron’s Casirivimab and Imdevimab and GSK’s Sotrovimab report effectiveness against the current variants. (Aug. 2021)
• Regeneron is more widely available and lower cost.
• Lilly’s Bamlanivimab and Etesevimab were effective against the original type of coronavirus but seem to be less effective against current variants. Distribution of Lilly’s mAbs is only in regions without those resistant variants (8/27/2021).
• The clinical research showed similar side effects (noted in the previous section).
• Infectious disease specialists will choose according to local conditions of variant types and availability of mAbs.

Q. When and where should mAbs treatment be given?
A. MAbs treatment should be given as soon as possible after testing shows COVID, and definitely within 10 days. This time sensitivity means that people usually do not have time to ‘shop around’ for other treatments. MAbs treatment should be given in an outpatient infusion center. The mAbs are infused into a vein over a few hours or can be given as a shot in the skin (subcutaneous). The medical team then watches the individual for up to an hour to see whether any side effects need to be treated.

Q. Are any of the mAbs better for an individual with sickle cell disease?
A. We do not know. Several members of MARAC have used mAbs for individuals with COVID and saw side effects and response just like those reported for people without SCD. No individuals with SCD were reported in the clinical research studies that led to approval of the mAbs.

Q. Are some people ineligible to get mAbs?
A. Eligibility criteria to receive mAbs are defined by the EUA. There is no known contraindication to receive the mAbs so long as they meet the eligibility criteria.
Q. Can I be vaccinated for COVID-19 after mAbs treatment for COVID-19?
A. As of 8-24-2021, the advice is to postpone COVID-19 vaccination for at least 90 days after treatment with mAbs for COVID-19. This is a precaution to avoid interference of mAbs with vaccine-induced immune responses. Updates to this recommendation may be made as additional information on the interaction between prior monoclonal antibody treatment and vaccine response becomes available.

Q. What are treatment alternatives to mAbs against COVID?
A. In the early phase, no alternatives to mAbs treatment have been shown to be helpful in this early phase soon after the diagnosis of COVID.
A. If COVID symptoms get worse and require hospitalization, several treatments might be used in the hospital: Remdesivir, convalescent plasma, Baricitinib, or dexamethasone. https://combatcovid.hhs.gov/i-have-covid-19-now/available-covid-19-treatment-options. However, the risks of death or permanent complications increase when a person has moderate or severe COVID-19 illness that requires hospitalization.

REFERENCES

Centers for Disease Control: Are you at higher risk for severe illness?
www.youtube.com/watch?v=qb7shu_sdQ0

General Resources

• HHS: Monoclonal Antibodies for High-Risk COVID-19 Positive Patients
  General information on monoclonal antibody treatments and other COVID-19 treatment options.
  https://combatcovid.hhs.gov/sites/default/files/documents/Administering-mAbs-072021.pdf
• COVID-19 Medication options https://www.health.state.mn.us/diseases/coronavirus/meds.html#mab
  accessed 8/31/2021
• In some regions, all three mAbs are authorized for emergency use in certain patients with COVID-19. In regions where more of the coronavirus is resistant (like the Delta variant), the Lilly combination is not used.

Regeneron - Casirivimab and Imdevimab
• Regeneron: Casirivimab and Imdevimab EUA Guidebook (PDF)
  Product information for providers and infusion sites.
• Regeneron: Authorized for FDA Emergency Use only Casirivimab and Imdevimab
• COVID-19: A treatment option. https://regeneronmax.widen.net/s/jbxqvn9b9c/20210614_pa_c_011

GSK Vir – Sotrovimab
• GSK Sotrovimab EUA for the Treatment of COVID-19 https://www.sotrovimab.com/

Eli Lilly - Bamlanivimab (BAM) and Etesevimab (ETE)
• Eli Lilly: Bamlanivimab and etesevimab for COVID-19
• https://www.covid19.lilly.com/bam-ete/hcp
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