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
www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/index.html

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. https://www.phe.gov/emergency/events/COVID19/investigation-MCM/Bamlanivimab-etesevimab/Pages/resumption-in-distribution-bamlanivimabetesevimab.aspx

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

SCDAA Medical and Research Advisory Committee Members

Miguel R. Abboud, MD
Professor of Pediatrics and Pediatric Hematology-Oncology
Chairman
Department of Pediatrics and Adolescent Medicine
American University of Beirut, Lebanon

Biree Andemariam, MD
Vice Chair, Sickle Cell Disease Association of America
Director, New England Sickle Cell Institute
Associate Professor of Medicine
University of Connecticut Health
Farmington, Connecticut

Shawn Bediako, PhD
Professor
Department of Psychology
University of Maryland Baltimore County
Baltimore, Maryland

Andrew Campbell, MD
Center for Cancer and Blood Disorders
Children's National Health System
Associate Professor of Pediatrics
George Washington University School of Medicine and Health Sciences
Washington, DC

Raffaella Colombatti, MD, PhD
Physician Azienda Ospedaliera-Università di Padova
Department of Womens' and Child Health
Clinic of Pediatric Hematology Oncology
Via Giustiniani 3 35129
Padova Italy

Lori Crosby, PsyD
Co-Director, Innovations in Community Research, Division of Behavioral Medicine & Clinical Psychology
Co-Director, CCTST, Community Engagement Core
Psychologist, Research, Behavioral Medicine & Clinical Psychologist
Cincinnati Children's
Professor, UC Department of Pediatrics
Cincinnati, Ohio

Deepika Darbari, MD
Center for Cancer and Blood Disorders
Children's National Health System
Professor of Pediatrics
George Washington University School of Medicine and Health Sciences
Washington, DC

Payal Desai, MD
Associate Professor
Director of Sickle Cell Research
The Ohio State University
JamesCare at Ohio State East Hospital
Columbus, Ohio

Edward Donnell Ivy, MD, MPH
Vice Chief Medical Officer, Sickle Cell Disease Assocation of America
Director of Community Outreach and Education
The Possibilities Clinic
Toronto, Ontario

James Eckman, MD
Professor Emeritus, Hematology & Medical Oncology
Emory University School of Medicine
Department of Hematology and Medical Oncology
Atlanta, Georgia

Mark Gladwin, MD
Professor and Chair
Department of Medicine
Founder, Pittsburgh Heart, Lung, and Blood Vascular Medicine Institute
University of Pittsburgh
Pittsburgh, Pennsylvania

Jo Howard, MB Bchir, MRCP, FRCPath
Head of Red Cell/Sickle Cell Service
Guy's and St Thomas' NHS Foundation Trust
London, United Kingdom

continued on next page

Lewis Hsu, MD, PhD
Co-Chair, Medical and Research Advisory Committee, Sickle Cell Disease Association of America
Chief Medical Officer, Sickle Cell Disease Association of America
Director of Pediatric Sickle Cell
Professor of Pediatric Hematology-Oncology
University of Illinois at Chicago
Chicago, Illinois

Baba Inusa
Professor of Paediatric Haematology
Lead Consultant Paediatric Sickle Cell and Thalassaemia
Evelina London Children's Hospital
Guy's and St Thomas' NHS Foundation Trust
Women and Children's Academic Health
Faculty of Life Sciences and Medicine
King's College
London, United Kingdom

Elizabeth Klings, MD
Associate Professor of Medicine
Director, Center for Excellence in Sickle Cell Disease
Director, Pulmonary Hypertension Center
Boston University School of Medicine
Boston, Massachusetts

Lakshmanan Krishnamurti, MD
Professor of Pediatrics
Director of Bone Marrow Transplant
Joseph Kuechenmeister Aflac Field Force Chair
Aflac Cancer and Blood Disorders Center
Children's Healthcare of Atlanta/Emory University
Atlanta, Georgia

Sophie Lanzkron, MD
Director, Sickle Cell Center for Adults
The Johns Hopkins Hospital
Baltimore, Maryland

Julie Makani, FRCP, PhD
Associate Professor
Department of Haematology and Blood Transfusion
Muhimbili University of Health and Allied Sciences
Dar es Salaam, Tanzania

Caterina P. Minniti, MD
Director, Sickle Cell Center Montefiore Health System
Professor, Departments of Medicine and Pediatrics
Albert Einstein College of Medicine
Bronx, New York

Genice T. Nelson, DNP, APRN, ANP-BC
Program Director, New England Sickle Cell Institute & Connecticut Bleeding Disorders Programs,
UConn Health, Farmington, Connecticut
Board Member, Sickle Cell Disease Association of America

Isaac Odame, MB ChB, MRCP(UK), FRCPath, FRCPCH, FRCPC
Professor, Department of Paediatrics
University of Toronto
The Hospital for Sick Children Division of Haematology/Oncology
Toronto, Ontario

Kwaku Ohene-Frempong, MD
Director Emeritus, Comprehensive Sickle Cell Center
Emeritus Professor of Pediatrics, University of Pennsylvania
President, Sickle Cell Foundation of Ghana
Emeritus Board Member, Sickle Cell Disease Association of America

Gwendolyn Poles, DO
Former Medical Director, Kline Health Center
Faculty, Internal Medicine Program
UPMC Pinnacle
Harrisburg, Pennsylvania
Board Member, Sickle Cell Disease Association of America

John D. Roberts, MD
Yale Adult Sickle Cell Program
Smilow Cancer Hospital at Yale New Haven
New Haven, Connecticut

Wally Smith, MD
Professor
Scientific Director, VCU Center on Health Disparities
Director, VCU Adult Sickle Cell Program
Department of Internal Medicine Division of General Internal Medicine
Virginia Commonwealth University
Richmond, Virginia

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