MARAC Statement: Temporary Suspension of Clinical Trials

March 1, 2021 - The Sickle Cell Disease Association of America’s Medical and Research Advisory Committee (MARAC) is aware of the announcement on February 16, regarding the temporary suspension of bluebird bio clinical trials of LentiGlobin Gene Therapy for Sickle Cell Disease and the pause of all commercial use of bluebird bio European gene therapy.

Additionally, on February 22, the National Heart, Lung, and Blood Institute (NHLBI) temporarily suspended their unrelated gene therapy trial—Pilot and Feasibility Study of Hematopoietic Stem Cell Gene Transfer for Sickle Cell Disease at Boston Children’s Hospital. The NHLBI stated that this temporary suspension was, “out of an abundance of caution” despite having no indications of harm.

On February 23, another gene therapy trial, Gene Transfer for Patients with Sickle Cell Disease, was also paused by the sponsor Aruvant.

MARAC has investigated the situation and met with bluebird bio to discuss the information available to the public. In the bluebird bio study, two patients developed blood cancer, and a third patient is under investigation for a related problem called myelodysplastic syndrome. The details of these patients are being examined by their doctors and the bluebird bio sponsors. Investigations are trying to determine whether the blood cancer can be linked to the gene therapy vector, the chemotherapy preparation for gene therapy, or damage of the host stem cell. No events occurred in the other clinical trials.

We value patient trust and patient concerns. SCDAA tries to express the voice of people living with sickle cell disease (SCD), and MARAC supports this mission with biomedical expertise. MARAC is monitoring developments and will continue to communicate findings to the SCD community. Nearly all the members of MARAC are involved in research to help those with SCD, and some who participated in developing this advisory statement are gene therapy investigators. The MARAC members with a potential conflict of interest due to their involvement in gene therapy clinical trials are listed on the following page.

MARAC acknowledges that there has been a history of clinical investigations that were unethical, including the infamous Tuskegee syphilis study, but this past week’s events highlight that clinical research is no longer in that era. The modern safeguards for clinical research are working. Preplanned “stopping rules” triggered a “pause” of enrollment by bluebird bio when unusual and concerning events occurred. The Data Safety and Monitoring Board for the NHLBI gene therapy study followed “out of an abundance of caution,” as did the Aruvant study. There were public announcements, and an intensive investigation is now underway to gather more information. The participants in the studies are being notified and are receiving appropriate medical care from the investigators.

Clinical research has been and continues to be the path for progress to improved SCD survival and quality of life. MARAC celebrates the decades of clinical research studies on which the progress in sickle cell care that we have today has been built — including penicillin, hydroxyurea, stroke screening and new medications.
SCDAA honors the SCD warriors who volunteer in clinical research. They have given their time so that others may benefit from new future treatments and cures. We pay tribute to all of those who have been lost to SCD, and we know many have died too young.

Disclosures:

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<thead>
<tr>
<th>Gene therapy study sponsor</th>
<th>Investigators</th>
<th>Other roles</th>
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<tr>
<td>bluebird bio</td>
<td>Julie Kanter, M.D.</td>
<td>Biree Andemariam, M.D., consultant Andrew Campbell, M.D., co-investigator, 2019 advisory board Baba Inusa, funded for ASCAT conference Elizabeth Klings, M.D., consultant on pulmonary function Sophie Lanzkron, M.D., chair of adjudication committee Kim Smith-Whitley, M.D., co-investigator Ahmar Zaidi, consultant/Honoraria</td>
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<td>Aruvant</td>
<td>Biree Andemariam, M.D., consultant (past) Lewis Hsu, M.D., Data Safety Monitoring Board</td>
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<td>NHLBI</td>
<td>Julie Kanter, M.D., protocol committee for BMTCTN-2001 Marsha Treadwell, Ph.D., consultant for Data Strategy Consortium</td>
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<td>Vertex / CRISPR Therapeutics</td>
<td>Miguel R. Abboud, M.D., Data Safety Monitoring Board Biree Andemariam, M.D., consultant Kim Smith-Whitley, M.D., co-investigator</td>
<td></td>
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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

continued on next page
Raffaella Colombatti, MD, PhD
Assistant Professor
Department of Women’s and Child’s Health
University of Padova
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 Psychology
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

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

Lewis Hsu, MD, PhD
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

continued on next page
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), FRCPCH, FRCP  
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

Crawford J. Strunk MD  
Director, Sickle Cell Disease and Hemoglobinopathy Clinic  
Pediatric Hematology/Oncology Program  
ProMedica Ebeid Children’s Hospital  
Toledo, Ohio

Immacolata Tartaglione, MD PhD  
Department of Woman, Child and General and Specialist Surgery  
Università degli Studi della Campania “Luigi Vanvitelli”  
Naples, Italy

Marsha Treadwell, PhD  
Director, Sickle Cell Care Coordination Initiative  
Regional Director, Pacific Sickle Cell Regional Collaborative  
Professor of Psychiatry and Pediatrics  
University of California San Francisco Benioff Children’s Hospital Oakland  
Oakland, California

Winfred C. Wang, MD  
Emeritus, St. Jude Faculty  
Member, Department of Hematology  
St. Jude Children’s Research Hospital  
Memphis, Tennessee

Russell E. Ware, MD, PhD  
Director, Division of Hematology  
Co-Director, Cancer and Blood Diseases Institute  
Director, Global Health Center  
Marjory J. Johnson Chair of Hematology Translational Research  
Cincinnati Children’s  
Professor, UC Department of Pediatrics  
Cincinnati, Ohio

Julie Kanter Washko, MD  
Associate Professor, Division of Hematology Oncology  
Director, Adult Sickle Cell Clinic  
University of Alabama at Birmingham  
Birmingham, Alabama

Kim Smith-Whitley, MD  
Professor of Pediatrics  
Director, Comprehensive Sickle Cell Center  
Clinical Director, Division of Hematology  
The Children’s Hospital of Philadelphia  
Philadelphia, Pennsylvania  
Board Member, Sickle Cell Disease Association of America

Wanda Whitten-Shurney, MD  
CEO & Medical Director  
Sickle Cell Disease Association, Michigan Chapter Inc.  
Detroit, Michigan  
Board Member, Sickle Cell Disease Association of America

Ahmar U. Zaidi, MD  
Assistant Professor of Pediatrics  
Comprehensive Sickle Cell Center, Children’s Hospital of Michigan  
Director of Physician Network Development, University Pediatricians  
Wayne State University/Central Michigan University School of Medicine  
Detroit, Michigan