RECOVER Treating Long COVID (TLC): Navigating the Pathway Forward

Goals of the Workshop

1. High-level scientific review of clinical and mechanistic data, with strong emphasis on community input and implications for clinical trial design.
2. Highlight opportunities for clinical trials based on what is known about mechanism, symptom burden and available interventions.
3. Summarize core findings of workshop discussions and integrate into description of how this effort will move forward.

Monday, September 23, 2024 (9 a.m.–5 p.m. EDT)

Retroactive lens of Long COVID, including lived experience, provider perspective, state of the art updates, and summary of ongoing activities.

9:00 Welcome and Opening Remarks: *Drs. Monica Bertagnolli, NIH and Julie Gerberding, FNIH*

9:15 Goals of the Workshop: *Drs. Jeanne Marrazzo, NIAID and Lindsey Baden, BWH/Harvard*

- The rationale for RECOVER-TLC
- How is RECOVER-TLC part of larger Long COVID research efforts?
- How will this workshop inform next steps?

9:30 RECOVER-TLC—Proposed Organizational Structure and Function: *Dr. Joe Breen, NIAID*

10:00 Living with Long COVID, Diverse Perspectives:

- *Christine Maughan, Patient Representative*
- *Angela Meriquez Vázquez, Childrens Partnership*
- *Liza Fisher, Patient Advocate*

10:45 Break

11:00 Long COVID Definitions and Impact on Clinical Trials

- Stage setting talk (10 min): *Dr. Jerry Krishnan, University of Illinois at Chicago*
- Panel discussion:
  - *Dr. Jerry Krishnan, University of Illinois at Chicago*
  - *Karyn Bishof, COVID-19 Longhauler Advocacy Project*
  - *Dr. Sharon Saydah, CDC*
  - *Dr. Serena Spudich, Yale*
  - Moderator: *Dr. Ian Simon, DHHS/OASH*
  - Possible topics:
    - Implications for clinical trials (inclusion/exclusion criteria)
    - Implications for regulatory decisions

12:00 Lunch

12:45 Overview of Observational Studies: Implications for Clinical Trial Design

- Stage setting talk (10 min): *Dr. Leora Horwitz, NYU*
- Clinical data from the observational studies:
  - *Dr. Mike Sneller, NIAID*
  - *Dr. Ziyad Al-Aly, VA/Wash U*
- Panel discussion
  - *Dr. Leora Horwitz, NYU*
  - *Dr. Michael Sneller, NIAID*
  - *Dr. Ziyad Al-Aly, VA/Wash U*
  - *Dr. Igor J. Koralnik, M.D, Northwestern University*
  - *Dr. Melissa Stockwell, Columbia University*
  - *Dr. Helen Ward, Imperial College*
  - *Dr. Simon Pollett, DoD*
  - *Patient advocate, TBD*
  - Moderator: *Dr. Serena Spudich, Yale*

2:00 Break

2:15 Pathobiology Studies: What is Known, What Information is Needed, What are the Challenges to Providing the Basis for Future Clinical Trials

- Immune activation/alterations: *Dr. Harlan Krumholz, Yale*
- Endothelial injury, thrombosis, complement activation**:** *Dr. Resia Pretorius, Stellenbosch University*
- Viral persistence: *Dr. Michael Peluso, UCSF*
- Biorepositories and candidate biomarkers by pathway: viral, inflammatory, and immunologic: *Dr. P. J. Utz*, *Stanford*
- Panel discussion (focusing on what has been done):
  - *Dr. Harlan Krumholz, Yale*
  - *Dr. Resia Pretorius, Stellenbosch University*
  - *Dr. Michael Peluso, UCSF*
  - *Dr. P.J. Utz, Stanford*
  - *Dr. Amy Proal, PolyBio*
  - Moderator: *Dr. Joe Breen, NIAID*

3:30 What Can Be Learned from ME/CFS, POTS, MIS-C and Other Related Syndromes to Inform the Design of Long COVID Clinical Trials

- *Dr. Avindra Nath, NINDS – ME/CFS*
- *TBD, POTS*
- *Dr. Adrienne Randolph, Harvard – MIS-C*

4:00 Panel Discussion on How to Use the Information from Observational and Pathobiology Studies, and ME/CFS, POTS, MIS-C, and Other Related Syndromes to Inform the Design of Future Clinical Trials

- Panelists:
  - *Hannah Davis, Patient-Led Research Collaborative (patient perspective)*
  - *Jaime Seltzer, MEAction Network*
  - *Dr. Alba Azola, JHU (clinical provider)*
  - *Dr. W. Ian Lipkin, Columbia University*
  - *Dr. Steven Deeks, UCSF*
  - Moderator: *Dr. H. Clifford Lane, NIAID*

5:00 Adjourn for the Day

Tuesday, September 24, 2024 (9 a.m.–5 p.m. EDT)

Discuss path forward including prioritization of interventions, study design, end points, etc.

9:00 Recap of Monday Highlights: *Dr. Lindsey Baden, BWH/Harvard*

9:15 Public Comment Period: In-person and virtual participants with lived experience or provider perspectives chosen at random from pool of volunteers to speak for 3 minutes on their perspectives

9:45 Leveraging Clinical Trials Already Underway or Planned

- Overview of RECOVER clinical trials: *Dr. Kanecia Zimmerman, Duke*
- Other Long COVID trials: Landscape overview: *Dr. Upinder Singh, University of Iowa*
- Panel discussion:
  - *Dr. Kanecia Zimmerman, Duke*
  - *Dr. Upinder Singh, University of Iowa*
  - *Dr. Amy Proal, PolyBio*
  - *Dr. Harlan Krumholz, Yale*
  - Moderator: *Dr. Eldrin F. Lewis, Stanford*

11:00 Break

11:15 Selecting & Prioritizing Possible Interventions

- Current landscape: *Dr. Julia Moore Vogel, Scripps*
- NCATS/C-Path CURE ID: *Dr. Heather Stone, FDA*
- Lessons from ACTIV agent prioritization: *Dr. Timothy G. Buchman, Emory*
- *RECOVER-TLC* agent submission portal: *Dr. Stacey Adam, FNIH*
- Panel discussion:
  - *Dr. Julia Moore Vogel, Scripps*
  - *Dr. Heather Stone, FDA*
  - *Dr. Timothy G. Buchman, Emory*
  - *Dr. Stacey Adam, FNIH*
  - *Dr. Josh Fessel, NCATS*
  - Moderator: *Dr. Sarah Read, NIAID*

12:30 Lunch

1:15 RECOVER-TLC Trial Design Challenges

<u>Populations</u>

- Stage setting talk: *Dr. Sally Hodder, West Virginia University*
- Panel discussion on need and populations disproportionately impacted by Long COVID, including rural areas:
  - *Angela Meriquez Vázquez, Children's Partnership*
  - *Dr. Sharon Saydah, CDC*
  - *Dr. Helen Ward, Imperial College*
  - Moderator: *Dr. Sally Hodder, West Virginia University*

2:00 Study Designs

- Stage setting talk: *Dr. Priscilla Hsue, UCLA*
- Panel discussion:
  - *Dr. Priscilla Hsue, UCLA*
  - *Dr. Christopher McAleer, AIM Immunotech*
  - *Dr. Thomas F. Patterson, UT San Antonio*
  - *JD Davids, Long COVID Justice*
  - *Dr. Lawrence Fine, NHLBI*
  - Moderator: *Dr. Dean Follmann, NIAID*
  - Possible topics:
    - Proof of concept vs large pivotal
    - Innovative trial designs, including remote trials, decentralized clinical trials
    - Trials focus – narrow, few symptom clusters, broad
    - Severity of Illness
    - Defining phenotypes/organ injury for trials

2:45 Endpoints

- Stage setting talk: *Dr. Alison K. Cohen, UCSF*
- Panel discussion:
  - *Dr. Alison K. Cohen, UCSF*
  - *Dr. Seth Lederman, Tonix*
  - *Dr. Linda Geng, Stanford*
  - *Dr. Todd Davenport, University of the Pacific*
  - Moderator: *Dr. Adrian Hernandez, Duke*
  - Possible topics:
    - What is measurable, meaningful, and will support regulatory decisions?
    - PROs vs objective
    - Timing of response by organ injury
    - Biospecimens
    - Biomarker

3:30 Break

3:45 RECOVER-TLC Trial Design Challenges (Continued)

Pediatric trials

- Stage setting speaker: *Dr. Melissa Stockwell, Columbia University*
- Panel discussion:
  - *Dr. Melissa Stockwell, Columbia University*
  - *Dr. Roberta DeBiasi, Children's National*
  - *Dr. Gail Pearson, NHLBI*
  - Moderator: *Dr. Sindhu Mohandas, Children's Hospital Los Angeles*

4:15 Recruitment Challenges

- Stage setting talk: *Dr. Kanecia Zimmermann, Duke*
- Panel discussion
  - *Dr. Kanecia Zimmermann, Duke*
  - *Dr. Jerry Krishnan, University of Illinois at Chicago*
  - *Dr. Catherine Blish, Stanford*
  - Moderator: *Dr. Sally Hodder, West Virginia University*

5:00 Adjourn

Wednesday, September 25, 2024 (9 a.m.–12 p.m. EDT)

How RECOVER-TLC plans to move forward

9:00 Recap of Tuesday Highlights Including Patient and Provider Input: *Dr. Lindsey Baden, BWH/Harvard*

9:15 Regulatory Perspectives

- FDA: *Dr. John Farley, FDA*
- EMA Perspective: *Dr. Marco Cavaleri, EMA*

9:45 Industry Perspective – *TBD*

10:00 Break

10:30 Panel Discussion on How Do We Get from Here to the Next Patient-Centered Long COVID Clinical Trials

- *Lisa McCorkell, Patient Led Research (patient perspective)*
- *Dr. Laurie Gutmann, Indiana University School of Medicine (clinical/research perspective)*
- *Dr. Clinton Wright, NINDS*
- *Dr. Yves Rosenberg, NHLBI*
- *TBD*
- Moderator: *Dr. John Beigel, NIAID*

11:30 RECOVER-TLC Next Steps and How to Proceed: *Dr. Jeanne Marrazzo, NIAID*

- Communication plans
- How clinical trials will be selected
- How to better incorporate patient input
- How to engage industry
- Target timeline (including timeline of results)

12:00 Adjourn