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Berkeley's Hub for Regulatory Science

Overview: Endpoints Working Group

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Review of Endpoints Working Group Goals and Objectives

Berkeley Public Health

Endpoints Working Group, April 2025

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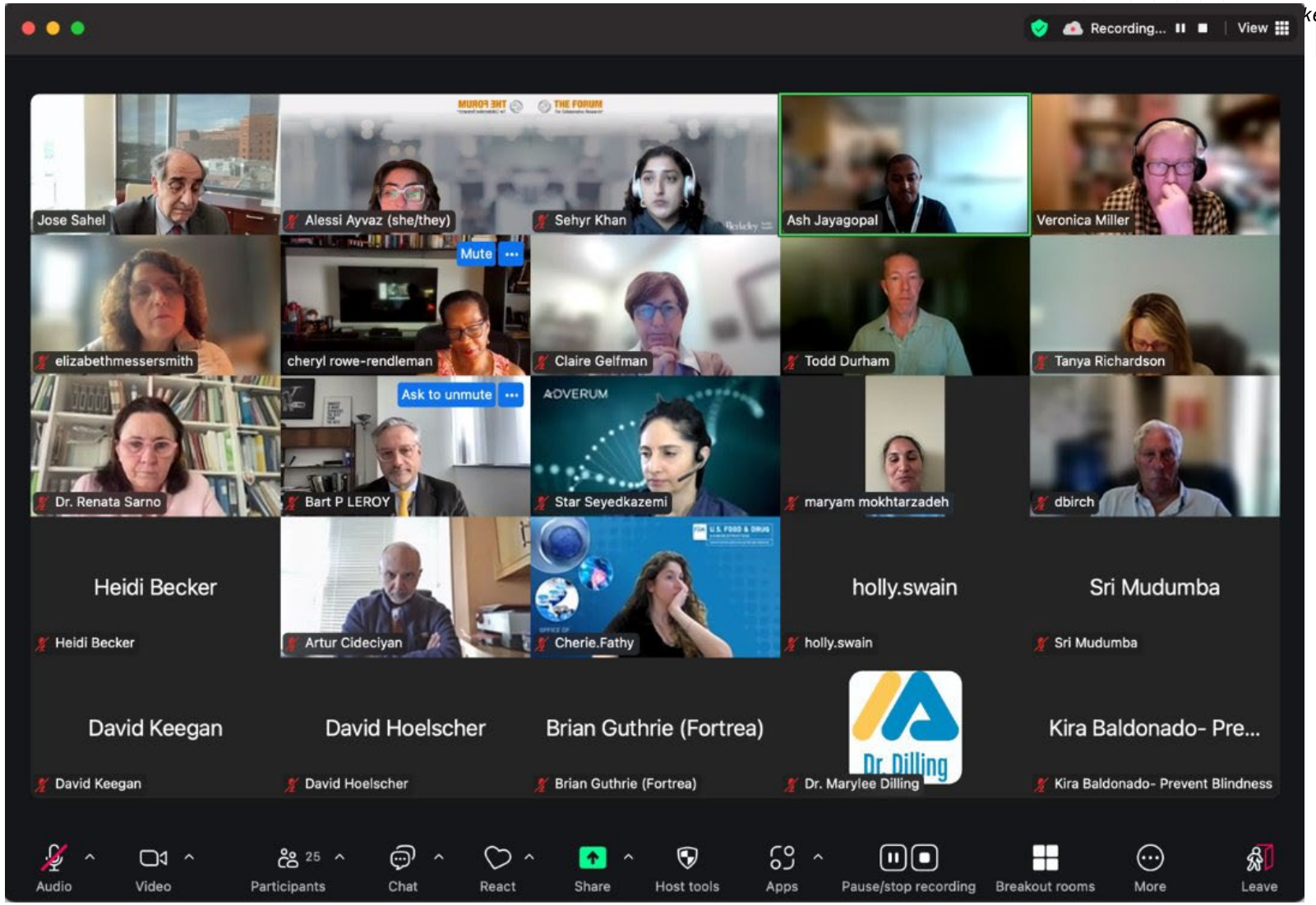

Endpoints (IRDs) Working Group

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- Led by Dr. Bart Leroy (Ghent University) and Dr. Ash Jayagopal (Opus Genetics)
- Members Include:
  - Alessi Ayvaz (Forum for Collaborative Research)
  - Allison Ayala (Jaeb Center for Health Research)
  - Artur Cideciyan (University of Pennsylvania)
  - Ash Jayagopal* (Opus Genetics)
  - Bart Leroy* (Ghent University)
  - Cherie Fathy (U.S. Food and Drug Administration, CBER)
  - Cheryl Rowe-Rendleman* (Omar Consulting Group)
  - Claire Gelfman* (Forum for Collaborative Research)
  - Daniel Chung* (SparingVision)
  - David Hoelscher (Fortrea)
  - David Keegan (Mater University/ERN-EYE)
  - Jim Wang* (Regeneron)
  - John Cavitt (Blue Gen Therapeutics Foundation)
  - Jose-Alain Sahel (UPMC Vision Institute)
  - Kali Stasi (Diorasis Therapeutics)
  - Kira Baldonado (Prevent Blindness)
  - Marylee Dilling (BCM Families Foundation)
  - Maryam Mokhtarzadeh (Regenxbio)
  - Nicholas Langevin (Boehringer Ingelheim)
  - Renata Sarno* (BCM Families Foundation)
  - Sehyr Khan (Forum for Collaborative Research)
  - Sri Mudumba (PYC Therapeutics)
  - Tanya Richardson* (Fortrea)
  - Todd Durham* (Foundation Fighting Blindness)
  - Veronica Miller (Forum for Collaborative Research)

Working Group Aims

- Review the regulatory landscape for IRD endpoints across agencies.
- Explore potential new endpoints dependent on the expected treatment outcome of a therapeutic and its mechanism of action.
  - Thus, endpoint selection for IRDs versus AMD must be disease-specific, outcome-specific, and treatment-specific.
- Explore pathways for validation of new endpoints including clinical and biomarkers

Full-field Stimulus Testing (FST)

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- FST: Assessment of whole visual field sensitivity by determining the lowest amount of perceivable light
- Emerging as a quantifiable endpoint to monitor both disease progression, as well as response to potential therapies:
  - LCA1 (Atsena)
  - LCA2 (Luxturna/Spark)
  - LCA5 (Opus)
  - LCA10 (Editas)
  - RUSH2A natural history study
- Additionally, it is predictive of results from the multi-luminescence mobility test (MLMT)

Request from ODF2

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- Define the patient population for whom FST is a suitable endpoint
- Collate the wealth of existing clinical data to propose FST testing as an acceptable endpoint in clinical trials for IRDs

Where we stand today

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- Standardization and Consensus on FST
- Role in Disease Staging and Clinical Trials
- Correlations with Other Clinical Outcomes
- FST as a Secondary or Supplementary Outcome
- Validation and Regulatory Considerations
- Collaboration and Expert Involvement

Draft Outline

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Introduction

- Rationale
- Consensus statement

Overview of FST

- FST Measures:
- FST does not measures:
- FST measurement in LCAs:
- FST limitations in LCAs:

FST as a Primary Outcome

- FST Administration in Leber Congenital Amaurosis
  - Characterization of LCAs
  - FST Administration in pediatric populations in LCA (age cutoff)
    - Ages 6-9
  - FST White in LCAs
  - Two-color DA FST in LCAs
    - B-R change
    - Thresholds of change
- FST Administration in Other Low Vision IRDs

FST anchored with other measurements

- MLMT
  - Rationale for anchoring with MLMT
  - Exploration of data analysis
- NEI-VFQ
  - Rationale for anchoring with MLMT
  - Exploration of data

FST as a Secondary Outcome

- In Retinitis Pigmentosa…
- In Other IRDs…
- **Future Directions**
- Establishing an MCID in prep.
- Looking at other endpoints

Thank You

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