Agenda

15 mins.	Session Introduction • Chairperson: Christian Lienhardt, WHO • Chairperson: Debra Hanna, CPTR
70 mins.	Critical Collaborations: Update on TB-ReFLECT • Rada Savic, UCSF
10 mins.	BREAK
45 mins.	Panel Discussion (moderator Christian Lienhardt) • Rada Savic, Payam Nahid, Dave Hermann, Patrick Phillips, Katherine Fielding, Amina Jindani
20 mins.	Closing Remarks • Debra Hanna

TB Re-analysis of Fluoroquinolone Executed Clinical Trials (TB-ReFLECT)

- CPTR and WHO Sponsorship
- Steering Committee
- UCSF executing analyses

Goal of TB-ReFLECT

Undertake a meta-analysis of the fluoroquinolones containing shorter regimen trials with the view to:

- Focus on improved understanding of the factors responsible for the variability in patients' response to treatment.
- Evaluate the endpoints of treatment outcome for:
  - Selection of new regimens to be tested in Phase III clinical trials
  - Optimization of statistical methods for comparing results between regimens
- Researchers will develop a framework linking clinically-relevant endpoints with the response of the bacteria to treatment

Benefits

- Improved understanding of the sources of variability in patients' response to treatment
- Determined predictable linkage between pathogen load dynamics and clinically-relevant endpoints in TB clinical trials.
- Improved selection of new regimens to be tested in Phase III clinical trials
- Optimized statistical methods for assessment of non-inferiority, together with the incorporation of PK/PD parameters into primary analyses

Potential Impact

- Envisioned to optimize:
  - Individualized dosing
  - Design of studies
  - Mechanistic models of pathophysiological processes

- With these tools, the TB drug development field can enter the Twenty-First Century by applying modern approaches, technology and resources.

TB-ReFLECT Collaborators

Dr. Gerry Davies (University of Liverpool)
Dr. Kathleen Eisenach (University of Arkansas for Medical Sciences)
Dr. Katherine Fielding (London School of Hygiene and Tropical Medicine)
Dr. Jan Gheuens (Bill & Melinda Gates Foundation)
Dr. Debra Hanna (Critical Path Institute)
Dr. Dave Hermann (Certara/Bill & Melinda Gates Foundation)
Lindsay Lehmann (Critical Path Institute)
Dr. Christian Lienhardt (World Health Organization)
Dr. Carl Mendel (TB Alliance)
Dr. Payam Nahid (University of California San Francisco)
Dr. Andrew Nunn (Medical Research Council, UK)
Dr. Piero Olliaro (World Health Organization)
Dr. Patrick Phillips (Medical Research Council, UK)
Dr. Klaus Romero (Critical Path Institute)
Dr. Rada Savic (University of California San Francisco)
Dr. Bob Wallis (Aurum Institute)

TB-ReFLECT Learnings & Next Steps

World Health Organization

Critical Path to TB Drug Regimens

Learnings:

- Ability to aggregate large data sets across institutions is fundamental to maximize learnings
- Consistency in data collection across trials is needed to expedite integrated learning
- These models are intended to evolve and will become even more precise with more detailed data (Chest X-ray readouts + biomarkers)

Next Steps:

- UCSF to complete analyses described
- Present on potential for impact on future trial design
- WHO and CPTR co-sponsored meeting focused on this program
- Publish the findings in high impacts journal to maximize messaging of this effort