

AMERICAN ASSOCIATION FOR
THE STUDY OF LIVER DISEASES



**Forum for
Collaborative HIV Research**

THE LIVER FORUM #2

21 APRIL 2015

VIENNA, AUSTRIA

SESSION 1: WELCOME & UPDATES

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- Acknowledgments
- Operating Principles
- Liver Forum Goals & Objectives
 - Updates since Liver Forum 1
- Objectives for Liver Forum 2

Joint Leadership



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STEERING COMMITTEE

facilitating collaborative research
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- Co-chairs
 - Gary Burgess, *Vectura*
 - Arun Sanyal, *VCU*
- FDA
 - Lara Dimick, *CDER/DGIEP*
 - Ruby Mehta, *CDER/DGIEP*
- EMA
 - Elmer Schabel, *BfArM*
- Carol Brosgart, *UCSF*
- Laurent Castera, *Hôpital Beaujon*
- Stephen Harrison, *Brooke Army Med Center*
- Markus Peck, *MedUni Wien*
- Scott Friedman, *Mount Sinai*
- Veronica Miller, *HIV Forum*
- Massimo Pinzani, *UCL*
- Detlef Schuppan, *Mainz Uni Med Center/BIDMC*
- Jeff Bornstein, *Biogen Idec*
- Eric Hughes, *BMS*
- David Shapiro, *Intercept*
- Bill Baldyga, Patient Representative
- Tracy Swan, Patient Advocate

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LIVER FORUM SPONSORS - 1

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LIVER FORUM SPONSORS - 2

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John Joseph Sninsky & Susan
Bardsley Sninsky



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FORUM STAFF

*facilitating collaborative research
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- *Rob Besaw, MPH
- *Brenda Rodriguez, MBA, MSc
- Nivedha Panneer, MPH
- Ben Hauschild, MPH
- Myrna Cozen, MPH
 - Visiting Scholar
- Students, Interns, Fellows

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LAST BUT NOT LEAST!

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- Margie and David Poole and IHL team

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LIVER FORUM OPERATING PRINCIPLES

Neutrality & Independence

Transparency & Accessibility

Inclusiveness & Collaboration

Efficiency & Productivity

NEUTRALITY & INDEPENDENCE

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- Ownership
 - Collective ownership
 - Equal voice
 - Safe space for discussion, dialogue, and deliberation
- Leadership
 - Recognized leaders from all stakeholder groups

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NEUTRALITY & INDEPENDENCE

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- Credibility
 - Recommendations based on sound ethical principles and scientific evidence
 - Let consensus evolve
 - Participation restricted to scientific experts from organizations with commitment to advancing the field
 - Not a venue for marketing, investors, journalists
 - Consensus information publicly available

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TRANSPARENCY & ACCESSIBILITY

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- Funding
 - All members invited to contribute according to ability to pay
 - Voluntary contributions
 - Seek as broad a funding base as possible
- Accountability
 - To member stakeholder groups
 - Frequent evaluation: Meeting the needs?
- Publication/dissemination

INCLUSIVENESS & COLLABORATION

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- Open to all organizations with an authentic commitment to the scientific advancement of the field
 - Value diversity
 - Expert input from all stakeholder groups
- Volunteered contributions by members
- Optimal resource utilization
- Share information as possible
- Avoid unintended duplication

EFFICIENCY & PRODUCTIVITY

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- Sustained disease specific focus
- Synchronous work process
 - “Information Democracy”
- Cross-pollination of ideas
- Standardization of research practices
- Design more efficient clinical trials
- Link silos!

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LIVER FORUM RULES

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- In-person collaborative sessions (vs meetings)
 - Closed – by invitation, guided by inclusiveness principle
 - Public dissemination only after vetting by participants
- Chatham House Rules
 - Comments are not for attribution
- Everyone brings expertise
 - Experts do not officially represent organizations or agencies
 - Comments are off-the-record
- Everyone contributes
 - No passive observers

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MANAGE ENTHUSIASM

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- Maximum 2 experts from each company for in-person meetings
- More opportunity for involvement within working groups

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THE LIVER FORUM GOALS & OBJECTIVES

THE LIVER FORUM: OVERALL GOALS

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- Independent and neutral venue
 - ongoing multi-stakeholder dialogue
 - facilitate more efficient regulatory path for diagnosis and treatment of NASH and fibrosis
- Facilitate best science-based decisions, in real time, regarding efficacy and safety
 - Break down inefficiencies
 - Increase clarity
 - Benefit to the whole field, especially the patient

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PRAGMATIC GOALS

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- Work towards acceptance of biomarkers (all diagnostic modalities) for
 - Defining disease stage
 - Diagnostic and prognostic
 - Patient selection; inclusion/exclusion criteria
 - Intervention
 - Predictive, pharmacodynamic, and endpoint surrogate markers
- Facilitate the establishment of a natural history cohort
 - Placebo arm data, other data sources

LIVER FORUM 1

NOVEMBER 2014

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- Official launch of The Liver Forum
 - Meet and get to know the players
 - Understand process and governance
- Understand regulatory perspectives
 - EMA and FDA
- Recommend initial working groups

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PROGRESS SINCE LF 1

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- Published LF1 meeting report
- Recruited new members
- Membership survey
 - elicit feedback
 - volunteers for working groups members and leadership
- Established Working Groups
 - Recruit leadership
 - Recruit working group members
 - Initiate discussions & deliberation towards first series of manuscripts
- Establish funding base
- Recruit additional staff

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LIVER FORUM 2 OBJECTIVES

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- Update on EU and US regulatory perspective/experience in this field
- Update on preliminary deliberations within working groups
 - Various stages
- Feedback on strategy/approach for working groups
- Feedback on strategies moving forward

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SESSION 2: REGULATORY PERSPECTIVES & UPDATES

Moderators: Gary Burgess, Arun Sanyal

Presenters/Discussants:

Elmer Schabel, BfArM/EMA

Lara Dimick, FDA



SESSIONS 3, 4, 5: WORKING GROUP UPDATES

WORKING GROUPS

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- Data Standardization
 - Joanne Imperial, Andrew Muir
- Definition of Disease Stages
 - Stephen Harrison and Sophie Megnien
- Pediatric Issues
 - Joel Lavine, Krishna Polu, Miriam Vos

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WHY, WHAT, AND HOW

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- Address gaps identified during Liver Forum 1
- Work towards overall goal of biomarker acceptance
- Start with small steps
 - What do we need to/can we put in place to help achieve the larger goal?
- WG's are interrelated
 - Strategic to focus on specific angle/perspective, then integrate

BIOMARKERS & ENDPOINTS (CHRIS LEPTAK, LF 1)

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Disease focused

- Natural history
- Absence of intervention
- Diagnostic
- Prognostic

Response to Intervention

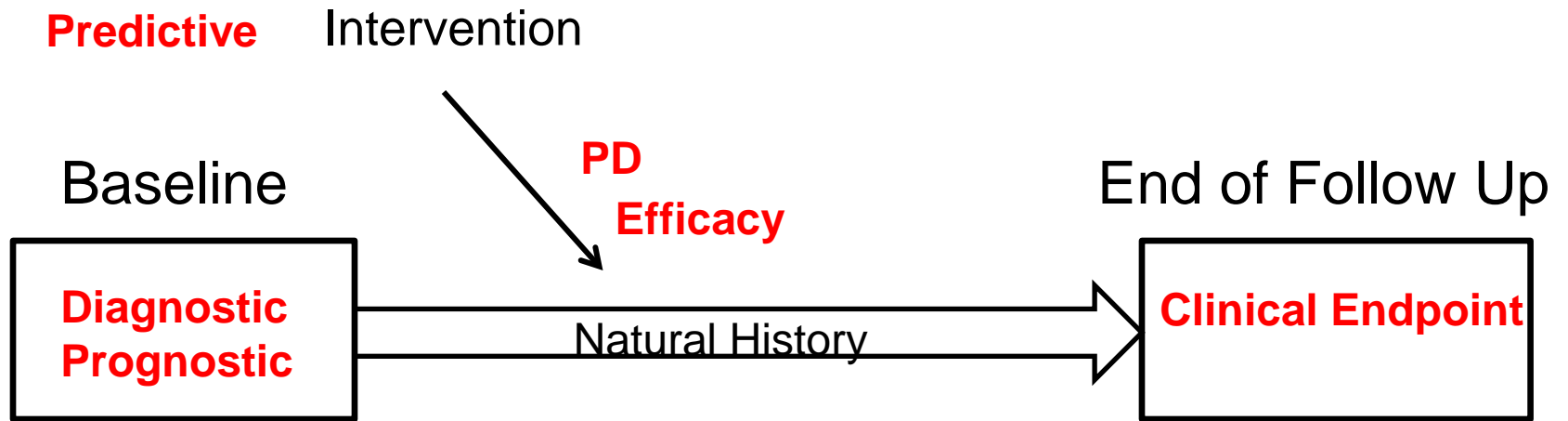
- Predictive
 - Efficacy
 - Safety
- Pharmacodynamic
 - Dose selection
- Efficacy
 - Predicts clinical outcome

Baseline

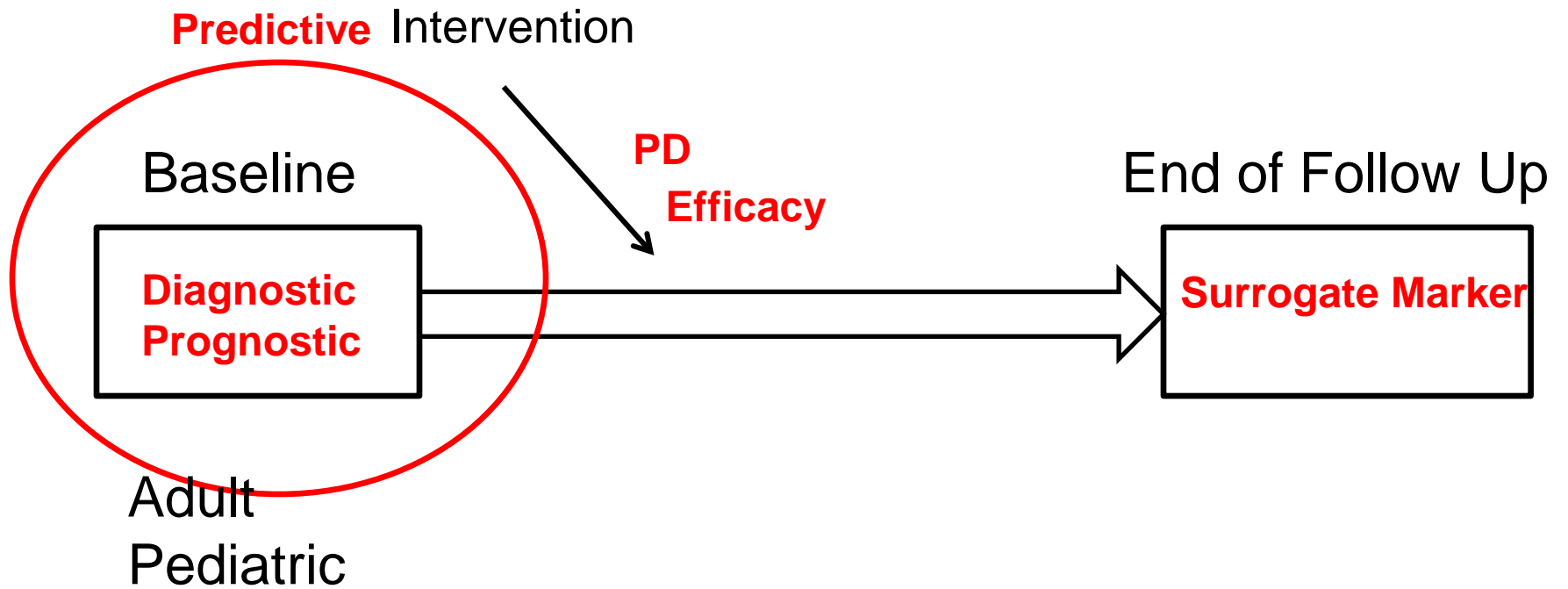
End of Follow Up



Adult
Pediatric



Adult
Pediatric



SESSION 3: TOWARD DATA DRIVEN COLLABORATION

Moderators: Veronica Miller, David Shapiro

Presenters/Discussants:

Bettina Hansen; Borje Darpö

Joanne Imperial; Scott Friedman; Rohit

Loomba, Rob Myers

DATA STANDARDIZATION WORKING GROUP

*facilitating collaborative research
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- Co-chairs: Joanne Imperial, Andrew Muir
- Working Group members:
 - Manu Chakravarthy
 - David DeBroda
 - Lara Dimick-Santos
 - Dean Hum
 - Sophie Megnien
 - Dan Peres
 - Stephen Rossi
 - David Shapiro
 - Brent Tetri

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TOWARD DATA-DRIVEN COLLABORATION

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- What can we learn from studies of surrogate endpoints in PBC trials?
- What can we learn from standardization of ECG/QT criteria for inclusion in NASH trials?
- Working group strategy and feedback

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DATA STANDARDIZATION WORKING GROUP

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Proposed Strategy

- Create overview of baseline variables in current clinical trials
 - What is level of variability?
 - Stratification?
- Explore potential of endpoints for future trials
 - Static vs. dynamic
- Consider multi-sponsor sub-studies within academic networks
 - Explore different funding mechanisms

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SESSION 4: SPEAKING A COMMON LANGUAGE: DEFINITIONS

Moderators: Markus Peck, Arun Sanyal

Presenters/Discussants:

Sophie Megnien, Stephen Harrison

Laurent Castera, Jude Oben, Rebecca Taub

DEFINITIONS WORKING GROUP

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- **Co-Chairs**
 - Stephen Harrison
 - Sophie Megnien
- **Working Group Members**
 - Helena Brett-Smith
 - Tony Coombs
 - Marcelo Costa
 - Lara Dimick
 - Greg Everson
 - Scott Friedman
 - Mike Hambleton
 - Dean Hum
- **Members, continued**
 - Joanne Imperial
 - Ruby Mehta
 - Melissa Palmer
 - Markus Peck
 - Dan Peres
 - Vlad Ratziu
 - Arie Regev
 - David Shapiro
 - Chinwe Ukomadu
 - Teresa Wright

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DISEASE DEFINITIONS WORKING GROUP

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Proposed Strategy

- Summarize current state-of-the-science
 - Where are the gaps, pitfalls?
- To what extent can we standardize/derive consensus based on current science?
- What opportunities exist for advancing the science?
 - Histological, radiological/imaging, functional
 - Dynamic vs. static
- What are the opportunities for collaboration?

DEFINITIONS WORKING GROUP

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Proposed steps

- NASH: define
- NASH: diagnose
- Gaps/Flaws of current methodologies
- Integration of new science into field

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SESSION 5: PEDIATRIC/ADOLESCENTS

Moderators: Carol Brosgart, Gary Burgess

Presenters/Discussants:

Joel Lavine, Krishna Polu, Miriam Vos

Dennis Grasela, Stefan Neubauer

PEDIATRIC ISSUES WORKING GROUP

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- Co-chairs
 - Joel Lavine
 - Krishna Polu
 - Miriam Vos
- Working Group members
 - Rajarshi Banerjee
 - Lara Dimick-Santos
 - Martine Kraus
 - Sophie Megnien
 - Ruby Mehta
 - Christine Murray
 - Stephanie Noviello
 - Debra Silberg

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PEDIATRIC WORKING GROUP

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- Proposed Strategies
- Address gaps in knowledge
 - Natural progression, long term consequences
- Biomarkers/diagnostics for pediatric and adolescent population
 - Urgency to replace liver biopsy
- Opportunities for collaboration

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SESSION 6: SUMMING UP & NEXT STEPS

Gary Burgess

Veronica Miller

Arun Sanyal