

Berkeley



HBV Forum Surrogate Endpoint Working Group

Co-chairs

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Working group members

- Ryan Taylor Anderson, MS – Forum Intern
- Nat Brown, MD - Hepatitis B Foundation Advisor
- Henry LY Chan, MD- Chinese University of Hong Kong
- Gavin Cloherty, PhD - Abbott
- Eric Donaldson, PhD – US FDA
- Geoffrey Dusheiko, MD -UCL
- Robert Gish, MD - Stanford
- Bettina Hansen, PhD - U Toronto
- Pietro Lampertico, MD, PhD - U Milan
- Oliver Lenz, PhD - Janssen
- Uri Lopatin, MD - Assembly Biosciences
- Eduardo Bruno Martins, MD, DPhil - Eiger
- Brian McMahon, MD – Alaska Native Medical Center
- Veronica Miller, PhD –Forum for Collaborative Research
- Charu Mullick, MD – US FDA
- Jeffrey Murray, MD, MPH – US FDA
- Michael Ninburg, MPA - Hepatitis Education Project
- Sandra Palleja, MD - PPD Inc.
- Jean-Michel Pawlotsky, MD, PhD – Henri Mondor Univ. Hospital
- Marion Peters, MD - UCSF
- Leland Ross Pierce, MD – US FDA
- Andrew Vaillant, PhD - Replicor
- Hwai-I Yang, PhD - Academia Sinica



Presentation Overview

- Objective of the working group
- Update on progress and collaborations
- Expansion of scope of the working group



Aims and Objectives

1. Assess the relationship of specific surrogate endpoints with long-term clinical outcomes, identify gaps, and recommend research to fill gaps to advance the regulatory process for HBV therapeutic interventions.
2. Review, discuss and formulate evolving consensus on HBV cure definition and appropriate surrogate endpoints for HBV Ph2b and Ph3 clinical studies.



First step

Perform a systematic literature review/meta-analysis describing links between **surrogate endpoints** and **long term clinical outcomes**.

– Starting with:

- A) Functional Cure: HBsAg seroclearance.
- B) Partial Cure: Undetectable HBV DNA, normal ALT, low HBsAg.



Status and next steps: literature review

- >100 papers (representing 175,298 patients and 1,104,027 person-years of follow-up) have been selected and data extracted
 - Summary spreadsheet, PowerPoint file with key figures and EndNote library



Status and next steps: literature review

- Ensure relevant papers are included
 - Literature review assessed by working group members
- Additional curation/check of the literature data
- Start meta-analyses



Beyond the literature review

- Organize a data base with patient level data to allow a better assessment of links between surrogate endpoint and long term clinical outcomes



Patient level Data

- Database owned by the HBV Forum and located at UC Berkeley.
 - Bettina Hanssen (U. Toronto)
- Scientific oversight committee (comprised by HBV Forum members and data contributors) “controls” database and decides on analyses to be performed.



Patient level Data: Update and next steps

- Produce a project concept paper
- Design a data collection template (i.e. which data to include)
- Develop preliminary statistical analyses plan
- Formalize the collaboration (e.g. confidentiality agreement, data transfer agreements)
- Reach out to industry and academic partners with relevant data to assess willingness to collaborate on this project.



Patient level Data: Update and next steps

Any suggestions on who might
have data to contribute?



Collaborations

- Multiple collaborations under development:
 - Industry partner to join efforts on literature review/meta-analyses
 - Multiple industry partners have been approached to share patient data
 - Generally positive response received
 - REVEAL (Prof. Hwai I Yang): agreed to share data
 - Bettina Hanssen (U Toronto): Perform literature meta-analyses and analyze patient level data



Extension of the working group scope

- The Diagnostics/Biomarkers WG will integrate with the Surrogate Endpoints WG
 - The Diagnostics/Biomarkers WG has assembled comprehensive matrix of available diagnostic tests.
- Scope and organizational set up of expanded group to be determined;
 - Potential topics include:
 - Value of novel markers (HBV RNA, HBcrAg) as clinical endpoints
 - Standardization of assays assessing novel markers (virologic, immunologic and liver disease markers)
 - Your favorite topic...



Summary

- Literature review is well underway with meta-analyses beginning soon
- Patient level data base is being set up
- Multiple collaborations are being explored
- Expanded scope of working group is being assessed

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Thank You!