Berkeley School of Public Health

Forum for Collaborative HIV Research

HBV Forum 1
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WG Update: Surrogate Endpoints

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Members

Facilitating collaborative research in drug development and health policy

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- Nat Brown, MD- Hepatitis B Foundation Advisor
- Henry LY Chan, MD- Chinese University of Hong Kong
- Gavin Cloherty, PhD- Abbott
- Eric Donaldson, PhD -FDA
- Geoffrey Dusheiko, MD -UCL
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- Bettina Hansen, PhD- U Toronto
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- Oliver Lenz, PhD- Janssen
- Uri Lopatin, MD Assembly Biosc
- Eduardo Bruno Martins, MD, DPhil- Eiger
- Jeffrey Murray, MD, MPH- FDA
- Michael Ninburg, MPA -Hep Education Project
- Sandra Palleja, MD -PPD, Inc.
- Jean-Michel Pawlotsky, MD, PhD- Paris
- Marion Peters, MD- UCSF
- Leland Ross Pierce, MD- FDA
- Andrew Vaillant, PhD Replicor

Aims and Objectives

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1. Assess the relationship of specific surrogate endpoints with long-term clinical outcomes, identify gaps, and recommend research to fill these 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.

Objective 1: Activity 1

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- Perform a systematic literature review/meta-analysis of references/data describing link between **surrogate endpoints** and **long term clinical outcome**.
  - Include references from all type of treatments and natural disease progression.
  - Focus on endpoints identified/prioritized (crf objective 2).
  - Starting with:
    A) HBsAg “loss” with or without anti-HBs “gain.”
    B) Low level HBsAg (quantified) .

Objective 1: Activity 1 *cont.*

- Define criteria for selection and "ranking" of reference (e.g. by level of evidence, obtaining expert input in relevance of papers,…)
- Perform sub analyses (age, race, GT, liver disease status,…) and include **all type of treatment and natural disease progression**.
- Data on HCV/HBV, HIV/HBV and HBV/HDV co-infected may be assessed later.

- Comparator: long term clinical outcome with current SOC.

Objective 1: Activity 2

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- Determine the regulatory perspective/requirements in terms of level of evidence needed to accept surrogate endpoints for long term clinical benefit.
  - what is required before registration and what could be provided post-approval.
  - Potentially include evidence required by payer and HTA bodies.

Objective 1: Activities 3-4

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3. Gap analyses assessing the available evidence vs. required evidence and determine which additional evidence would facilitate HBV cure development.

4. Identify, promote and facilitate opportunities to create additional evidence (e.g. in collaboration with HBV cohorts, cross pharma initiatives, EASL, AASLD, APASL,…)

Objective 2: Activity 1

- Define cure definitions (including surrogate endpoints) to be endorsed by the HBV Forum and develop/prioritize list of (surrogate) endpoints for Ph2b/3 studies:
  - Review of literature, conference proceedings, etc. from different stakeholders (e.g. AASLD-EASL workshop, regulatory documents, clinical evidence,…)
  - Achieve consensus within the HBV Forum.
  - Assess the available level of evidence of these surrogate markers with respect to long term clinical outcome (link to Objective 1).

Outcomes and Products

- **Deliverable:**
  - Peer-reviewed manuscript(s).
  - Reference set collection of data (format to be determined).

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Timelines

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Objective 1:

- Activity 1: Literature review of clinical outcome data for HbsAg ("loss" and low level) and collection of data - Q1 2017.
  - Created a shared Box folder containing the references received from working group members; 48 and counting
  - Currently refining and populating a master spreadsheet with data from these publications
- Activity 2-4: 2017.

Objective 2:

- Activity 1: present first consensus proposal at next HBV forum meeting.

Questions

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