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HBV Biomarkers Database Working Group

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Forum for Collaborative Research

Berkeley Public Health

Background

- Clinical development of novel HBV therapeutics and combination regimens is challenged by heterogeneity of chronic hepatitis B virus infection

- Clarity is urgently needed to understand heterogeneity across hepatitis B clinical trials, with respect to patient populations, biomarkers measured, etc

Objectives

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- Perform a landscaping literature review of hepatitis B trials
- Characterize heterogeneity with respect to demographic, clinical, and biomarker information across hepatitis B trials
- Translate into visualizations that illustrate trial heterogeneity
- Input from regulatory agencies and patients
- Propose to correlate our findings with other recommendations (eg Endpoints guidance)

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Workstreams

Trial-Level

Aim: to understand heterogeneity across hepatitis B trials of novel therapeutics and combination regimens

Patient-Level

Aim: to facilitate future hepatitis B drug development and collective learning by assembling a database of clinical trials data

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DAC Advisors

Regulatory Science
Data Science
Statistics
Novel Analytics

FCR Data & Analysis Center (DAC)
DAC Team and Platform

DAC Project Portfolio

Liver Forum – MASH Placebo Database

Liver Forum – Digital Histology AI/ML

HIV Forum

HBV Forum

Annual Workshops

Data Science
RWD-RWE
ML-AI
Causal Inference
ETC

Berkeley Public Health

The DAC Platform: A safe place for data sharing and analysis

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- Data protection by design & by default
- Built on UC Berkeley's SRDC system which is approved for ePHI and highly sensitive data
- Deep collaborations with experts in UC Berkeley's Privacy, Human Subjects, Information Security, and VC Research Offices
- Virtual machines, HPC cluster, and parallel file system storage

Name of Trial	NCT ID	Sponsor	Trial Status *(discontinued, completed, ongoing)*	Latest Data *(publications, conference proceedings)*	Phase	Randomized Trial?	Masking?	Combination Trial? *(excludes NrtI or IFN as backbone drugs)*	Backbone Drug(s) *(NrtI, IFN, or placebo)*	Novel Investigational Compound(s)	Drug Category *(antiviral or immune modulator)*
A Study of JNJ 73763989+JNJ 56136379+Nucleos(t)Ide Analog (NA) Regimen Compared to NA Alone in e Antigen Negative Virologically Suppressed Participants With Chronic Hepatitis B Virus Infection	NCT04129554	Janssen	Completed	w.natap.org/2022/AASLD/AASI	2b	YES	Double Masked	YES	ETV, TDF, TAF	JNJ-3989 JNJ-6379	antiviral antiviral
A Study of Different Combination Regimens Including JNJ-73763989 and/or JNJ-56136379 for the Treatment of Chronic Hepatitis B Virus Infection (REEF-1)	NCT03982186	Janssen	Completed	om/science/article/abs/pii/S24681	2b	YES	Double Masked	YES	ETV, TDF, TAF	JNJ-3989 JNJ-6379	antiviral antiviral
A Study of JNJ-73763989, JNJ-56136379, Nucleos(t)Ide Analogs, and Pegylated Interferon Alpha-2a in Virologically Suppressed Participants With Chronic Hepatitis B Virus Infection (PENGUIN)	NCT04667104	Janssen	Completed	w.natap.org/2022/AASLD/AASI	2b	NO	NONE	YES	TDF, TAF, ETV, PEG-IFN-a	JNJ-3989 JNJ-6379	antiviral antiviral
An Efficacy, Safety, and Pharmacokinetics Study of JNJ-56136379 in Participants With Chronic Hepatitis B Virus Infection	NCT03361956	Janssen	Completed	om/content/early/2023/01/24/gu	2	YES	Triple Masked	NO	ETV, TDF, Placebo	JNJ-6379	antiviral
Study of ARO-HBV in Normal Adult Volunteers and Patients With Hepatitis B Virus (HBV)	NCT03365947	Janssen	Completed	hepatology.eu/article/S0168-82	2a	YES	Double Masked	NO	TDF, ETV	JNJ-3989	antiviral
A Study of GSK3228836 in Participants With Chronic Hepatitis B (CHB)	NCT04449029	GSK	Completed	.nejm.org/doi/full/10.1056/NEJI	2b	YES	Single Masked	NO	ETV, TDF, TAF, 3TC, ADV, FTC	bepirovirsen	antiviral
Study of Sequential GSK3228836 and Peginterferon Treatment in Participants With Chronic Hepatitis B (CHB) (B-Together)	NCT04676724	GSK	Completed	summaries/research-summaries	2b	YES	NONE	NO	NrtI & PEG-IFN-a	bepirovirsen	antiviral
Safety, Tolerability and Antiviral Activity of Selgantolimod in Virally-Suppressed Participants With Chronic Hepatitis B	NCT03491553	Gilead	Completed	direct.com/science/article/pii/S	2	YES	Double Masked	NO	ETV, TDF, TAF, 3TC, TEL	selgantolimod	immune modulator
Safety and Efficacy of GS-4774 in Combination With Tenofovir Disoproxil Fumarate (TDF) for the Treatment of				https://pubmed.ncbi.nlm.nih.gov/30930022/							

Working Group Call #1

- HBV Forum convened a working group call October 2023 to strategize on research priorities and questions for this project:

Forum	Industry	Regulatory	Co-Leads & Co-Chairs
Veronica Miller Chris Hoffman Margot Yann Mitchell Leus	Jerome Bouquet, GSK Jay Greene, GSK Andrea Cathcart, Vir Rémi Kazma, Roche Katie Kitrinos, Assembly Ryan Yan, Assembly John Fry, Consultant Cynthia Wat, Consultant	Poonam Mishra, FDA Wen Zeng, FDA	Markus Cornberg Doug Mayers Oliver Lens Marion Peters

Key Variables Discussed

- **Duration of therapy:** are we treating patients for an adequate time period, and do we need to treat for longer to achieve the endpoint the trial is evaluating?
- **Biomarkers Measured:** what biomarkers were measured, what assays were used, and what were the details of the assay?
  - HBV RNA
  - HBcrAg
  - HBcAg
  - Immune markers

Next Steps

- Finalize landscaping literature review strategy
  - Generate questions that we might want to ask of the data
  - Variables of interest
  - Phases of trials to include
- Continue outreach with sponsors around clinical data sharing
  - Consider ‘middle ground’ strategy of requesting summary statistics from sponsors

Further Discussion

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- **Inclusion of Phase 1 Trials?**
  - The landscaping literature review initially focused only on Phase 2 trials
  - Patient populations differ in Phase 1 vs. in Phase 2 – is there value for including?

- **Data 'Middle Ground'?**
  - Could the working group approach companies with a very specific question about their trial data and request summary statistics generated by the sponsor?
  - Serves as a 'middle ground' in lieu of sharing patient-level clinical datasets

Thank You!