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HBV Biomarkers Database Working Group

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Forum for Collaborative Research

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



- 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

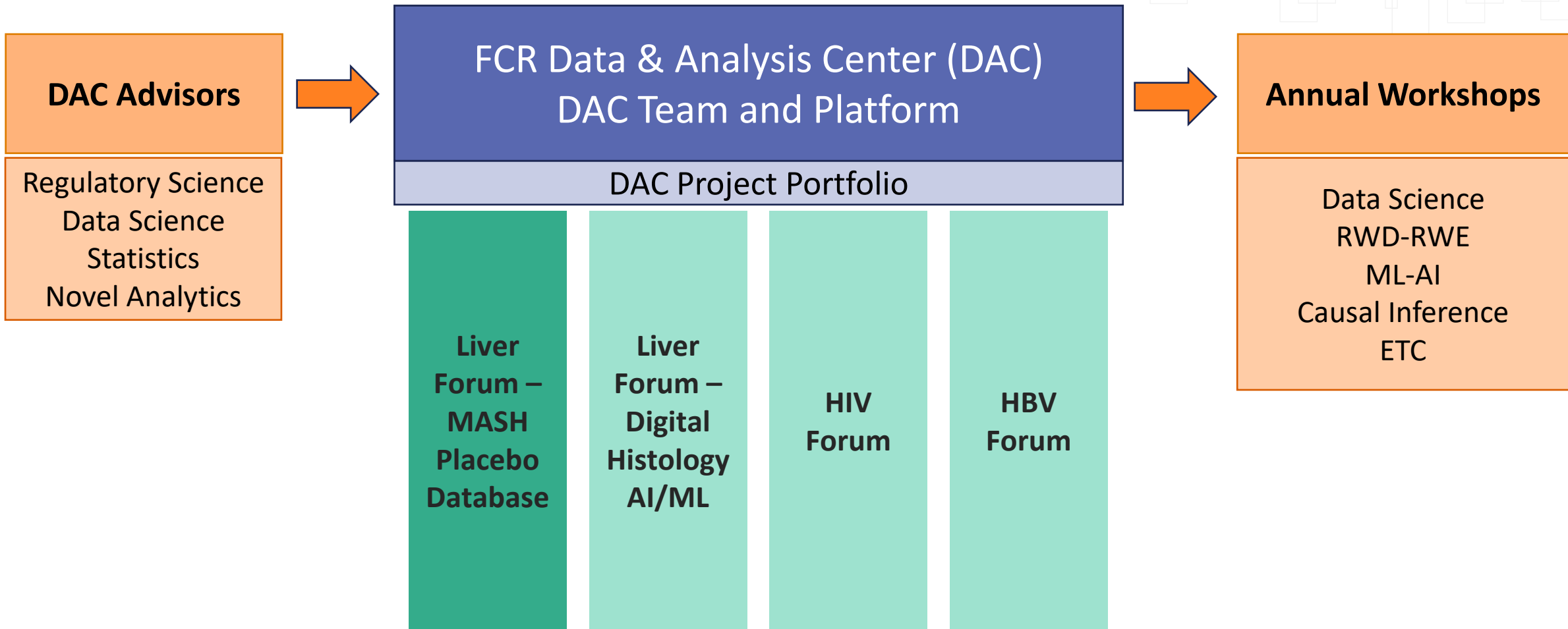
Aim: to understand heterogeneity across hepatitis B trials of novel therapeutics and combination regimens

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



- 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 | www.natap.org/2022/AASLD/AASLD | 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 | https://doi.org/10.1016/j.jhep.2022.05.011 | 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 | www.natap.org/2022/AASLD/AASLD | 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 | www.gilead.com/content/early/2023/01/24/gilead-sci/101010 | 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 | www.eurjhep.com/article/S0168-8278(22)00082-8 | 2a | YES | Double Masked | NO | TDF, ETV | JNJ-3989 | antiviral |
| A Study of GSK3228836 in Participants With Chronic Hepatitis B (CHB) | NCT04449029 | GSK | Completed | https://doi.org/10.1056/NEJMoa2207000 | 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 | www.gilead.com/press-releases/2022/08/2022-08-22-gsk-3228836 | 2b | YES | NONE | NO | NrtI & PEG-IFN-a | bepirovirsen | antiviral |
| Safety, Tolerability and Antiviral Activity of Selgantolimod in Virologically Suppressed Participants With Chronic Hepatitis B | NCT03491553 | Gilead | Completed | https://pubmed.ncbi.nlm.nih.gov/30930022/ | 2 | YES | Double Masked | NO | ETV, TDF, TAF, 3TC, TEL | selgantolimod | immune modulator |

| | | | | | | | |
|----------------------------|--------------------|-------------------------------|---------------------------------|----------------|---------------------------------|------------|---|
| Clinical Trial Information | Inclusion Criteria | Primary Efficacy Endpoint Def | 2ndary Endpoints & Viro Biomark | Immune Markers | Host Markers (genetics, epigene | ALT Flares | + |
|----------------------------|--------------------|-------------------------------|---------------------------------|----------------|---------------------------------|------------|---|

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 Kitrinis, 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

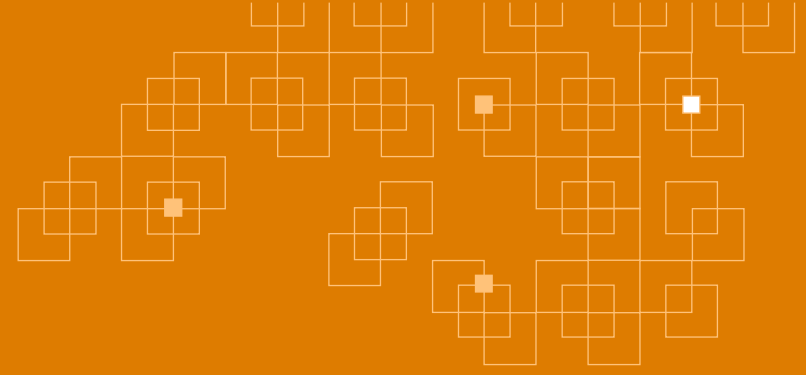


■ Inclusion of Phase 1 Trials?

- 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!