Session 4

Matching the Mechanism of Action to the HBV Subpopulation: Key to Successful Development

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Working Group Launch

- **Title:** Matching the Mechanism of Action to the HBV Subpopulation: Key to Successful Development
- **Co-Leads:**
  - Michael Biermer, Janssen Pharmaceuticals
  - Jordan Feld, Toronto Centre for Liver Disease
- Initial impetus was Anuj Gaggar recognizing the importance of HBV patient heterogeneity
  - How does patient heterogeneity relate to HBV treatment?

Working Group Aim

- To advance drug development for HBV treatments by better understanding the relationship between mechanisms of action and patient heterogeneity
  - NUCs = administered equally across HBV patients
  - Future agents hoping to achieve functional cure may require **more individualized approaches depending on HBV subpopulation**
  - This is particularly true in the development program…
    - Studying the **'right drug'** in the **'wrong population'** could lead to discarding a very effective therapy

HBV Subpopulations

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- Achieving functional cure w/ future treatments (and treatment combinations) may depend on the HBV subpopulation(s):
  - Phase of disease
  - HBeAg status
  - Comorbidities (cirrhosis, NASH)
  - HBV genotype
  - Demographic factors: age, sex, region/race, age of infection etc
  - Host genetics…TBD

Implications for Trial Design

- Need to think mechanistically and strategically when designing trials:
  - Rationale based on target & MOA…useful when well understood
  - Small pilot studies in different subpopulations to understand treatment effects **and MOA(s)**, only then leading to larger trials in the 'right/most promising' population(s) (more investment of time, money, resources)
    - Balance of speed/efficiency vs risk of missing a signal
  - Adaptive trial designs might prove useful
    - Platform trials
    - Ancillary translational studies to understand MOA – allows better alignment of drug with pop'n

Working Group Outputs

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- We are open to suggestions:
  - Webinar as a starting point
  - Summary paper