



**THE FORUM**  
For Collaborative Research<sup>SM</sup>

# Early Learnings from NUC Stop Studies

**Bruce Given, Arrowhead Pharmaceuticals**

HBV Forum 5

April 10, 2019

Vienna, Austria

**Berkeley** Public  
Health

# Objectives for this session

- Consider what implications arise for upcoming finite therapy trials arising from recent Stop Nuc studies
  - What safety considerations may arise?
  - Are there likely to be predictors of response?
  - In arms with background Nucs, are they continued or stopped?
  - Is CHB without hepatitis off therapy considered a positive outcome?

# Patient characteristics (generally)

- Long-term NUC treated patients
  - Most studies in HBeAg negative patients after long-term therapy
  - DNA <LLOQ or target not detected (TND)
  - No cirrhosis known or suspected
  - ALT usually 'normal'\*
- Stop the NUC and follow

\* Considerable variability in normal ranges or degree of allowed elevation

# Basically 4 possible outcomes

## ■ Outcome 1 (CHB, no hepatitis):

- DNA remains <2000 IU
- If ALT changes not perceived as flare

## ■ Outcome 2 (“Functional cure”)

- Viral parameters +/- show increases, DNA often remains suppressed



- Often mild host response or can flare



- DNA <LLOQ and HBsAg clearance

## ■ Outcome 3 (CHB, no hepatitis)

- Viral parameters show increases



- Host response/Flare



- DNA <2000 IU, ALT ‘normal’

## ■ Outcome 4 (CHB, hepatitis)

- Viral parameters show increases, often with flare, HBeAg seroreversion possible



- High DNA and/or severity of flare requires NUC re-start

# Some factors of interest

- Any baseline predictors?
  - DNA <LLOQ vs TND?
    - Time in that DNA status?
  - HBV RNA or HBcrAg levels?
  - HBsAg levels?
  - Genotype?
  - Age, race, gender, etc?
  
- Clearance rates increase with time

# Efforts to manage risk

- Close follow-up
- Baseline factors to avoid
  - Cirrhosis
  - Others?
- Clear re-treatment rules
- Other measures to take?

# Objectives for this session

- Consider what implications arise for upcoming finite therapy trials arising from recent Stop Nuc studies
  - What safety considerations may arise?
  - Are there likely to be predictors of response?
  - In arms with background Nucs, are they continued or stopped?
  - Is CHB without hepatitis off therapy considered a positive outcome?