Stopping NUCs
how to move forward? (with incomplete knowledge...)

Dr Kosh Agarwal
Institute of Liver Studies
King’s College Hospital
London

HBV Forum 2021
Stopping NA therapy before HBsAg loss in HBeAg-negative patients

Potential outcome predictors
Age, time to undetectable HBV DNA, and duration of viral suppression under NA, HBsAg levels at NA baseline and NA cessation, type of NA (TDF vs. ETV), HBV DNA levels during reactivation phase, re-treatment strategy, and HBV genotype

- **Treatment phase** (> 3 years)
  - Nucleos(t)ide analog (NA)

- **Lag-phase** (<1-12 months)
  - Risk of severe flare?

- **Reactivation phase** (~ 3 months)
  - HBV DNA
  - ALT

- **Consolidation phase** (~ 12 months)

- **Long-term outcome**
  - D) Chronic hepatitis B requiring re-treatment (~40%)
  - C) Indeterminate state not fulfilling immediate re-treatment criteria (~10–20%)
  - B) Sustained virologic response (true ‘healthy carrier’ state) ± HBsAg level decline ~20–30%
  - A) HBsAg loss (~20% after 2–3 years of follow-up)

**Limit of HBV DNA detection**

**TIME**

*Lampertico P and Berg T, Hepatology 2018*
Viral and immune factors associated with successful withdrawal in HBeAg–ve HBV

N=27 – 30% lost SAg/ 82% not retreated

Low SAg
Decreased cccDNA Transcription
Functional HBV specific T cells at baseline

Garcia-Lopez et al J Hep 2020
'When all think alike, no one thinks very much…’
W Lippman

No clinical consensus
Not a big uptake in clinical practice – pts!

What endpoint? – surely SAg loss
Low SAg <100 – lower the better
Conflicting evidence re newer viral biomarkers
Viral/ host heterogeneity confusing
Transcriptional activity vs invigorated T cell response*
Pragmatic criteria (HBV EAg loss, HBSAg<100, composite)
Standardise – ie everyone and then watch…
or consider MOA driven rules

*'Dylan’ refined proposal Berg T, Lampertico P J Hep in press