

The background of the slide features a dark purple color with a pattern of faint, light purple molecular structures. These structures consist of interconnected circles of various sizes, representing atoms, and lines representing chemical bonds. The overall effect is a scientific and network-like aesthetic.

Liver Connect 2022:

Stopping Nucleos(t)ide Therapy
HBV Case Discussion

Disclosures

- Grants/Research Support: Assembly Biosciences, BMS, Eli Lilly, Enanta, Gilead, Janssen, Merck, and Novo Nordisk
- Consultant/Advisor: Aligos, Arbutus, Arrowhead, Assembly Biosciences, Biomarin, Galmed, Gilead, Glaxo, Janssen, Madrigal, NeuroBo, Poptest, Redhill, and Virion

AASLD HBV Guideline: Stopping Nucleos(t)ide Therapy

	Parameters	Cirrhosis
HBeAg-positive	<ul style="list-style-type: none">• HBeAg seroconversion• Undetectable HBV DNA• Normal ALT → for ≥ 12 months	No
HBeAg-negative	<ul style="list-style-type: none">• HBsAg clearance	No

Note: EASL and APASL Guidelines allow for individualized stopping in HBeAg-negative patients after HBV DNA undetectable for ≥ 2 years (APASL) or 3 years (EASL)

Pros and Cons of NA Discontinuation in HBeAg- Patients

Pro

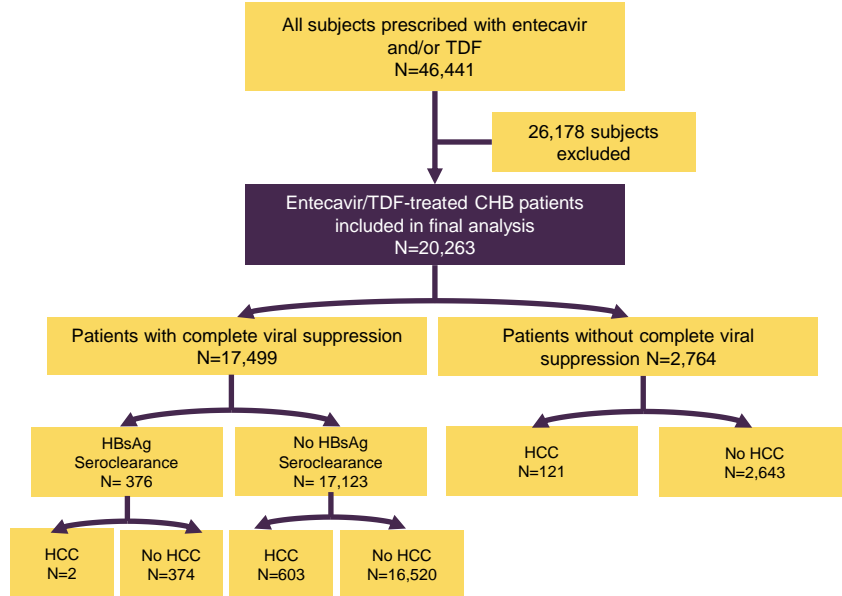
- Increased chance of HBsAg loss*
- Finite therapy
 - Less side effects
 - Decreased costs
- Improved prognosis?

Con

- Virologic/clinical flares
- Potential decompensation
- Possible progressive disease and adverse outcomes if recurrence not recognized

Is Prognosis Better After HBsAg Clearance?

Impact of HBsAg Seroclearance on Nucns on Incidence of HCC: N=20,263



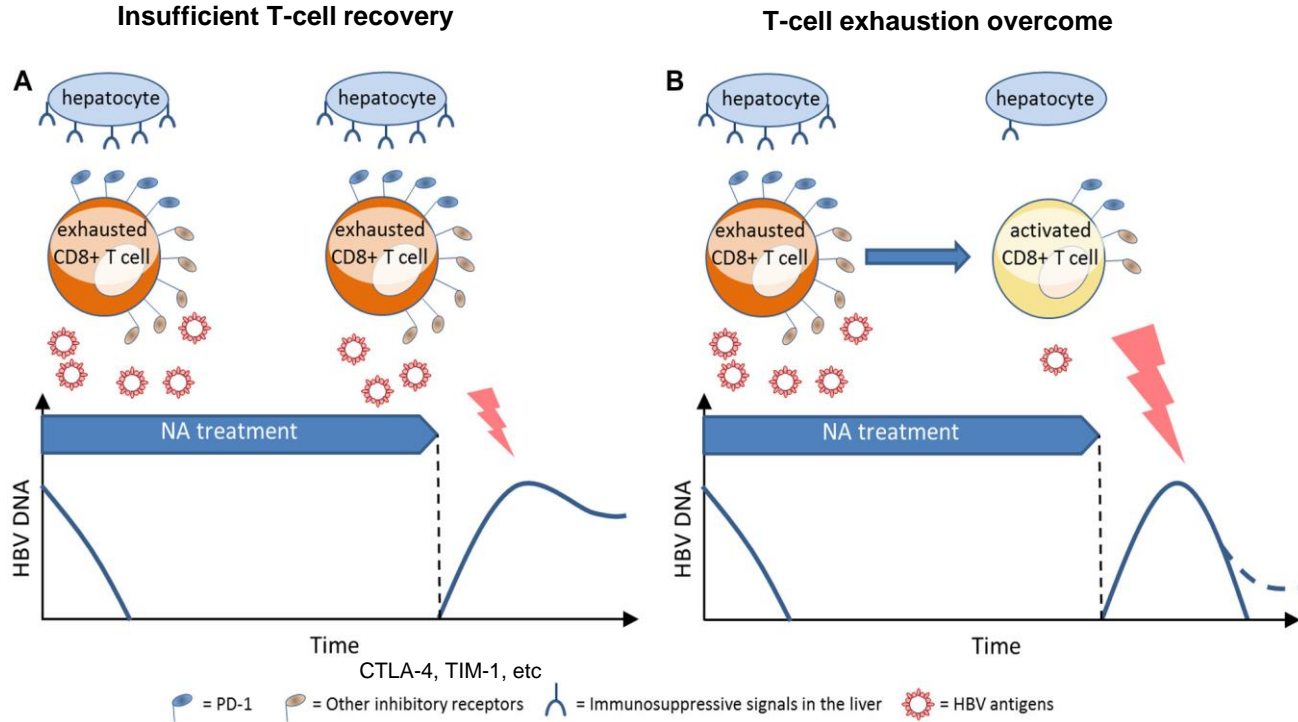
Multivariate analysis

Viral Suppression	aHR	P value
Complete viral suppression	Referent	
Incomplete viral suppression	1.69	<0.001
HBsAg seroclearance	0.24	0.045

Other significant factors: age, male, cirrhosis

Discontinuation of NA's in Chronic HBeAg-Negative CHB

The Concept of T-Cell Exhaustion



Case #1

- 60 year old Caucasian man with chronic hepatitis B
- Informed of his status in his late 20's at time blood donation; no known FH
- History of GERD, cholecystectomy age 53 for GB polyp (hyperplastic)
- HBeAg negative, anti-HBe positive
- Treated with entecavir for >10 years; pre-treatment e status unknown
- HBV DNA consistently undetectable
- Fibroscan 5.1 kpa
- Ultrasound every six months negative
- Quantitative HBsAg December 2021 = 61 IU/mL
- Would you stop therapy?
- What would you tell the patient about the chances of clearing HBsAg if he stops?

Case #2

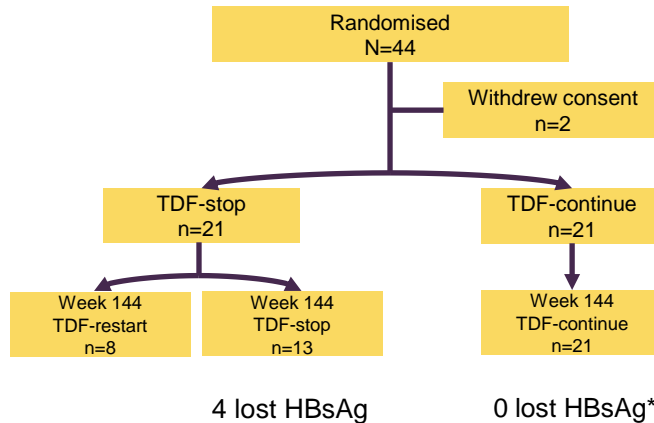
- A 47 year old Chinese man who was found to have HBV infection at age 13 prior to vaccination: HBsAg+ since then
- Parents, 2 siblings stated to be HBV negative
- HBeAg negative, anti-HBe positive
- Ultrasound normal
- Fibroscan 4.0 kpa CAP 247

	<u>HBV DNA (IU/mL)</u>	<u>ALT (U/L)</u>	<u>gHBsAg (IU/mL)</u>
Jan 2020	847	12	—
April 2021	4750	11	> 1000

- Would you start treatment in this patient?
- Started TAF June 2021
- Feb 2022 HBV DNA < 10 IU/mL, ND

Long Term Response After Stopping TDF in Non-Cirrhotic HBeAg- Patients – FINITE Study

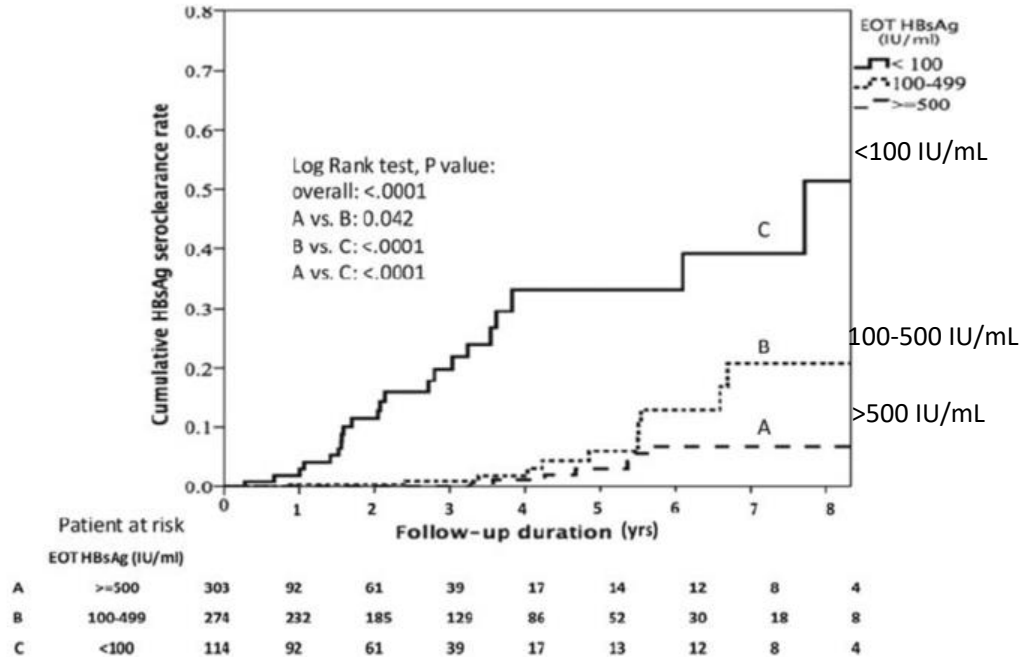
- Non-cirrhotic and < F3 HBeAg- patients, n=44
- TDF for > 4 years, HBV DNA suppression for > 3.5 years
- Randomized to continuation versus stop (n=21 each group)
- Patients who stopped were to remain off therapy for 144 weeks



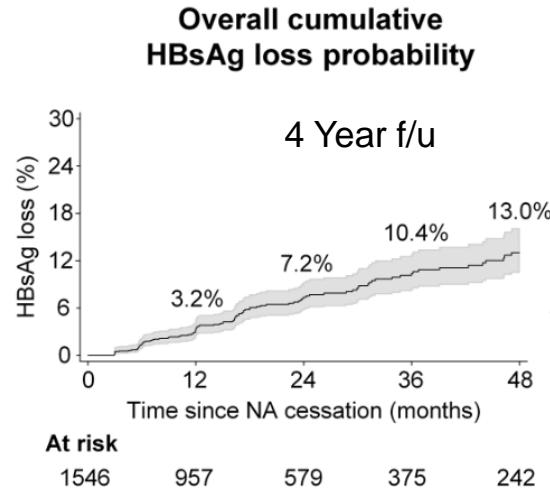
Stopping NA therapy may provide an expedited path to HBsAg clearance

Incidence and Predictors of Seroclearance of HBsAg Clearance After Discontinuation of NA Therapy, n=691

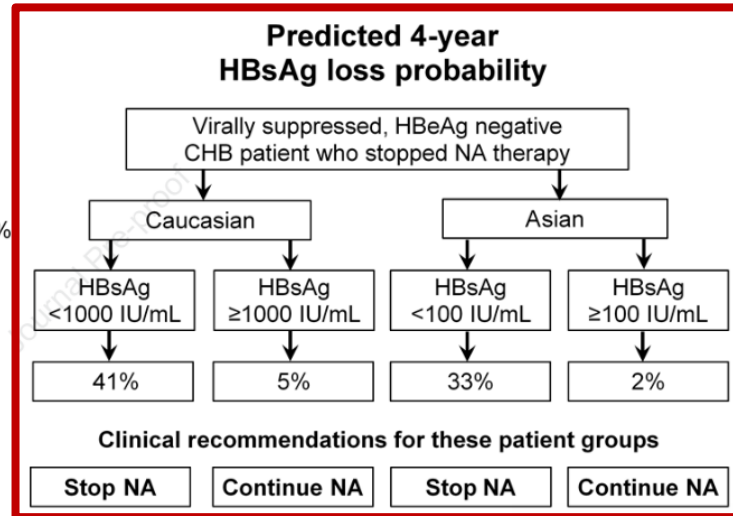
**Overall 6 year seroclearance 13%
(9% cirrhosis, 16% non-cirrhosis)**



Off-Therapy Response After NA Withdrawal in Patients With CHB: An International, Multi-Center, Multi-Ethnic Cohort RETRACT-B Study: Over 900 Patients

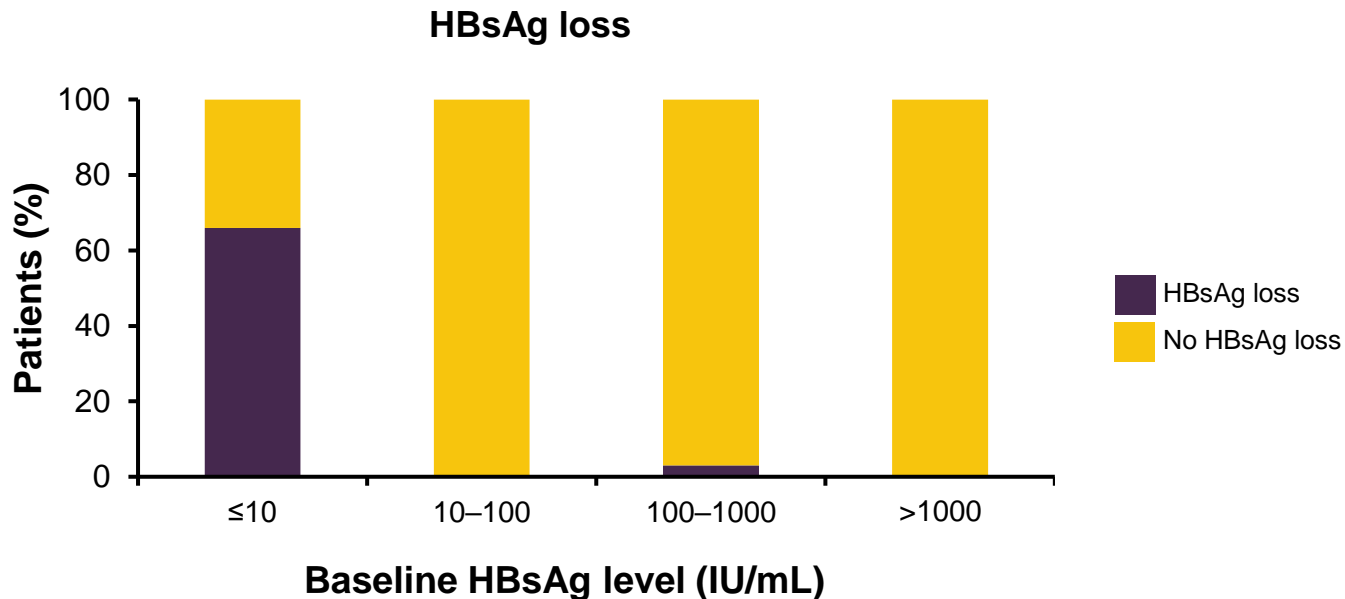


A Useful Algorithm Derived From Study



19 patients developed hepatic decompensation after NA cessation (8/184 [4.3%] of patients with cirrhosis vs. 11/1,368 [0.8%] of patients without cirrhosis, $P < .001$) with an incidence rate of 0.48 per 1000 person-years.

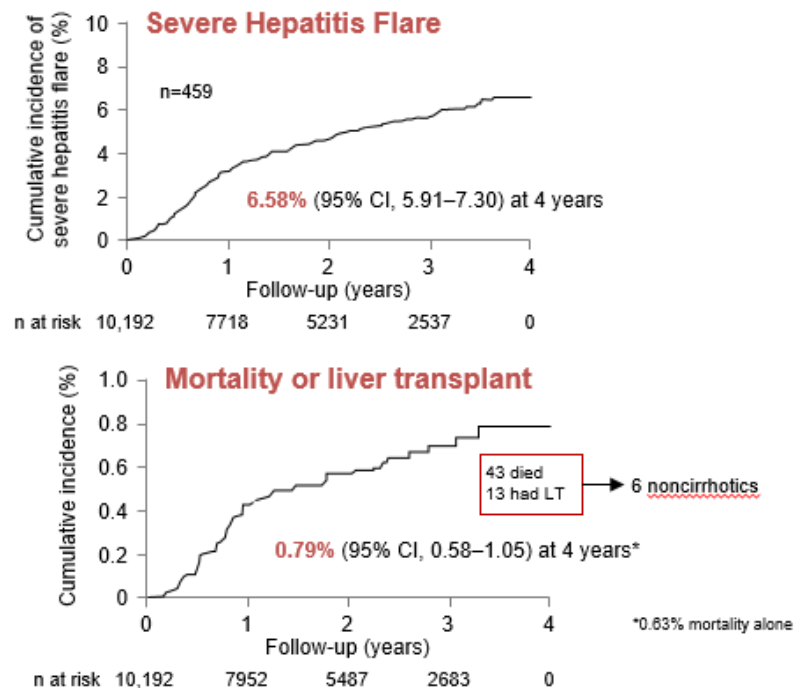
Final Results of HBV-STOP: Results of Stopping Therapy, n=110



<u>Baseline HBsAg</u>	<u>HBsAg loss</u>	
HBsAg ≤10 IU/mL (n=8)	6/8 (75%)	P<0.001
HBsAg >10 IU/mL (n=99)	1/99 (1%)	

Severe Hepatitis Flare and Mortality After Discontinuation of Oral Antiviral Treatment in Patients With CHB: Taiwan National Health Insurance Lab Database, n = 10,192

Off-therapy follow-up and event occurrences



Risk factors for severe flare

- Age, per 10 years
- Male gender
- Cirrhosis
- History of decompensation

Risk factors for mortality

- Age, per 10 years
- Cirrhosis
- Hypertension

Takeaways for Stopping Nucleotide Therapy

- Can be considered after 3-5 years of full viral suppression
- It's appropriate to make patients aware of the option
- Informed discussion with patient should include result of a quantitative HBsAg level (now commercially available)
 - Other markers, e.g. HBcrAg, HBV RNA being studied but not available
- Inflection point for realistic chance of clearing 10-100 IU/mL
- Decision to stop should be as much patient driven as clinician driven