2020 VIRTUAL GI AND LIVER SYMPOSIUM

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Update: Hepatitis B
Abstracts from AASLD and EASL

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Disclosures

- I receive institutional grant support from Gilead Sciences Inc.

Outline

1. Updates on developments with established first-line HBV therapies
2. Updates on safety and efficacy of withdrawal therapy for treated patients
3. Updates on novel therapies in the pipeline for HBV

Updates on Established Therapies

Longitudinal real-world study on estimated glomerular filtration rate changes in entecavir versus tenofovir disoproxil fumarate-treated chronic hepatitis B patients: a REAL-B study

BACKGROUND & AIMS

- There is conflicting data on whether TDF is associated with higher risk of renal impairment than ETV
- The long-term renal effect of oral NAs in diverse real-world cohorts is unknown
- **AIM**: to determine the longitudinal eGFR in a large cohort of CHB patients by type of NA and factors associated with eGFR decline

METHODS

- Retrospective study of 6189 adult treatment-naïve CHB patients with ≥12 months of follow-up at 22 centers
  - TDF (n=2482)
  - ETV (n=3707)
- Assessed eGFR by CKD-EPI formula at baseline and every 6 months
- Patients were propensity matched (PSM) on:
  - Age, gender, DM, HTN, cirrhosis, baseline eGFR, and follow-up time
  - Stratified on eGFR ≥60 and <60
- Multivariable generalized linear modeling and Cox regression models

Mak LY, et al. AASLD TLMdX 2020; Oral #21

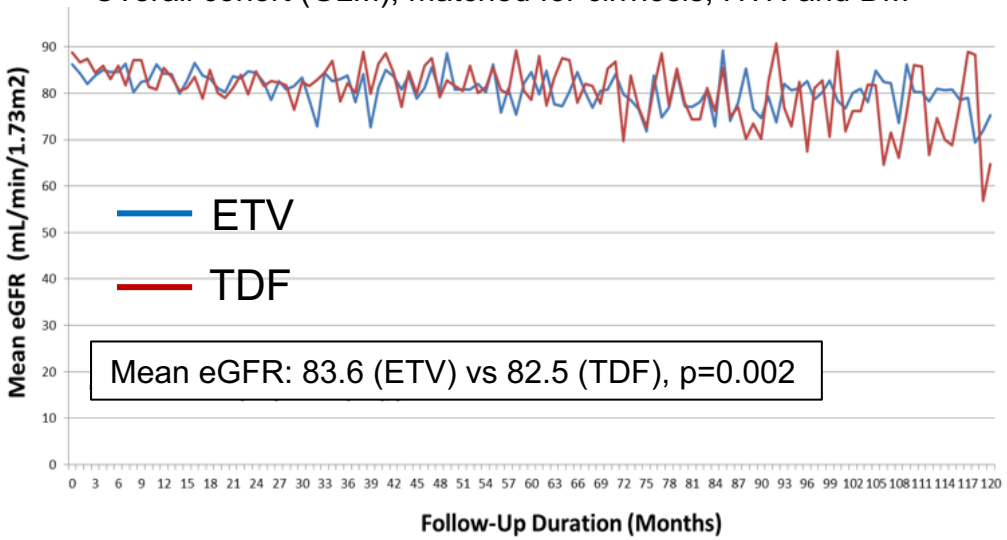
Longitudinal real-world study on estimated glomerular filtration rate changes in entecavir versus tenofovir disoproxil fumarate-treated chronic hepatitis B patients: a REAL-B study

RESULTS

- ETV-treated patients at baseline were older, more likely to be cirrhotic, had more DM/HTN, and had lower baseline eGFR
- Multivariable risk factors for renal impairment (defined as CKD upstaging by ≥1 stage) identified in PSM cohorts:

PSM	Variable	HR	p value
eGFR<60	TDF (vs ETV)	1.3 (1.1-1.4)	<0.001
eGFR<60	ALT	1.0 (1.0-1.0)	0.04
eGFR<60	Albumin	0.90 (0.85-0.96)	0.001
eGFR<60	TDF (vs ETV)	2.6 (1.0-6.8)	0.05

Overall cohort (GLM), matched for cirrhosis, HTN and DM



When data was stratified by age (≥50 vs <50 years), lower GLM-adjusted mean eGFR for TDF group was only seen with the older age group.

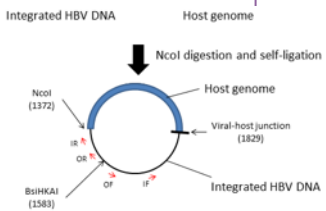
CONCLUSION **The lower mean eGFR over 10 years among TDF-treated suggests TDF should be used cautiously in patients at higher risk of renal impairment, particularly those older than 50 years.**

Mak LY, et al. AASLD TLMdX 2020; Oral #21

Long term nucleos(t)ide analogue therapy reduced the extent of HBV DNA integration in chronic hepatitis B patients

BACKGROUND & AIMS

- HBV DNA integration has been associated with development of HCC in HBV-infected
- Impact of NAs on HBV DNA integration is unclear
- **AIM**: to study the effect of long-term NA treatment on the extent of HBV DNA integration in CHB patients



METHODS

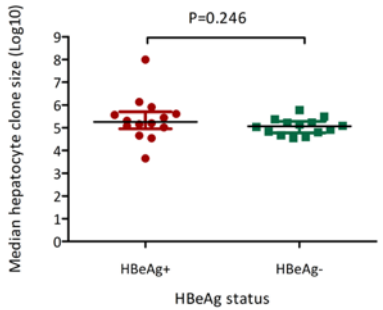
- Paired biopsy study (n=28)
  - Biopsies collected before treatment and 1 year after treatment
  - 5 had biopsy at 10 years
- Inverse PCR method used to identify integrated DNA
  - Identifies the viral-host junction
  - Presence of HBV-human DNA junctions was verified by Sanger sequencing
  - **Hepatocyte clone size** = the # of detectable bands containing a particular integration at the greatest dilution X dilution factor

Chow N, et al. AASLD TLMdX 2020; Oral #22

Long term nucleos(t)ide analogue therapy reduced the extent of HBV DNA integration in chronic hepatitis B patients

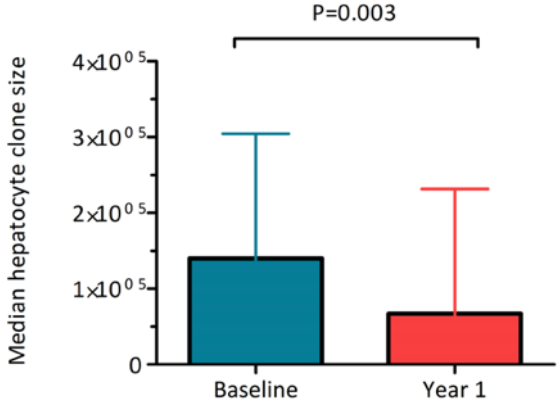
RESULTS

- Patient characteristics
  - 14 HBeAg-positive and 14 HBeAg-negative
  - 75% male
  - Mean age 40 years
  - Treatment: lamivudine (11), telvibudine (7), entecavir (10)
- Integration was detectable in all baseline and 1-year biopsies



No correlation between hepatocyte clone size and:

- Pre-treatment HBeAg status, age, serum and intrahepatic HBV DNA, cccDNA
- On-treatment reduction in serum and intrahepatic HBV DNA



- Median 42.5% reduction in median clone size between baseline and 1-year biopsies
- 3 of 5 10-year biopsies had undetectable HBV DNA integration

CONCLUSION **Therapy with NAs significantly reduced the clone size of infected hepatocytes, with long-term NUC therapy demonstrating marked impact on HBV DNA integration.**

Chow N, et al. AASLD TLMdX 2020; Oral #22

Tenofovir vs entecavir on post-operative recurrence-free and overall survival of patients with hepatitis B virus-related hepatocellular carcinoma

BACKGROUND & AIMS

- Studies suggest that TDF treatment may be associated with a significantly lower risk of HCC compared with ETV in patients with CHB
- **AIM**: to compare TDF and ETV on recurrence-free and overall survival among patients after curative hepatectomy for HBV-related HCC

METHODS

- Historical cohort study of 1,695 consecutive patients in Korea between 2010 and 2018
- After curative hepatectomy for HBV-related HCC (BCLC stage 0 or A), patients received NA therapy
  - ETV (n=813)
  - TDF (n=882)
- Recurrence-free and overall survival were compared between groups
  - Propensity score-matched analysis
  - Multivariable-adjusted Cox regression analysis

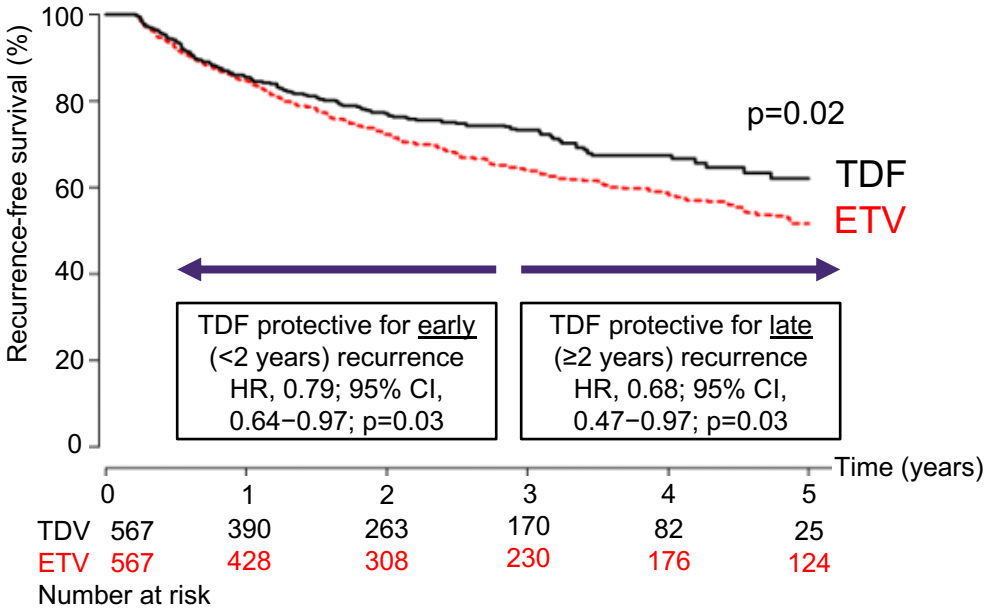
Choi J, et al. DILC 2020; AS094

Tenofovir vs entecavir on post-operative recurrence-free and overall survival of patients with hepatitis B virus-related hepatocellular carcinoma

RESULTS

- Mean age among patients was 54.8 years and 1,294 (76.3%) were male
- HCC recurrence was significantly less with TDF
  than with ETV (figure)
  - Median duration of follow-up: 37.6 months
- Overall mortality was significantly lower with TDF than with ETV
  - PS-matched analysis: p=0.03
  - Multivariable analysis: HR 0.62; 95% CI 0.44−0.88; p=0.01
- TDF therapy was an independent protective factor for both early and late HCC recurrence

Recurrence-free survival in the PS-matched patients



CONCLUSION **Among patients who undergo curative hepatectomy for HBV-related HCC, TDF therapy was associated with significantly better recurrence-free and overall survival vs ETV therapy.**

Choi J, et al. DILC 2020; AS094

Tenofovir alafenamide fumarate therapy for the prevention of hepatitis B vertical transmission in highly viremic mothers with chronic hepatitis B

BACKGROUND & AIMS

- Prevention of mother-to-child transmission (MTCT) is critical to viral elimination
- TAF has a better safety profile compared to TDF
- **AIM**: to investigate the efficacy and safety of TAF to prevent vertical transmission of CHB

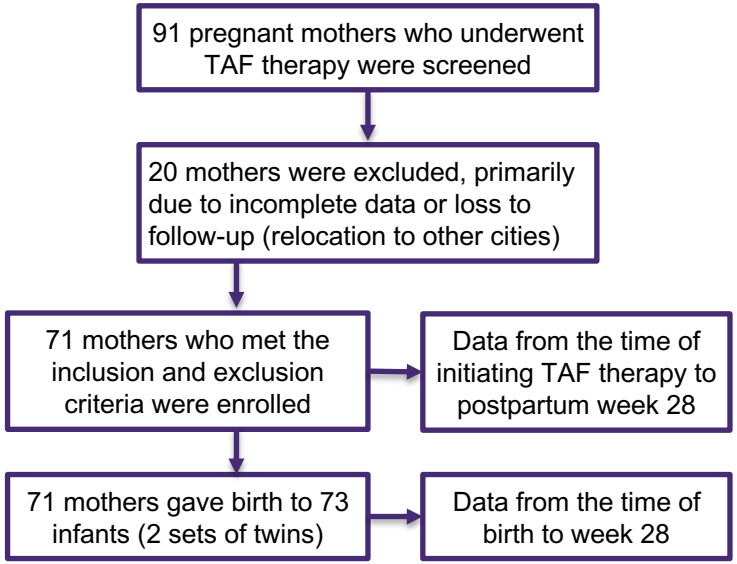
METHODS

- Multicenter, single-arm, retrospective real-world cohort study
  - 7 centers across China
  - Included mothers older than 20, mono-infected, HBeAg-positive with HBV DNA>200,000 IU/mL
  - Received TAF from 2nd or 3rd trimester until delivery
- All infants received HBIG and HBV vaccine (birth, one and 6 months
- Primary endpoint: MTCT rate at 24-28 weeks of age
- Secondary endpoint: HBV DNA reduction at delivery, infant malformation rates, and adverse events up to post-partum 28 weeks

Ding Y, et al. AASLD TLMdX 2020; Oral #20

Tenofovir alafenamide fumarate therapy for the prevention of hepatitis B vertical transmission in highly viremic mothers with chronic hepatitis B

RESULTS



Maternal Treatment Effects with TAF

Variables	Baseline	Delivery	p value
HBV DNA	7.78 $\log_{10}$ IU/mL	4.1 $\log_{10}$ Iu/mL	<0.001
HBsAg titer	2.89	1.93	0.005
ALT	32.6 U/L	22.8 U/L	0.24
Creatinine	53 umol/L	56 umol/L	0.04

- At delivery 85.9% achieved HBV DNA <200,000 IU/mL
- All met primary end-point: 0% mother-to-child transmission, 0% congenital abnormalities
- At 24-28 weeks infant height, weight, head circumference comparable to national infant standards
- No serious adverse events in mothers or infants
- 66% breastfeeding - did not increase risk of infant HBV infection
- 15% of mothers had a post-partum ALT flare with ALT peak of 140 U/L

CONCLUSION **TAF may be another option to prevent HBV perinatal transmission but require more data, cost considerations, and long-term follow-up given well-established safety data with TDF.**

Ding Y, et al. AASLD TLMdX 2020; Oral #20

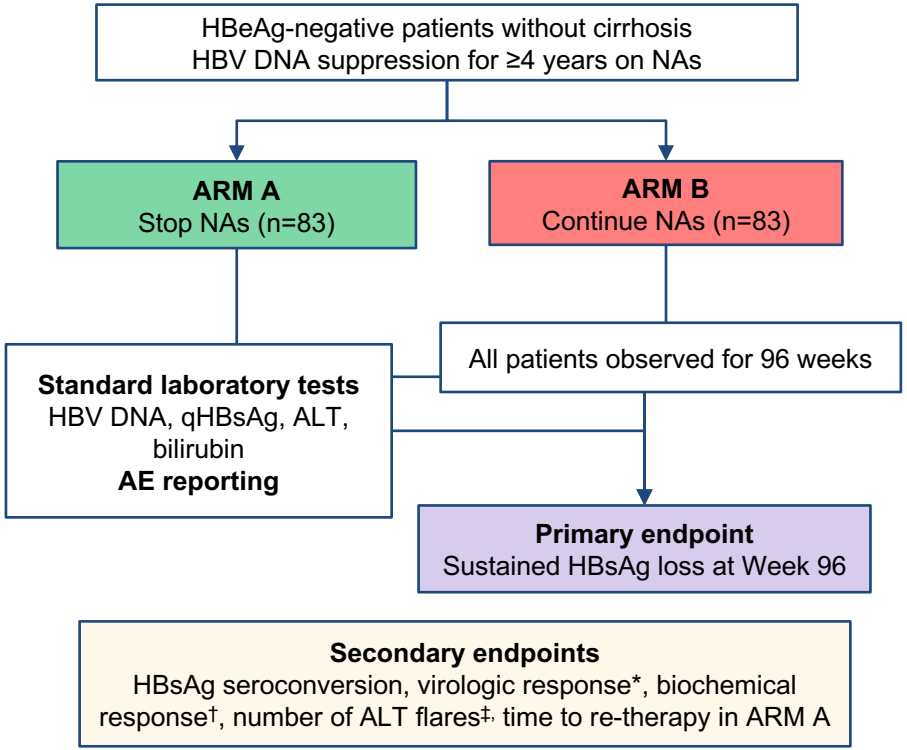
Updates on Withdrawal Therapy

Response to discontinuation of long-term nucleos(t)ide analogue treatment in HBeAg-negative patients: Results of the Stop-NUC trial

BACKGROUND & AIMS

- Discontinuation of long-term suppression of HBV replication with NAs can result in durable immune control of HBV replication in HBeAg-negative patients
- **AIM**: to assess the effect of NA discontinuation in HBeAg-negative patients in a prospective, multicentre, randomized trial
  - The Stop-NUC study (EudraCT-Nr.: 2013-004882-15)

METHODS



van Bömmel F, et al. DILC 2020; LBO06

Response to discontinuation of long-term nucleos(t)ide analogue treatment in HBeAg-negative patients: Results of the Stop-NUC trial

RESULTS

- Full analysis set: 79 patients in each arm
- HBsAg loss at Week 96 post-NA discontinuation
  - ARM A: 8/79 (10%)
  - ARM B: 0/79
- HBsAg loss at Week 96 post-NA discontinuation
  - ARM A: 6/79 (8%)
  - ARM B: 0/79

Predictive value of HBsAg levels at discontinuation

HBsAg loss	Baseline HBsAg <1,000 U/mL	Baseline HBsAg ≥1,000 U/mL	p value
No	18 (72%)	53 (98.1%)	0.001
Yes	7 (28%)	1 (1.9%)	

All patients in ARM A but none in ARM B experienced an HBV DNA flare >20 IU/mL after NA discontinuation

Parameter at Week 96	ARM A	ARM B	p value
HBV DNA ≤20 IU/mL	24/79 (31%)	79/79 (100%)	<0.001
ALT flare	28/79 (35%)	0	–
NA re-installed	11/79 (14%)	N/A	–
No NA indication†	54/79 (68%)	N/A	–

No patient in ARM A had a severe SAE possibly related to NA discontinuation

CONCLUSION **The STOP-NUC study demonstrates the potential of discontinuation of long-term NA treatment for inducing durable immune control and functional cure in HBeAg-negative patients.**

van Bömmel F, et al. DILC 2020; LBO06

Randomized trial of 192 weeks of tenofovir with or without peginterferon alfa for the first 24 weeks followed by protocolized withdrawal in adults with chronic HBV

BACKGROUND & AIMS

- Prior studies on NA withdrawal after prolonged treatment are limited by retrospective design and non-protocolized withdrawal and retreatment
- **AIM**: to evaluate safety and efficacy of 192 weeks of TDF alone or in combination with 24 weeks PEG-IFN alfa-2a followed by *protocolized treatment withdrawal*

Hepatitis B Research Network (HBRN) Immune-Active Trial
ClinicalTrials.gov ID NCT01369212

METHODS

HBeAg-negative or -positive with active disease on labs/biopsy
No prior antiviral therapy for ≥24 weeks

Day 0 to Week 192 Treatment Phase | **Week 192 to 240 Withdrawal Phase**

201 enrolled

- **TDF only N=102** → N=51 Withdrawn
- **TDF + Peg-IFN N=99** → N=60 Withdrawn

Withdrawal Criteria
- HBV DNA <1000 for 24 wks
- Absence of cirrhosis
- HBeAg negative by wk 144
- Anti-Hbe positive by wk 180

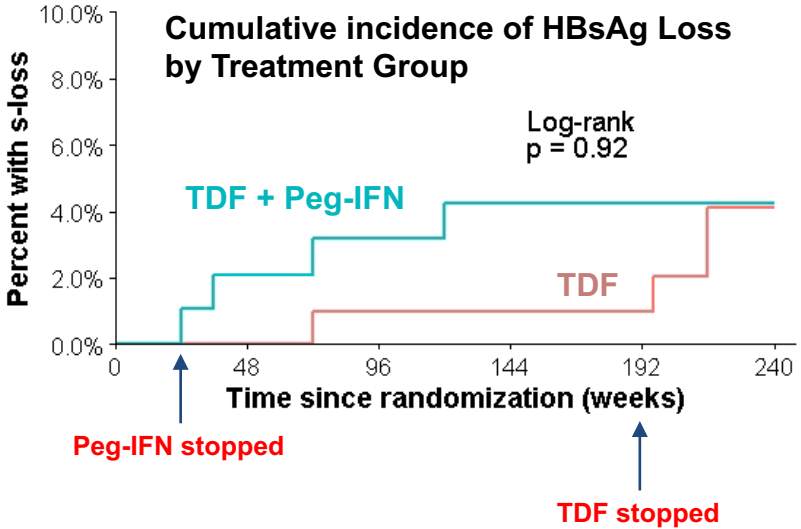
Retreatment Criteria
- Any clinical decompensation
- Tbili ≥3.0 or dbili ≥1.0
- HBV DNA≥10000 + ALT elevation

Primary endpoint: HBsAg loss
Secondary endpoints: HBeAg loss, ALT normalization, HBV DNA <20 and <1000, frequency of ALT flares and adverse events

Terrault N, et al. AASLD TLMdX 2020; Oral #19

Randomized trial of 192 weeks of tenofovir with or without peginterferon alfa for the first 24 weeks followed by protocolized withdrawal in adults with chronic HBV

RESULTS



Primary Outcome: HBsAg Loss

ITT Analysis	TDF N=102	TDF + Peg-IFN N=99	p value
Wk 192	1 (1.0%)	4 (4.3%)	0.21
Wk 240	4 (4.5%)	5 (5.7%)	0.74

Timing of ALT flares* by treatment group

	TDF	TDF + Peg-IFN
Participants with ALT flares	N=24 (24%)	N=31 (31%)
First 24 weeks	5 (19%)	19 (58%)
Week 24-192	3 (11%)	0 (0%)
Withdrawal phase TDF stopped	19 (70%)	14 (42%)
Withdrawal phase TDF continue	0 (0%)	0 (0%0

*ALT ≥300 (M) and ≥200 (F) AND >3x baseline

CONCLUSION **Achievement of HBsAg loss was not significantly enhanced by combination Peg-IFN for 24 weeks with long-term TDF followed by withdrawal, though longer follow-up is needed.**

Terrault N, et al. AASLD TLMdX 2020; Oral #19

HBsAg loss is higher among Caucasians compared to Asians after stopping nucleos(t)ide analogue therapy: results from a large, global, multi-ethnic cohort of patients with chronic hepatitis B (RETRACT-B Study)

BACKGROUND & AIMS

- Heterogeneity between studies questions feasibility of NA cessation with reported HBsAg loss ranging 0-47% across studies
- There is a need for analysis on a global scale for robust statistical power
- **AIM**: to evaluate clinical and virological outcomes following cessation of NA therapy in a large, global, multi-center, multi-ethnic cohort of patients with CHB

METHODS

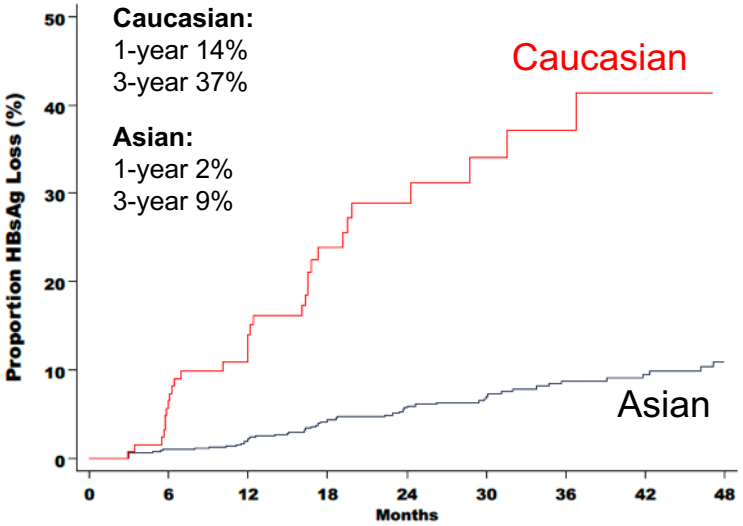
- Ongoing retrospective cohort study of CHB patients who discontinued NUC from 2001 - 2020
  - 12 participating centers in North America, Europe, Asia
- Inclusion / Exclusion
  - Inclusion: HBeAg negative and HBV DNA undetectable at time of NUC cessation
  - Excluded: co-infection with HCV, HDV or HIV, received Peg-IFN 1 year prior to NA cessation
- Primary outcomes: Off-treatment HBsAg loss and NA re-treatment
  - Predictors: age, sex, **race**, NA type, HBeAg status at start of therapy
  - Kaplan-Meier and Cox-regression

Hirode G, et al. AASLD TLMdX 2020; Oral #23

HBsAg loss is higher among Caucasians compared to Asians after stopping nucleos(t)ide analogue therapy: results from a large, global, multi-ethnic cohort of patients with chronic hepatitis B (RETRACT-B Study)

RESULTS

- N=1541 CHB patients who discontinued
- Mean age 53 y, 73% male
- **10% Caucasian, 88% Asian, 2% Other**
- 43% Genotype B (missing=43%)
- 77% HBeAg negative, 5% with cirrhosis
- Majority treated with ETV (60%) or TDF (29%)
- Off-treatment follow-up: 5 visits and median total follow-up 17 months
- Cumulative incidence of HBsAg loss of 12% and retreatment rate of 50% at 3-years
- Age over 50 years only predictor of retreatment
- *15 patients decompensated and 12 deaths during follow-up (9 liver-related)*



Race was the only independent predictor of HBsAg loss: 5.8 times higher among Caucasians compared to Asians (HR=5.8, 3.6-9.5).

CONCLUSION **Stopping long-term NUC Is feasible but close monitoring is essential and there is risk, albeit low of severe flares and even death. HBsAg loss appears to be higher in Caucasians.**

Brakenhoff S, et al. AASLD TLMdX 2020; Oral #158

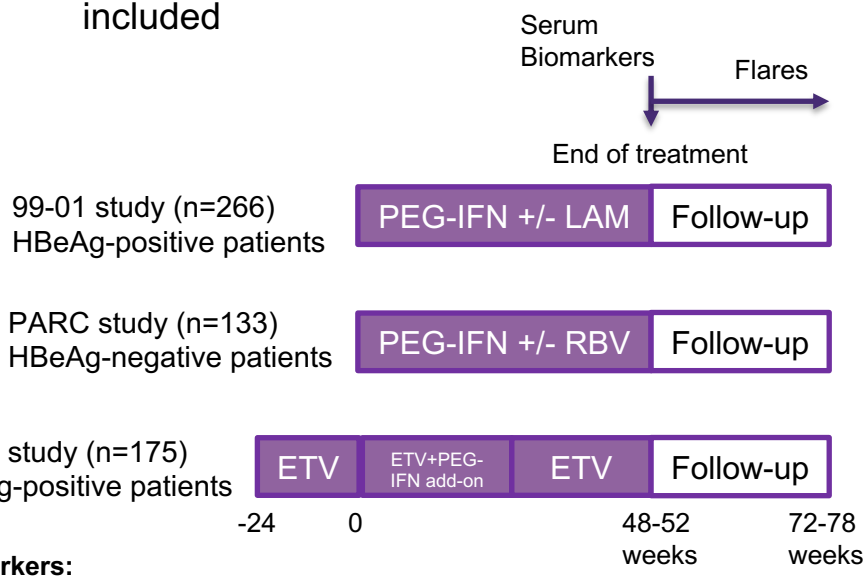
End of treatment HBsAg, HBcrAg and HBV RNA levels predict risk of off-treatment ALT flares in patients with chronic hepatitis B

BACKGROUND & AIMS

- Off-treatment ALT flares are frequently observed after treatment withdrawal
- Biomarkers for intrahepatic replication outside of HBV DNA (often low or undetectable) are needed to stratify risk of flares
- **AIM**: to assess whether serum HBsAg, HBcrAg, and HBV RNA at end of treatment can be used to predict risk of ALT flares and virological outcomes

METHODS

- Participants from three global RCTs were included



Serum biomarkers:
HBsAg (Abbott Architect)
HBcrAg (Lumipulse)
HBV RNA (RACE-based RT-PCR)

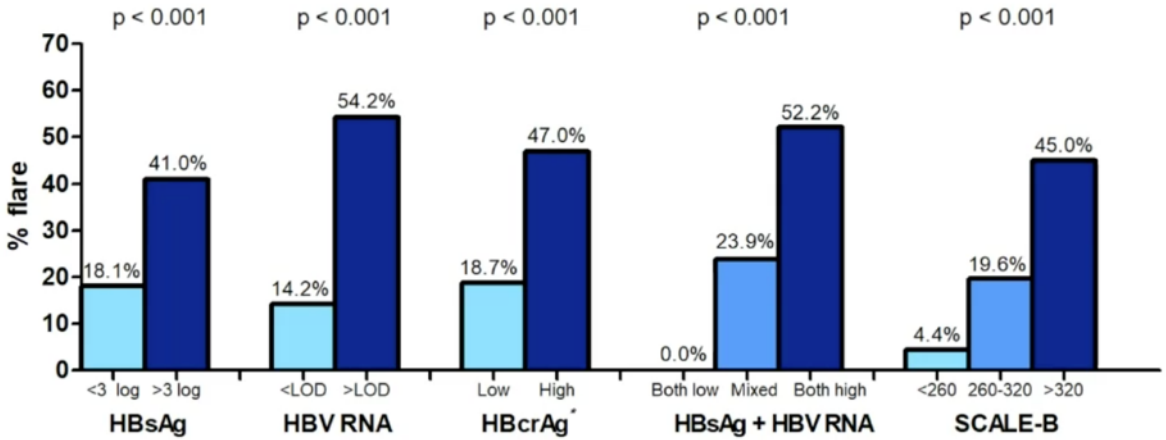
Flares:
ALT ≥ 5x ULN during the 1st six months after treatment cessation

Brakenhoff S, et al. AASLD TLMdX 2020; Oral #158

End of treatment HBsAg, HBcrAg and HBV RNA levels predict risk of off-treatment ALT flares in patients with chronic hepatitis B

RESULTS

Characteristics (N=344)	%
Age (median)	34
Male	75.3%
HBV Genotype A B C D	 23.3% 7.3% 13.4% 52.3%
Sustained response	16.6%
HBsAg loss	1.7%
ALT flare	35.5%

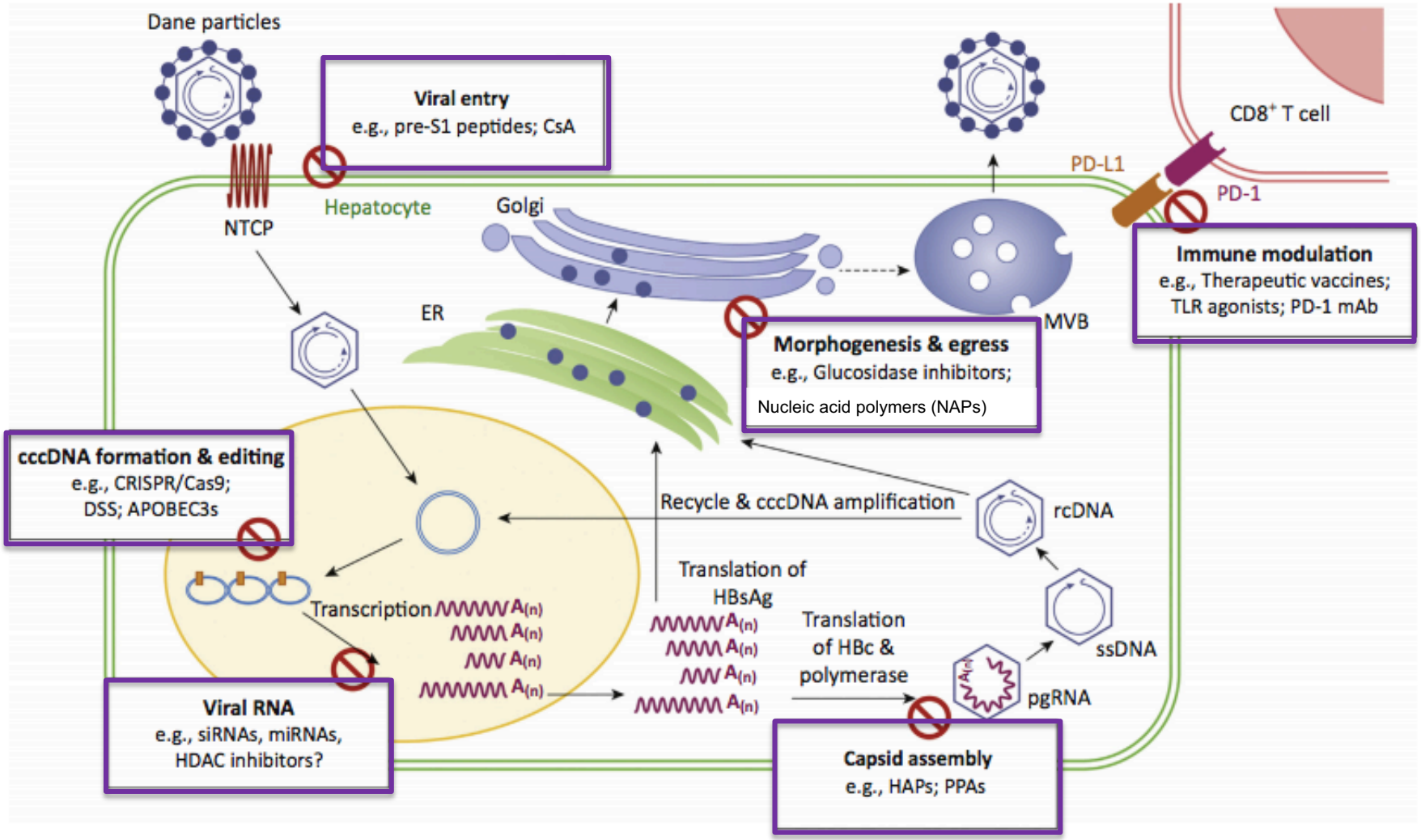


- ↑ biomarker levels were associated with ↑ ALT flares
- ↓ biomarker levels were associated with ↑ sustained response
- HBsAg loss was only observed in patients with low levels of biomarkers

CONCLUSION **Novel biomarkers may be utilized in clinical practice to select patients for finite therapy and identify those who require more intensive post-withdrawal monitoring for flares.**

Brakenhoff S, et al. AASLD TLMdX 2020; Oral #158

Updates on Novel Therapies


Dane particles
Viral entry
e.g., pre-S1 peptides; CsA
NTCP
Hepatocyte
Golgi
ER
MVB
CD8+ T cell
PD-L1
PD-1
Immune modulation
e.g., Therapeutic vaccines;
TLR agonists; PD-1 mAb
Morphogenesis & egress
e.g., Glucosidase inhibitors;
Nucleic acid polymers (NAPs)
cccDNA formation & editing
e.g., CRISPR/Cas9;
DSS; APOBEC3s
Recycle & cccDNA amplification
rcDNA
Translation of
HBsAg
Transcription
Translation
of HBc &
polymerase
ssDNA
pgRNA
Viral RNA
e.g., siRNAs, miRNAs,
HDAC inhibitors?
Capsid assembly
e.g., HAPs; PPAs

Short-term treatment with RNAi therapy, JNJ-3989, results in sustained HBsAg suppression in patients with chronic hepatitis B receiving nucleos(t)ide analogue treatment

BACKGROUND & AIMS

- RNAi therapy with JNJ-3989 silences HBV RNA transcripts from episomal cccDNA and integrated HBV DNA
- In a Phase 2a study in patients with CHB (AROHBV1001), treatment with JNJ-3989 (3 monthly doses 25–400 mg) + an NA demonstrated antiviral activity with reductions in serum viral parameters[1]
- **AIM**: to evaluate 9-month follow-up data for patients from AROHBV1001 treated with ≥100 mg JNJ-3989

METHODS

- 40 HBeAg+ or HBeAg-, NA-experienced or -naïve CHB patients received subcutaneous JNJ-3989 100, 200, 300 or 400 mg
  - on Days 1, 27 and 57
- All patients received an NA on Day 1 and continued throughout the study
- Safety and viral parameters were assessed
  - Viral parameters: HBsAg, HBeAg, HBV DNA, HBV RNA, HBcrAg
- For all parameters, sustained suppression was defined as a ≥1.0 $\log_{10}$ reduction from Day 1 or a value <LLOQ at Day 336
  - ~9 months after last dose of JNJ-3989

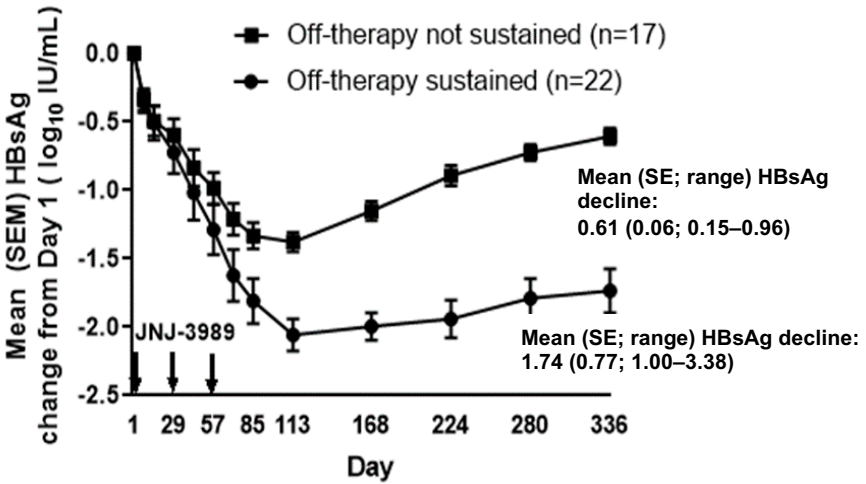
Gane EJ, et al. DILC 2020; GS10

Short-term treatment with RNAi therapy, JNJ-3989, results in sustained HBsAg suppression in patients with chronic hepatitis B receiving nucleos(t)ide analogue treatment

RESULTS

- Patient demographics:
  - 73% male; 85% Asian; median age 45 years*; 65% HBeAg-; 80% NA-experienced
- No deaths, treatment discontinuations or drug-related SAEs
  - Most common drug-related AEs were mild injection site AEs (17.5%)

JNJ-3989	100 mg	200 mg	300 mg	400 mg
Mean (SE) HBsAg nadir	1.72 (0.18)	1.79 (0.14)	2.04 (0.20)	1.90 (0.18)
≥1.0 log_{10} HBsAg reduction at nadir from Day 1, n (%)	39 (98) (range 1.11–3.77)			



- Sustained suppression of HBV RNA, HBeAg and HBcrAg was seen in 58%, 64% and 42% of patients with available data, respectively

CONCLUSION **JNJ-3989 (100–400 mg) with an NA was well tolerated with a ≥1.0 log_{10} reduction in HBsAg at nadir achieved in 98% of patients. A subset of patients had sustained HBsAg suppression ~9 months after the last RNAi dose.**

Gane EJ, et al. DILC 2020; GS10

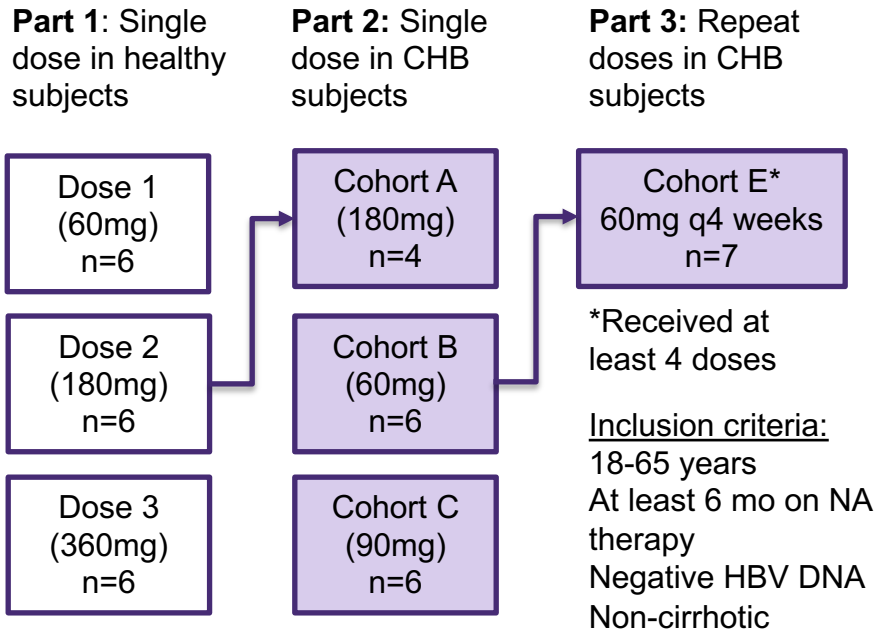
Safety and pharmacodynamics of the GalNAc-siRNA AB-729 in subjects with chronic hepatitis B infection

BACKGROUND & AIMS

- AB-729 is a RNAi agent with proprietary liver targeting technology based on GalNAc ligand interaction with ASGPr for subcutaneous drug delivery
- In preclinical models, AB-729 inhibited HBV replication, reduced all transcripts and lowered all HBV antigens, across genotypes
- **AIM**: to present preliminary safety and pharmacodynamic data on NA-treated virally suppressed patients with chronic HBV who received single or multiple dose regimens at varying dose levels/intervals

METHODS

- Phase I (open-label) study



Yuen MF, et al. AASLD TLMdX 2020; Oral #83

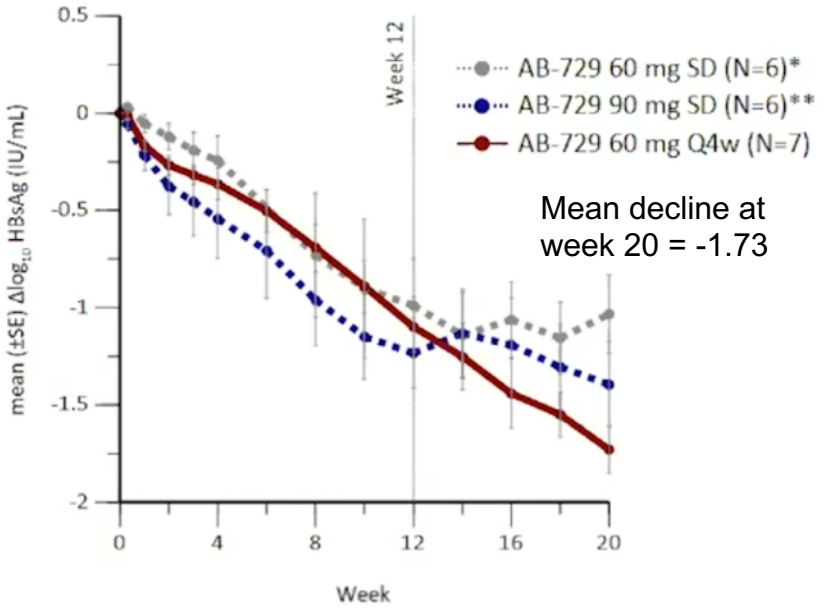
Safety and pharmacodynamics of the GALNAC-siRNA AB-729 in subjects with chronic hepatitis B infection

RESULTS

Characteristics and Outcomes by Dose Cohort

	60 mg	90 mg	180 mg	60 mg q4
Baseline mean HBsAg (IU/mL)	2095	822	8577	5372
Week 12 mean HBsAg decline	-0.99	-1.23	-1.10	-1.10
HBsAg <100 IU/mL	3/6	5/6	0/4	4/7
HBsAg <10 IU/mL	1/6	1/6	0/4	1/7

- No SAEs or discontinuations due to AEs
- No treatment-related Grade 3 or 4 AEs
- Injection site adverse events were mild or moderate and transient



CONCLUSION **For AB-729, mean HBsAg concentrations continuously declined up to week 12 before reaching a plateau with no clear dose response, supporting a dosing interval >4 weeks. Kinetics of HBsAg decline were similar between single and repeat dose cohorts.**

Yuen MF, et al. AASLD TLMdX 2020; Oral #83

Antiviral activity and safety of the hepatitis B core inhibitor ABI-H0731 administered with a nucleos(t)ide reverse transcriptase inhibitor in patients with HBeAg-negative CHB infection

BACKGROUND & AIMS

- While NRTIs are the standard of care for patients with CHB, on-treatment viral suppression is rarely followed by off-treatment sustained response
- The HBV core protein inhibitor ABI-H0731 in combination with an NRTI is currently being evaluated in Phase 2 clinical studies as finite treatment for CHB
- **AIM**: to present antiviral activity and safety for HBeAg-negative patients included in the double-blind, placebo-controlled ABI-H0731-201 study in NRTI-suppressed patients with CHB

METHODS

- **Inclusion criteria**:
  - HBV DNA ≤LLOQ for ≥6 months
  - HBsAg >1,000 IU/mL
  - ALT ≤ 5x ULN
  - Metavir F0−F2
- **Study design**:
  - Patients were randomized 3:2 for 24 weeks:
    - ABI-HO731 (300 mg QD) + NRTI
    - Placebo + NRTI
- **Efficacy endpoint**:
  - HBV DNA
  - HBV pgRNA
- **Safety endpoint**:
  - AEs
  - Laboratory abnormalities

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RESULTS

	ABI-H0731 + NRTI (N=16)		Placebo + NRTI (N=10)	
	Baseline	Week 24	Baseline	Week 24
HBV DNA (COBAS TaqMan 2.0), n (%)				
≥20 IU/mL	0	1 (6)	0	0
<20 IU/mL, TD	6 (38)	2 (13)	3 (30)	4 (40)
<10 IU/mL, TND	10 (63)	13 (81)	7 (70)	6 (60)
HBV DNA (LLOQ 5 IU/mL), n (%)				
TD	6 (38)	1 (6)	2 (20)	3 (30)
TND	10 (63)	15 (94)	8 (80)	7 (70)
HBV pgRNA (LLOQ 35 U/mL), n (%)				
<LLOQ	13 (81)	15 (94)	9 (90)	10 (100)
HBcrAg, mean (SD) in Log_{10} kU/mL	0.29 (0.90)	0.23 (0.81)	0.54 (0.70)	0.38 (0.87)
HBsAg, mean (SD) in Log_{10} IU/mL	2.99 (0.56)	3.09 (0.55)	3.35 (0.65)	3.35 (0.64)
ALT, mean (SD) in U/L	27 (14)	22 (7)	21 (10)	21 (12)

- Subjects were predominantly male (62%) and Asian (81%)
  - Mean (range) age was 48 (34–64) years
- More patients treated with ABI-H0731 + NRTI achieved HBV DNA TND vs placebo + NRTI
- AEs and laboratory abnormalities were similar in both treatment groups and were of mild/moderate severity
- No SAEs or discontinuations due to AEs were reported

CONCLUSION **24 weeks of treatment with ABI-H0731 + NRTI resulted in a higher proportion of HBeAg- patients achieving viral suppression by highly sensitive assays compared with placebo + NRTI, with a favorable safety and tolerability profile.**

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HBsAg reduction by nasal administration of a therapeutic vaccine containing HBsAg and HBcAg (NASVAC) in patients with chronic HBV infection: the results of 18 months follow up

BACKGROUND & AIMS

- NASVAC is an experimental therapeutic vaccine that targets HBsAg and HBcAg
- Follow-up data after NASVAC nasal vaccine administration up to 6 months were presented in 2019, demonstrating a 16-18% reduction in HBsAg levels
- **AIM**: to present updated data for the impact of NASVAC on anti-HBs induction and HBsAg reduction at 18 months of follow-up

METHODS

- At total of 71 subjects received 10 doses of NASVAC (once every 2 weeks) through an open-label clinical trial in Japan
  - 29 were on NA therapy; 22 reached the 18-month mark
  - 42 were treatment-naïve carriers; 33 reached 18-months
- Outcomes at 18-months:
  - HBsAg reduction rate
  - Anti-HBs positivity
  - HBsAg loss

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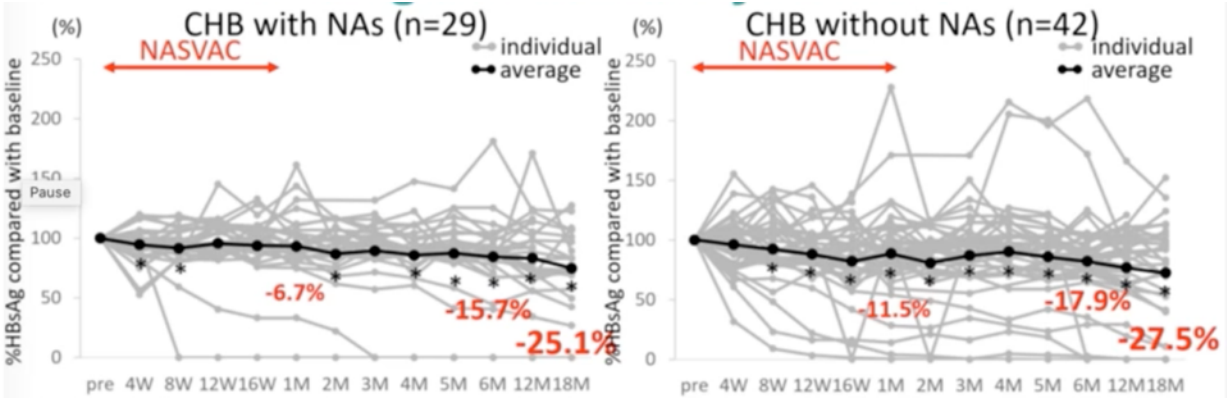
RESULTS

- Patient demographics:
  - NA group: 70% men, median 54 years, 75% HBeAg-neg
  - Untreated: 50% women, median 53 years, 95% HBeAg-neg
  - Most HBV GT C
- There were no severe AEs
- HBV DNA remained suppressed in the treated group and decreased about 19% in untreated
- HBcrAg declined slightly but change was not statistically significant



Outcome	6 mo	18 mo
HBsAg reduction	75.9%	72.3%
Anti-HBs positivity	34.5%	31.8%
HbsAg loss	6.9%	9.1%

6 mo	18 mo
76.2%	78.9%
59.5%	57.6%
4.8%	12.1%

CONCLUSION **Longer follow-up showed better outcomes in HBsAg reduction and achievement of HBsAg loss. Nasal administration of NASVAC could be an effective and safe immune therapy for achieving functional cure.**

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Thank you!

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Hepatitis B SIG Presentation

HBV: Current Management Controversies and the Road to a Cure

Hepatitis Debrief