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VTP-300
HBV therapeutic progress and plans

Non-confidential data presentation

January 2022

This presentation includes express and implied “forward-looking statements,” including forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. Forward looking statements include all statements that are not historical facts, and in some cases, can be identified by terms such as “may,” “might,” “will,” “could,” “would,” “should,” “expect,” “intend,” “plan,” “objective,” “anticipate,” “believe,” “estimate,” “predict,” “potential,” “continue,” “ongoing,” or the negative of these terms, or other comparable terminology intended to identify statements about the future. Forward-looking statements contained in this presentation include, but are not limited to, statements about our product development activities and clinical trials, our regulatory filings and approvals, our ability to develop and advance our current and future product candidates and programs, our ability to establish and maintain collaborations or strategic relationships or obtain additional funding, the rate and degree of market acceptance and clinical utility of our product candidates, the ability and willingness of our third-party collaborators to continue research and development activities relating to our product candidates, our and our collaborators’ ability to protect our intellectual property for our products. By their nature, these statements are subject to numerous risks and uncertainties, including factors beyond our control, that could cause actual results, performance or achievement to differ materially and adversely from those anticipated or implied in the statements. You should not rely upon forward-looking statements as predictions of future events. Although our management believes that the expectations reflected in our statements are reasonable, we cannot guarantee that the future results, performance or events and circumstances described in the forward-looking statements will be achieved or occur. Recipients are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date such statements are made and should not be construed as statements of fact.

Certain information contained in this presentation and statements made orally during this presentation relate to or are based on studies, publications, surveys and other data obtained from third-party sources and our own internal estimates and research. While we believe these third-party studies, publications, surveys and other data to be reliable as of the date of this presentation, it has not independently verified, and makes no representations as to the adequacy, fairness, accuracy or completeness of, any information obtained from third-party sources. In addition, no independent source has evaluated the reasonableness or accuracy of our internal estimates or research and no reliance should be made on any information or statements made in this presentation relating to or based on such internal estimates and research.

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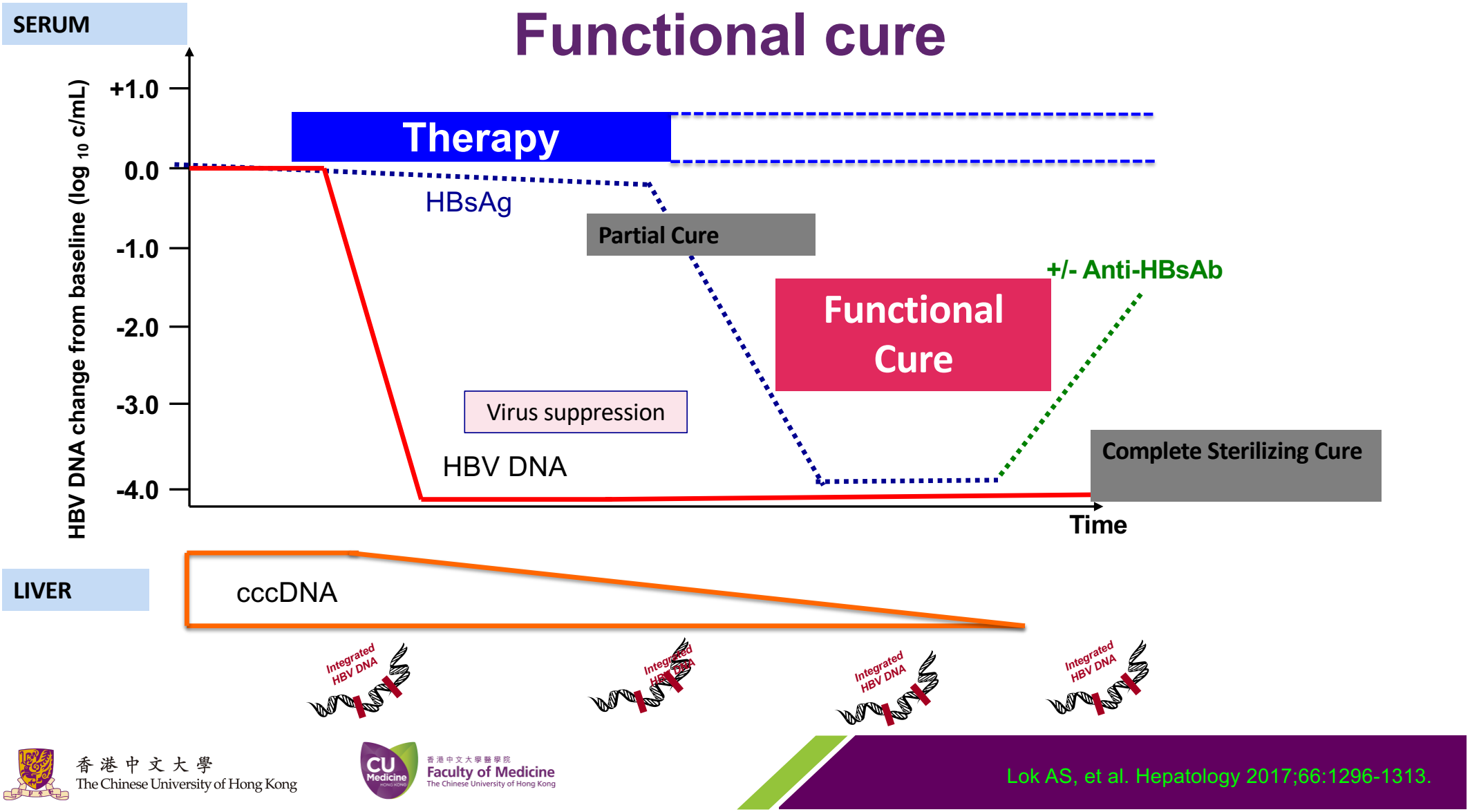
The progress to chronic HBV functional cure

Dr Henry LY Chan

Functional cure



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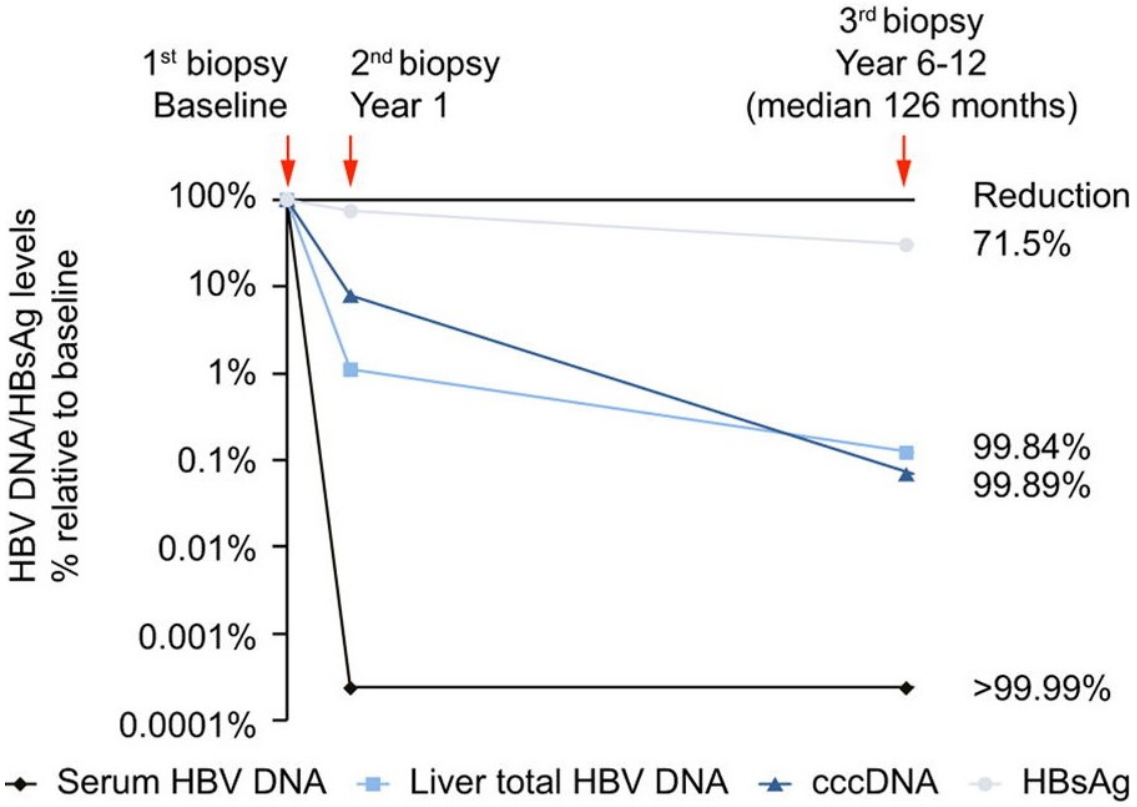
Lok AS, et al. Hepatology 2017;66:1296-1313.

Continuous HBV DNA suppression can slowly deplete cccDNA but is insufficient to lead to HBsAg loss



43 chronic hepatitis B patients on continuous NA therapy with undetectable HBV DNA

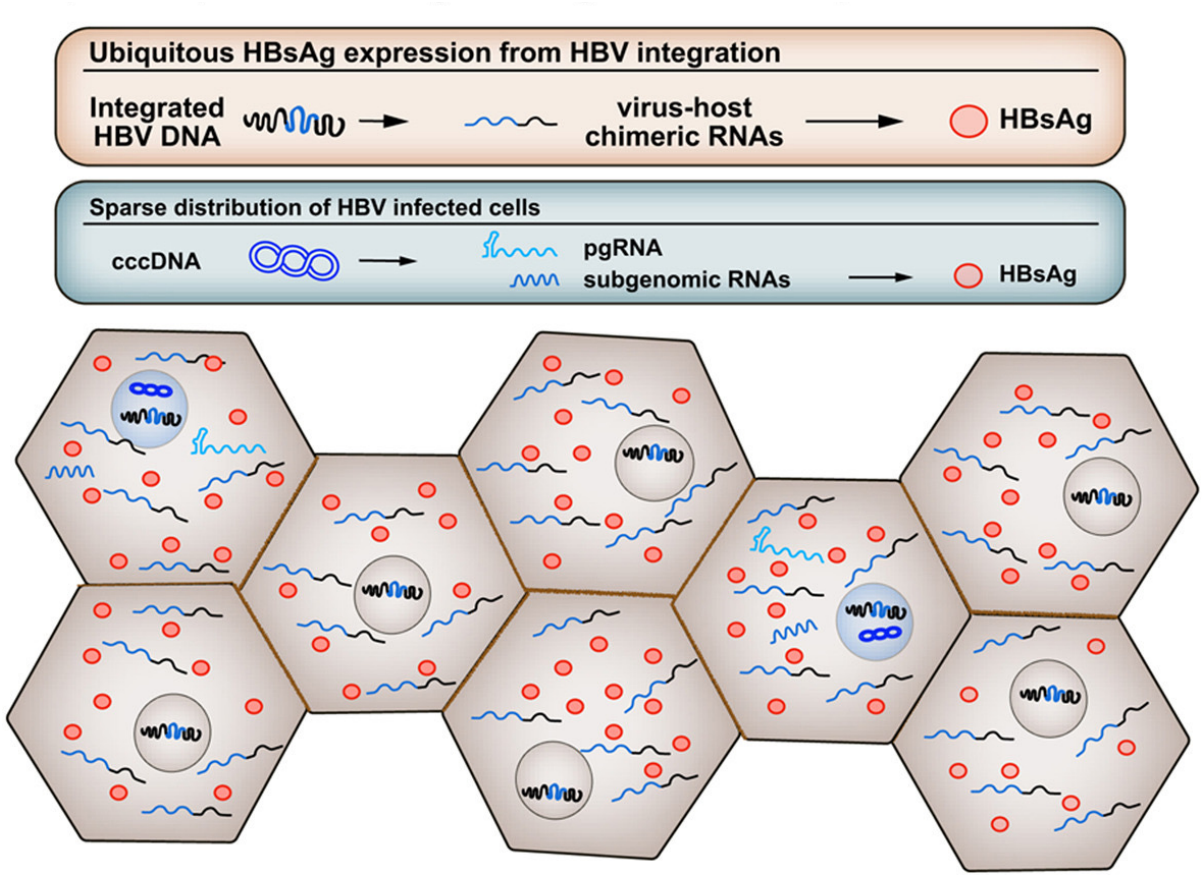
Compared to baseline levels, there was reduction of

- HBsAg levels by 0.54 log (71.46%)
- ihHBV DNA levels by 2.81 log (99.84%)
- cccDNA levels by 2.94 log (99.89%)

49% having cccDNA levels below the detection limit; 1 patient had HBsAg loss

Lai CL, et al. J Hepatol 2017;66:275-81.

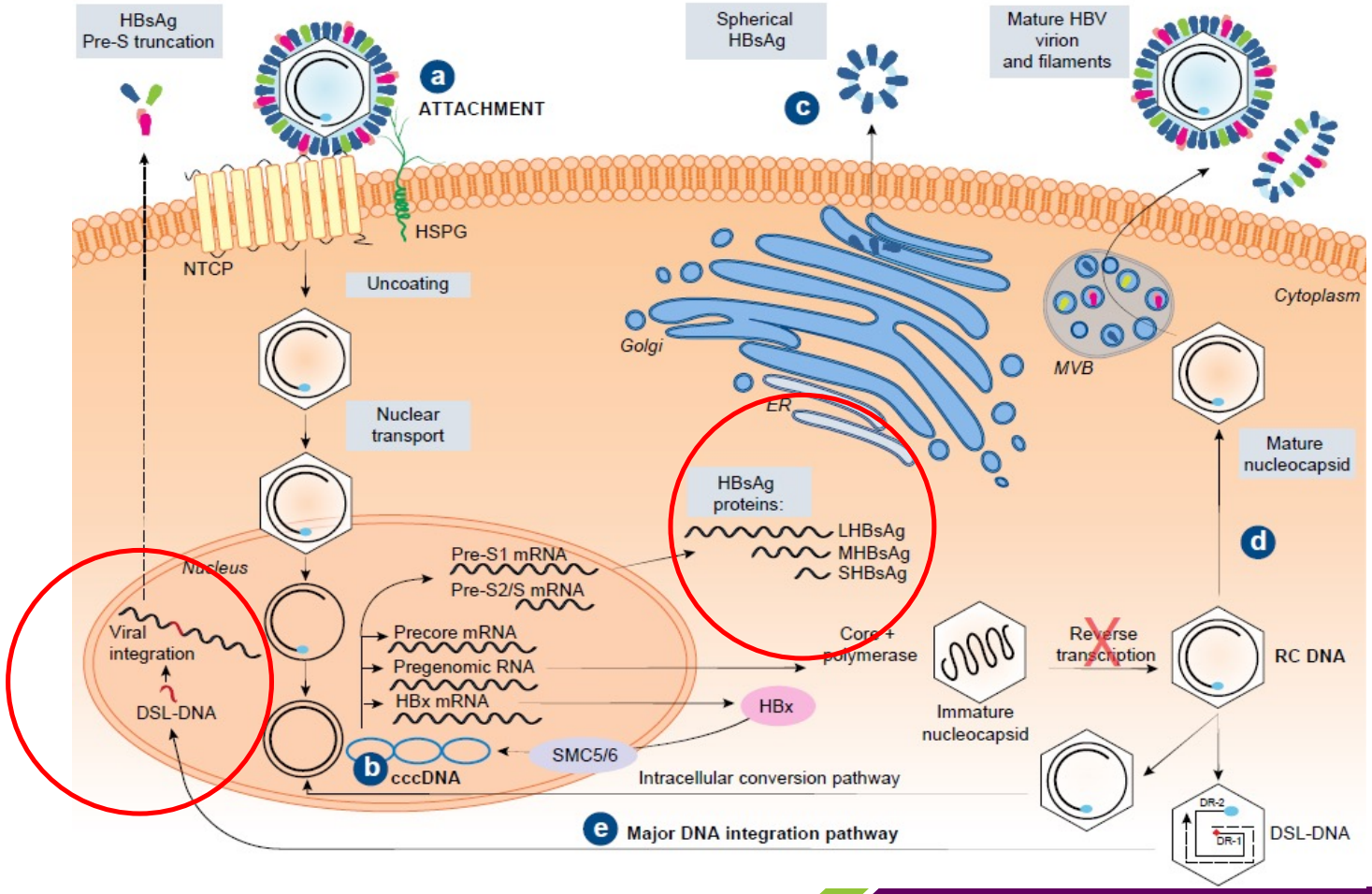
HBsAg derived from integrated HBV DNA in HBeAg negative patients with low viral load



- HBV RNA and antigen expression are ubiquitous in the liver despite low viremia.
- Levels of the viral transcriptional template cccDNA are not sufficient for ubiquitous HBV RNA and antigen expression.
- Ubiquitous viral antigen expression is associated with virus-host chimeric transcription.
- Intrahepatic viral DNA and RNA levels are consistent with widespread HBV integration.

Meier MA, et al. J Hepatol 2021;75:840-7.

Functional cure = clearing of cccDNA + intrahepatic integrated HBV DNA



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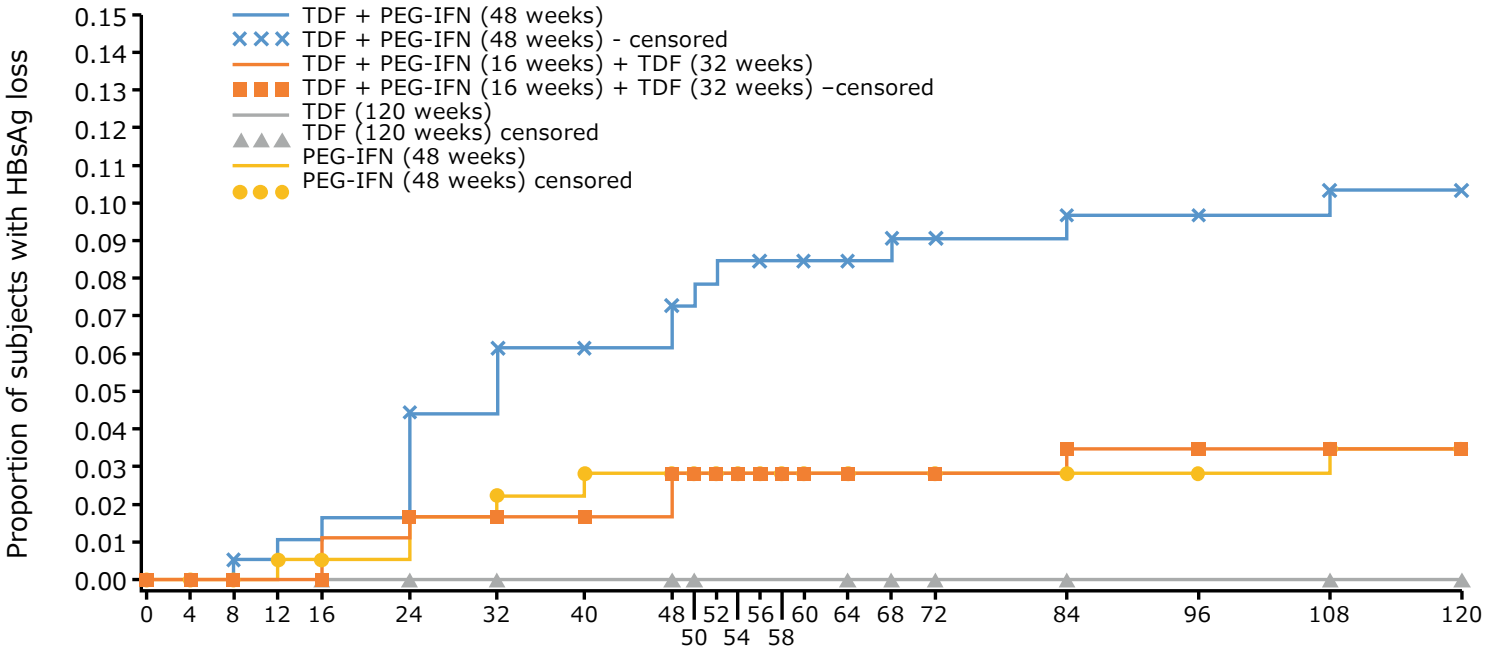
Cornberg M, … Chan HL. J Hepatol 2017;66:398-411

TDF and PEG-IFN combination may modestly increase HBsAg seroclearance



Number at risk

TDF+PEG-IFN(48weeks)	186	183	181	179	178	177	169	165	164	160	159	158	154	149	145	142	137	135	132
									161	159	158								
TDF+PEG-IFN(16weeks)+TDF(32weeks)	184	183	181	179	179	177	175	172	171	165	162	160	155	151	151	147	142	138	132
									167	164	161								
TDF(120weeks)	185	184	179	179	179	178	176	175	175	171	171	171	171	170	169	168	165	165	163
									173	171	171								
PEG-IFN(48weeks)	185	182	180	180	178	177	170	168	166	165	164	163	161	159	159	154	146	144	142
									165	165	163								

The rate of HBsAg loss in group A was significantly higher than rates in group C (P < 0.001) or group D (P = 0.002). The rate of HBsAg loss in group B did not significantly differ from that in group C or group D

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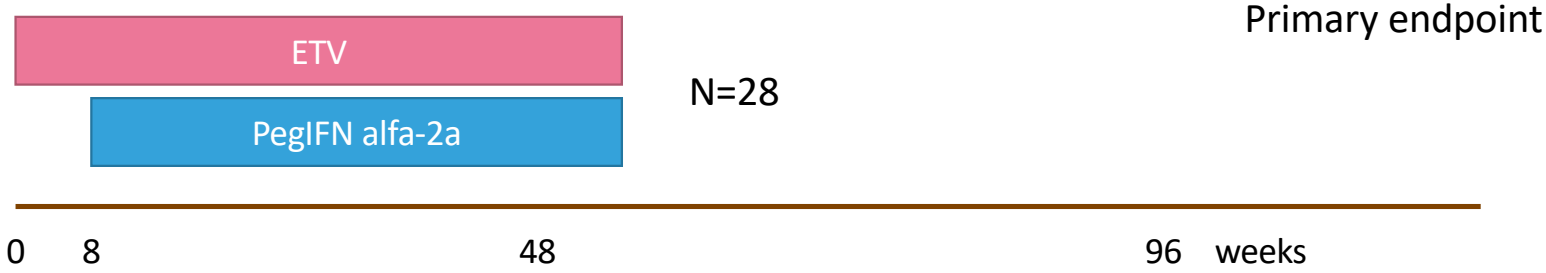
Ahn SH et al. *Dig Dis Sci.* 2018; 63: 3487-3497.

Poor response to ETV + PegIFN combination therapy in adults

Age >18 yo, HBeAg +ve,
HBV DNA > 7 log IU/ml,
ALT <1.5x ULN



	Week 48	Week 96
HBsAg loss	0%	0%
HBeAg seroconversion	4%	4%
HBV DNA <20 IU/ml	18%	0%
HBV DNA ≤1000 IU/ml	93%	0%

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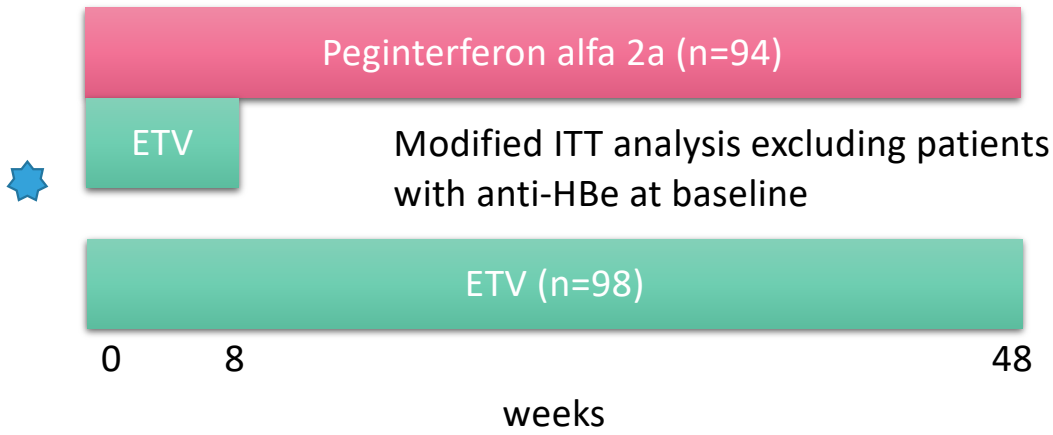
Feld JJ, et al. Hepatology 2019;69:2338-48.

Peginterferon increases HBeAg seroconverision and HBsAg loss among patients with low HBeAg title on ETV

HBeAg positive CHB on ETV x 9-36 mos
HBV DNA <1000 copies/ml + HBeAg <100 PEIU/ml



Outcome	Peginterferon α2a	Entecavir	P
HBeAg seroconversion	14.9%	6.1%	0.047
HBeAg loss	38.1%	33.3%	0.64
HBsAg loss	8.5%	0	0.0028
HBsAg seroconversion	4.3%	0	0.056

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Ning Q, et al. J Hepatol 2014;61:777

Low HBsAg at switch from ETV increases HBsAg loss to 1-year Peginterferon

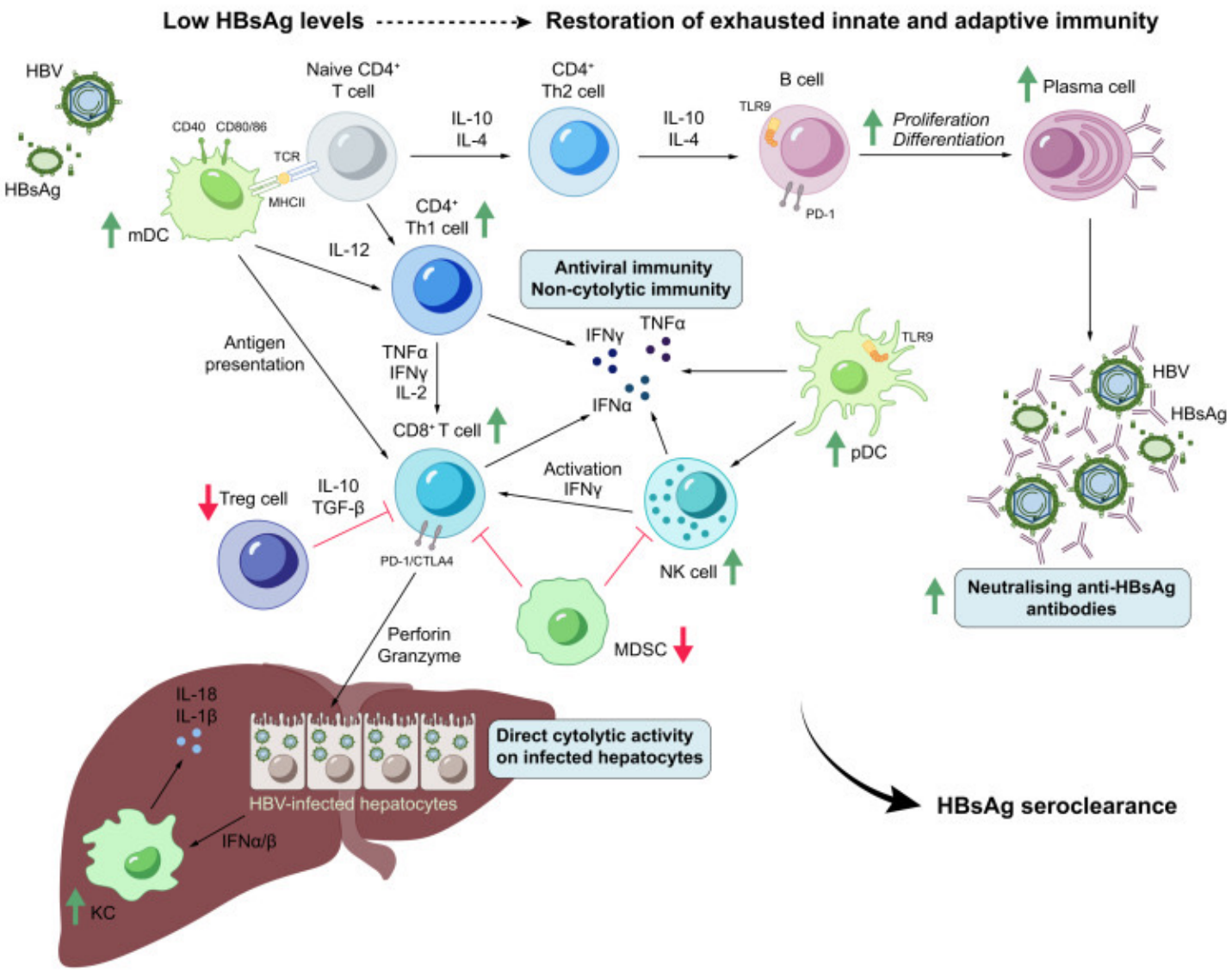
	Ning Q, et al	Wu P, et al	Chan HL, et al
Location	China	China	Hong Kong
N	94	303	41
HBeAg positive pts switched from ETV to PIFN	HBeAg <100 PEIU/ml	HBeAg loss	HBeAg seroconversion
HBsAg loss after 1-year peginterferon			
Overall	8.5%	11.5%	15%
HBsAg <1500 IU/ml	20%	25.4%	20%
HBsAg <500 IU/ml	-	-	50%

Ning Q, et al. J Hepatol 2014;61:777;
Hu P, et al. J Clin Transl Hepatol 2018;6:25-34;
Chan HL, et al. J Viral Hepat 2019;26:126-35.

Low viral load and HBsAg level is associated with best response to peginterferon

	De Niet	Cao	Li	Zeng
Location	Netherlands	China	China	China
Design	Open-label, RCT, prospective	Patient choice, prospective	Retrospective cohorts	Patient choice, prospective
Patient	HBV DNA <20000 IU/ml; ALT <5x ULN	HBeAg negative; HBV DNA <2000 IU/ml, ALT normal; HBsAg <1000 IU/ml	HBeAg negative; HBV DNA <100 IU/ml; ALT normal; HBsAg <100 IU/ml	HBeAg negative, HBV DNA <200 IU/ml; ALT normal; HBsAg <20 IU/ml
Treatment	PegIFN + ADV/TDF x 48 weeks	PegIFN x 72-96 weeks	PegIFN x 72 weeks	PegIFN x 48 weeks
HBsAg seroconversion	3%	38%	60%	94%

De Niet A, et al. Lancet Gastroenterol Hepatol 2017;2:576-84; Cao, et al. Hepatology 2017;66:1058-66; Li MH, et al. World J Gastroenterol 2016;8:637-43; Zeng QL, et al. Open Forum Infect Dis 2020;7:ofaa208.



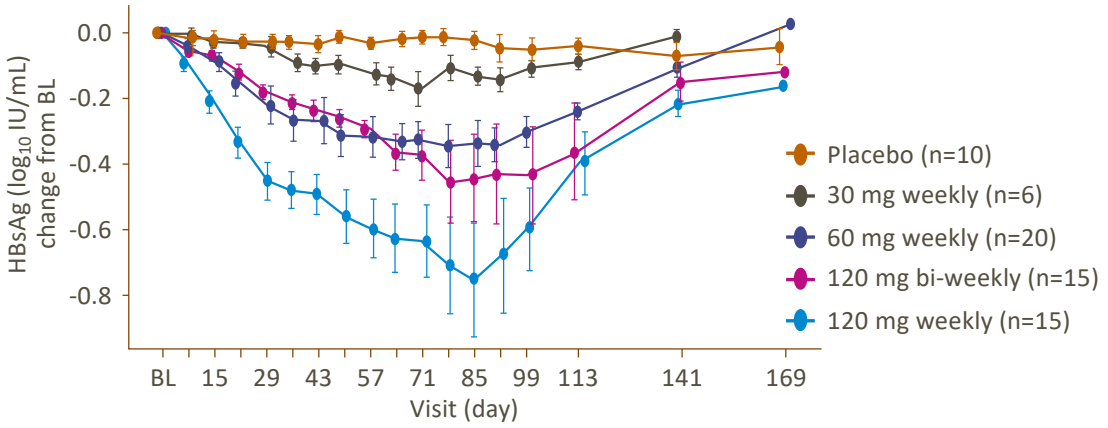
- HBsAg seroclearance is an immune mediated phenomenon that can be facilitated by a low HBsAg level
- Future HBV cure strategy
  - Reduction in HBsAg level
  - Boosting of immune response

Tout I, et al. J Hepatol 2020;73:409-22.

RNA interference by antisense oligonucleotide Early clinical data

- Phase 2a, multicenter, randomized, double-blind, placebo-controlled study in Asia-Pacific region
- Multiple-dose, 12 weeks SC injection of GSK3389404; HBeAg +/- NA treated non-cirrhotic CHB patients with HBsAg >50 IU/ml and ALT ≤2x ULN

Dose-dependent change from BL in HBsAg (log_{10} IU/mL) over time



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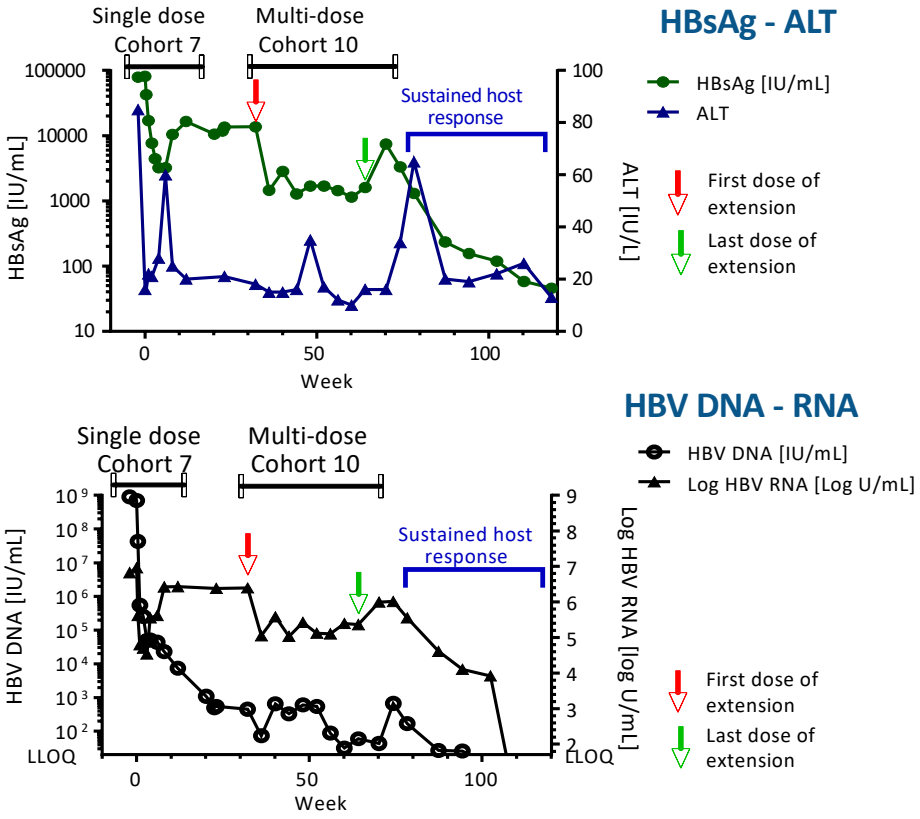
Yuen M-F, et al. AASLD 2019, Boston, USA. #695

RNA interference therapy with ARC-520 injection leads to HBsAg reduction, triggering a flare preceding functional cure

Case study: HBeAg positive patient with HBsAg seroclearance



- 8 CHB (5 HBeAg-neg, 3 HBeAg-pos) received up to 9 doses of 4 mg/kg ARC-520 once every 4 weeks with daily ETV; ETV continued post ARC-520 and followed for a further 12 months after last ARC-520 dose
- 1 HBeAg positive and 1 HBeAg negative patient achieved HBsAg loss
- Mild ALT elevations off ARC-520 therapy coincided with sustained host responses in 2/3 HBeAg-positive and 2/5 HBeAg negative patients

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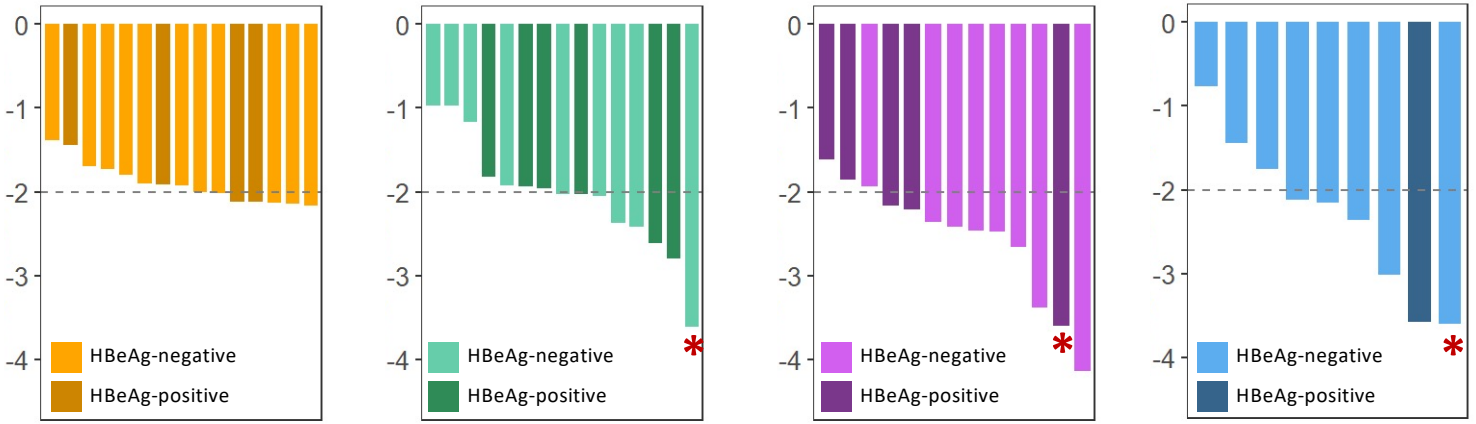
Yuen MF, et al. Gut 2021 [Epub ahead of print].

Concurrent Initiation of VIR-2218 and PEG-IFNα Combination Achieved Greatest Reductions in HBsAg Through Week 24

	Cohort 1	Cohort 2	Cohort 3	Cohort 4
	VIR-2218 only	**VIR-2218 lead-in + PEG-IFNα (12 wk)**	**VIR-2218 + PEG-IFNα (24 wk)**	**VIR-2218 + PEG-IFNα (≤ 48 wk)**
Week 4, n	15	15	17	13
Mean Change in HBsAg (log_{10} IU/mL)	-0.51	-0.51	-0.92	-1.01
Week 12, n	14	15	16	11
Mean Change in HBsAg (log_{10} IU/mL)	-1.39	-1.42	-1.98	-2.05
At Week 24, n	15	15	13	9
Mean Change in HBsAg (log_{10} IU/mL)	-1.89	-2.03	-2.55	-2.30

HBsAg change from baseline at Week 24 (log_{10} IU/mL)



*Participant achieved HBsAg < LLOQ (0.05 IU/mL)

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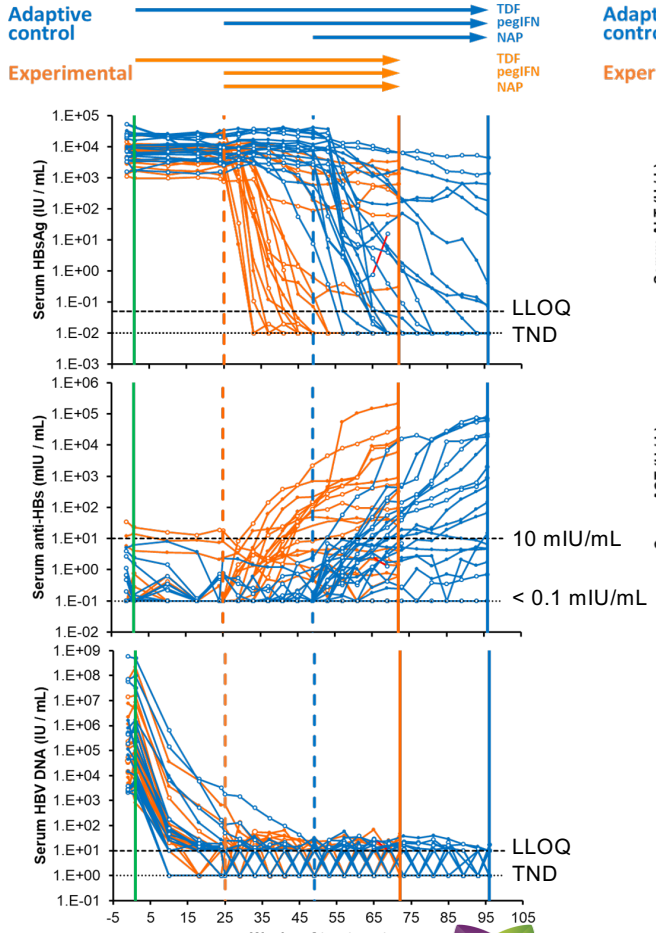
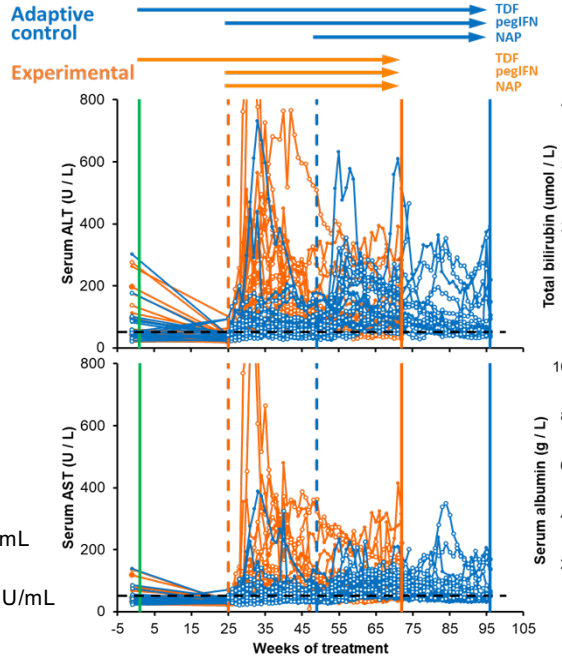
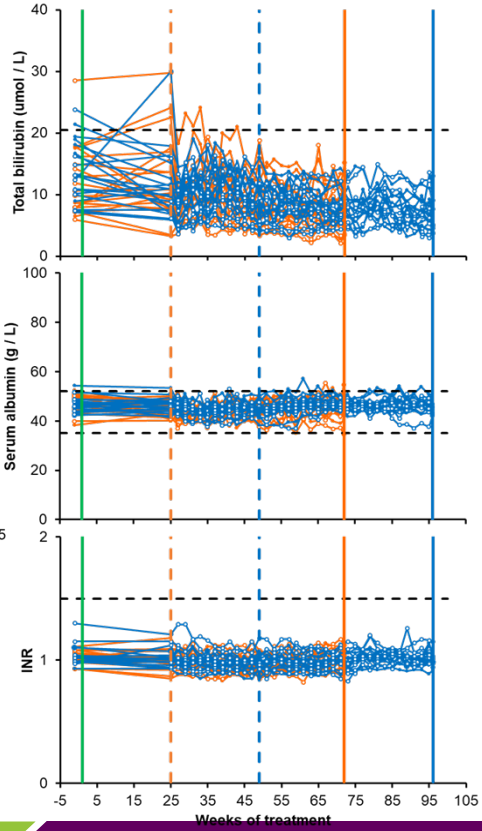
Sequential combination of nucleic acid polymer (iv REP 2139-Mg and REP 2165-Mg), TDF and pegIFN in HBeAg-negative CHB







HBsAg loss

- EOT 60%
- Post tx FU 42%

ALT elevation in 95% patients, correlated with initial HBsAg decline, self-resolved/declined with continuing NAP therapy

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Bazinet M, et al. Gastroenterology 2020;158:2180-94.

Approach to functional cure

Nucleos(t)ide analogues
?? Capsid assembly modulator (CAM)

? RNA interference (siRNA or ASO)
? Nucleic acid polymer (NAP)

? Therapeutic vaccine
? Anti-PD1/PD-L1
? TLR 7/8 agonist
? Peginterferon

The role of immunotherapeutics as a component of chronic HBV therapeutic combination

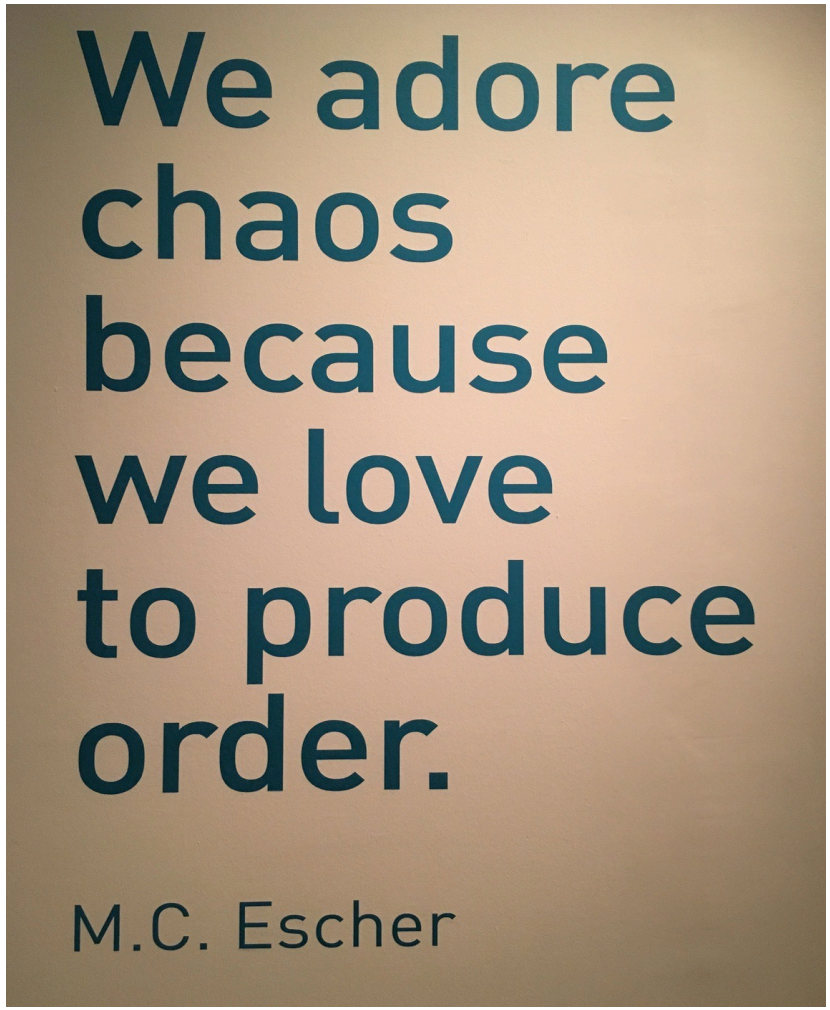
Dr Kosh Agarwal

Disclosures:

Advisory/ Speaker Bureau:

Arbutus/ Assembly/ Abbvie/ Aligos/ Biotest/Janssen/ Roche/ BI/ DrugFarm/ Gilead/GSK Intercept/ Immunocore/ Merck/ Springbank/ Shinoigi/ Sobi/ Vir

I am involved in multiple early phase studies



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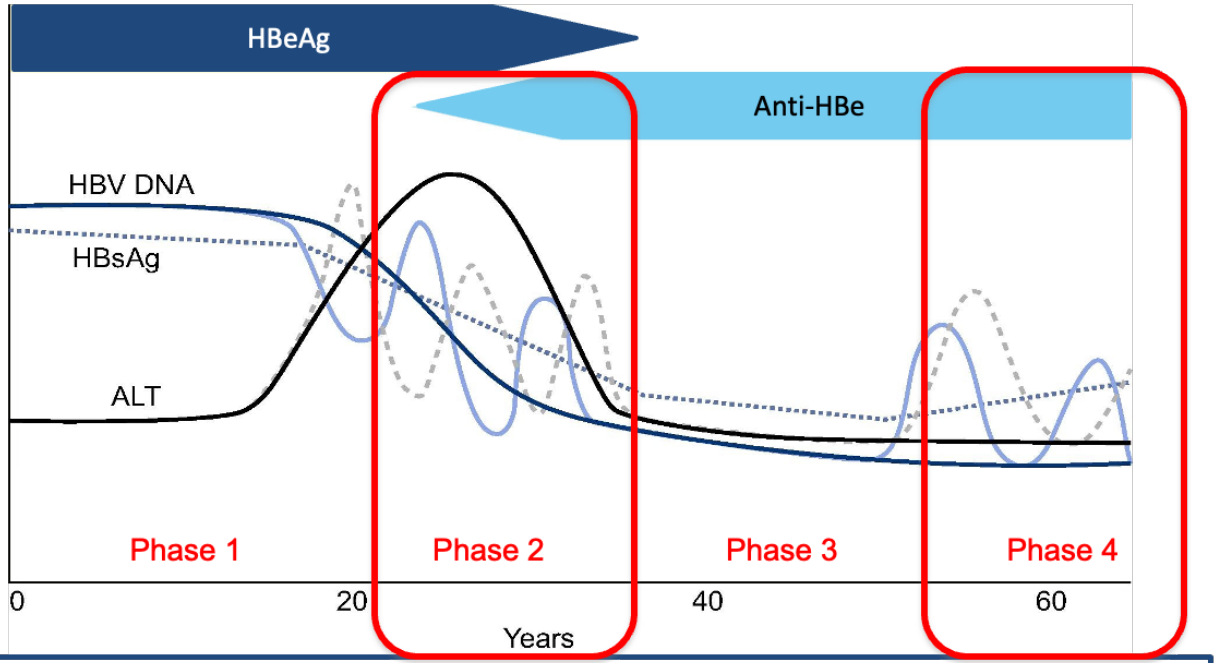
Phases of chronic HBV infection: infection vs hepatitis



New nomenclature	HBeAg-positive chronic HBV infection	HBeAg-positive chronic hepatitis B	HBeAg-negative chronic HBV infection	HBeAg-negative chronic hepatitis B
Old nomenclature	Immune tolerant	Immune reactive	Inactive carrier	HBeAg-negative chronic hepatitis

Lok A, et al. J Hepatol 2017;67:847–61;
EASL CPG HBV. J Hepatol 2017;67:370–98 – KEY MESSAGE – READ ME!

Garnering much information on HBV biomarkers this is translating into standard practice - soon

ORIGINAL ARTICLE

WILEY JVH

HBsAg and HBcrAg as predictors of HBeAg seroconversion in HBeAg-positive patients treated with nucleos(t)ide analogues

B. Wang[1] | I. Carey[1] | M. Bruce[1] | S. Montague[1] | G. Dusheiko[1,2] | K. Agarwal[1]

Multicenter Study > Aliment Pharmacol Ther. 2021 Mar;53(6):733-744. doi: 10.1111/apt.16258. Epub 2021 Jan 19.

Incremental value of HBcrAg to classify 1582 HBeAg-negative individuals in chronic infection without liver disease or hepatitis

Maurizia R Brunetto[1], Ivana Carey[2], Benjamin Maasoumy[3], Cristina Marcos-Fosch[4], André Boonstra[5], Gian Paolo Caviglia[6], Alessandro Loglio[7], Daniela Cavallone[1], Caroline Scholtes[8], Gabriele Ricco[1], Antonina Smedile[6], Mar Riveiro-Barciela[4], Florian van Bömmel[9], Annemiek van der Eijk[5], Fabien Zoulim[8], Thomas Berg[9], Markus Cornberg[3], Pietro Lampertico[7], Kosh Agarwal[2], Maria Buti[4]

HEPATOLOGY

AASLD

HEPATOLOGY, VOL. 72, NO. 1, 2020

Pregenomic HBV RNA and Hepatitis B Core-Related Antigen Predict Outcomes in Hepatitis B e Antigen–Negative Chronic Hepatitis B Patients Suppressed on Nucleos(T)ide Analogue Therapy

Ivana Carey[1], Jeffrey Gersch[2], Bo Wang[1], Christiana Moigboi,[1] Mary Kuhns[2], Gavin Cloherty,[2] Geoffrey Dusheiko[1], and Kosh Agarwal[1]

Clinical Gastroenterology and Hepatology aga

SYSTEMATIC REVIEWS AND META-ANALYSES

Hepatitis B Core-Related Antigen to Indicate High Viral Load: Systematic Review and Meta-Analysis of 10,397 Individual Participants

Published April 29, 2020 • DOI: https://doi.org/10.1016/j.cgh.2020.04.045

Clinical Gastroenterology and Hepatology 2021;■:■–■

Prediction of Sustained Response After Nucleo(s)tide Analogue Cessation Using HBsAg and HBcrAg Levels: A Multicenter Study (CREATE)

Milan J. Sonneveld,[*] Jun Yong Park,[‡] Apichat Kaewdech,[§] Wai-Kay Seto,[‖] Yasuhito Tanaka,[¶] Ivana Carey,[#] Margarita Papatheodoridi,[**] Florian van Bömmel,[‡‡] Thomas Berg,[‡‡] Fabien Zoulim,[§§] Sang Hoon Ahn,[†] George N. Dalekos,[‖‖] Nicole S. Erler,[¶¶] Christoph Höner zu Siederdissen,[##] Heiner Wedemeyer,[***] Markus Cornberg,[***] Man-Fung Yuen,[‖] Kosh Agarwal,[#] Andre Boonstra,[‡] Maria Buti,[***] Teerha Piratvisuth,[§] George Papatheodoridis,[**] and Benjamin Maasoumy,[***] for the CREATE Study Group

Clinical Infectious Diseases

BRIEF REPORT

IDSA hivma

Circulating Pregenomic Hepatitis B Virus RNA Is Primarily Full-length in Chronic Hepatitis B Patients Undergoing Nucleos(t)ide Analogue Therapy

Courtesy of I Carey KHP

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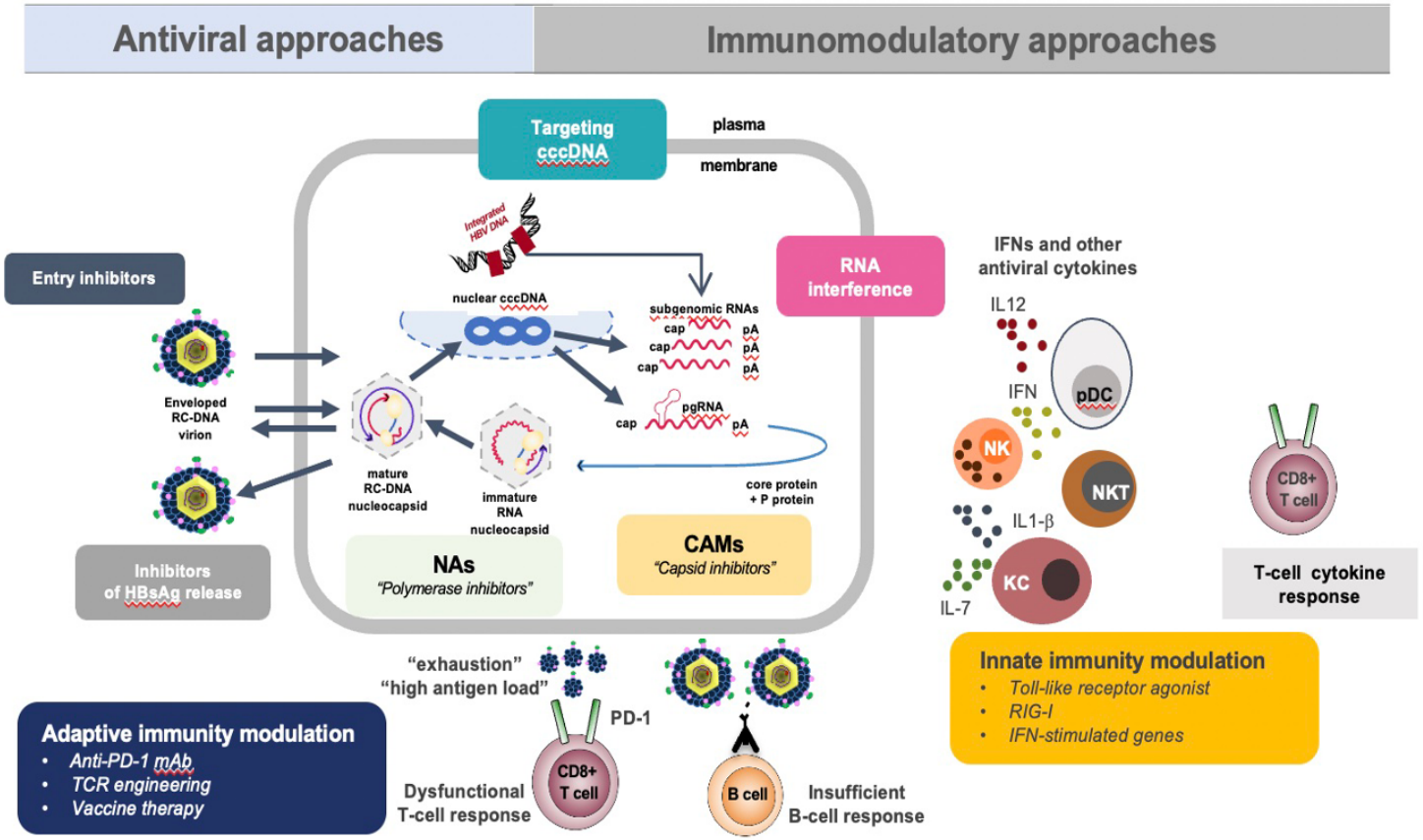

Figure adapted from Levrero M, et al. Curr Opin Virol 2016;18:135-143 and Brahmania B, Janssen HL. Lancet Infect Dis 2016;16(2):e10-e21. Reproduced with permission from Elsevier Inc.
cccDNA, covalently closed circular deoxyribonucleic acid; CAM, capsid assembly modulator; DNA, deoxyribonucleic acid; HBsAg, hepatitis B surface antigen; HBV, hepatitis B virus; IFN, interferon; IL, interleukin; NA, nucleos(t)ide analog; NKT, natural killer T cell; PD-1; programmed death 1; pDC, peripheral dendritic cell; TCR, T cell receptor; RIG-1, retinoic acid-inducible gene 1.

1. Levrero M, et al. Curr Opin Virol 2016;18:135-143. Brahmania B, Janssen HL. Lancet Infect Dis 2016;16(2):e10-e21.

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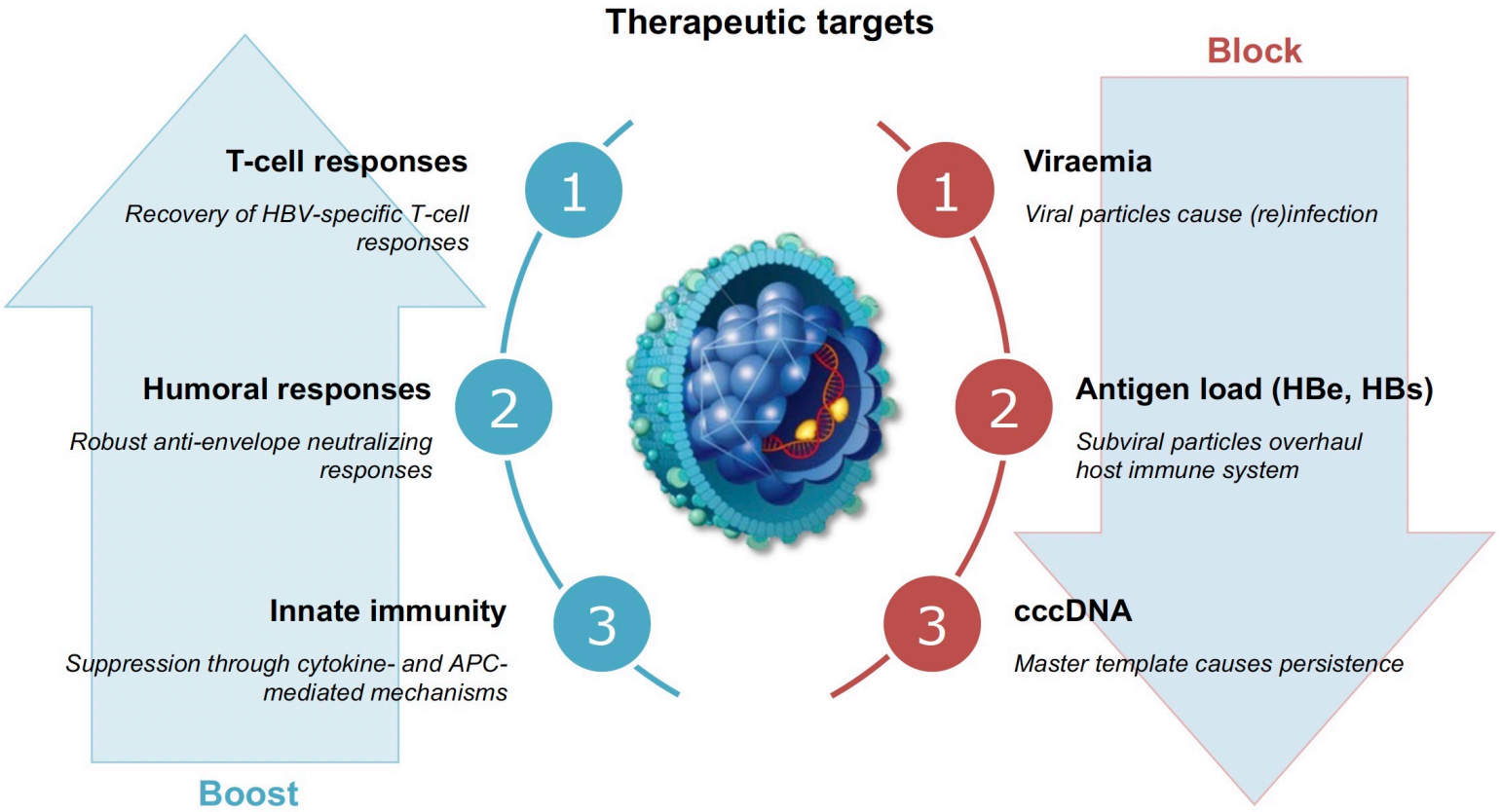
HBV Treatment Strategies



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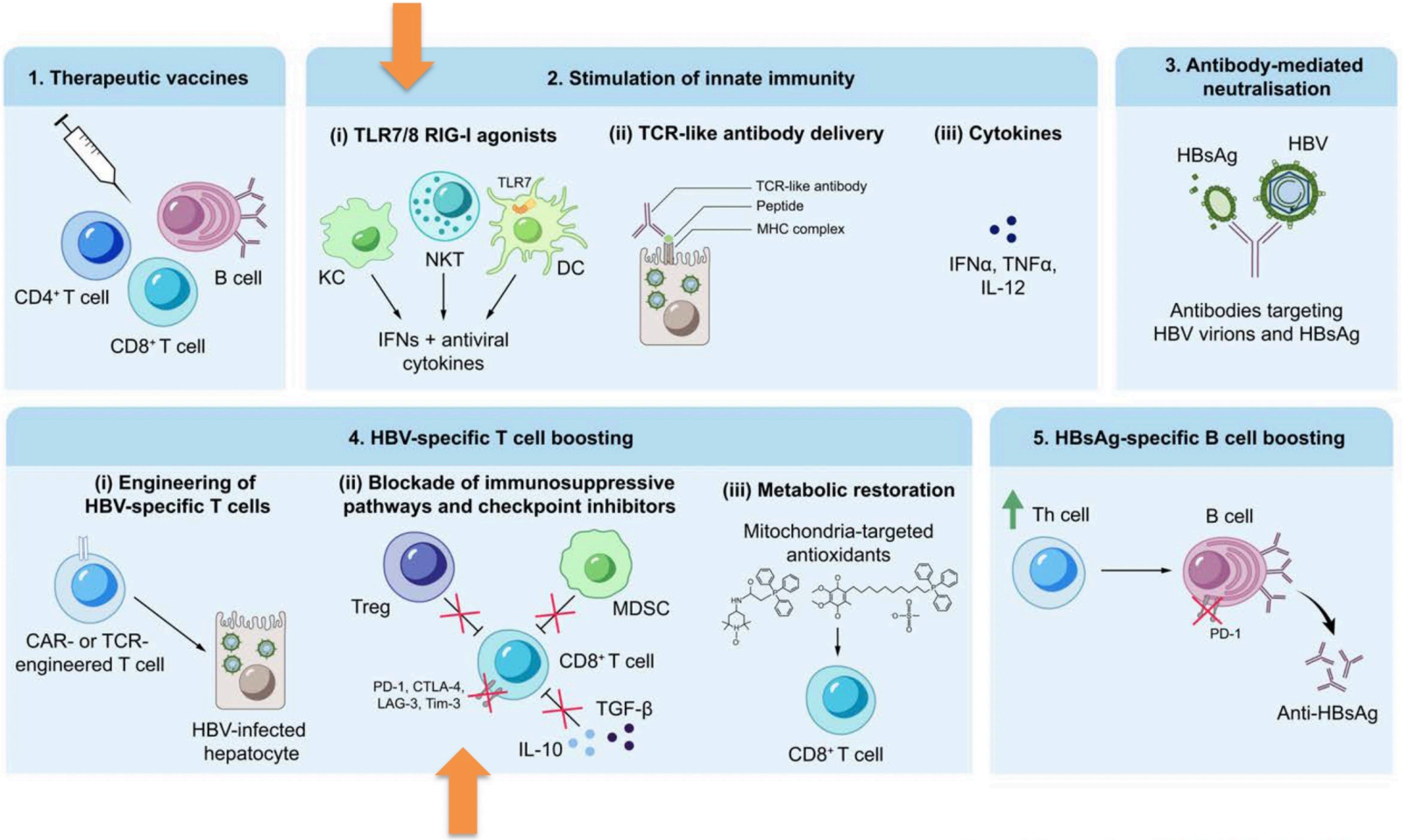
Overview of immune modulation therapies for HBV



Tout, J Hepatology 2020 73(2): 409-422

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An ideal therapeutic vaccination approach

Vaccine:

- *incorporating core, pol and surface antigens*
- *inducing multispecific broadly cross-reactive T cells*
- *inducing functional B cells and neutralizing antibodies*
- *accompanied by immunomodulation to overcome HBV-specific immune exhaustion*

Therapeutic vaccine trials in chronic hepatitis B

Homologous vaccines

-	HepT cell	peptide + adjuvant	Phase I
-	INO-1800	DNA-vaccine	Phase I
-	CVI-HBV-002	DNA-vaccine	Phase I/II
-	HB-110/100	DNA-vaccine	Phase I
-	ppdpSC18	DNA-vaccine	Phase I/II
-	HBO2-VAC-ADN	DNA-vaccine	Phase I/II
-	Theravax	protein + adjuvant	Phase Ib
-	GS-4774	protein + adjuvant	Phase II
-	ePA-44	peptide + adjuvant	Phase II
-	ABX 203	protein	Phase II/III
-	TG1050	adeno vector vaccine	Phase II

failed

Heterologous prime – boost vaccines

-	pSG2.HBs/MVAHBs	DNA-vaccine + MVA	Phase Ib/II (S only, no Ab) failed
-	***TherVac B***	**protein + MVA (broad)**	**preclinical PoC**

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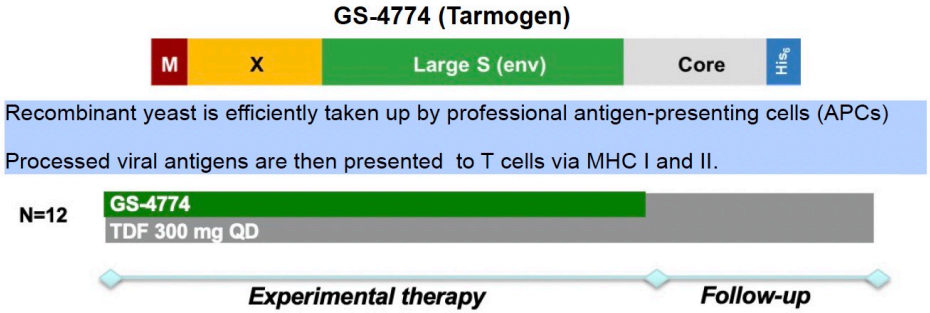
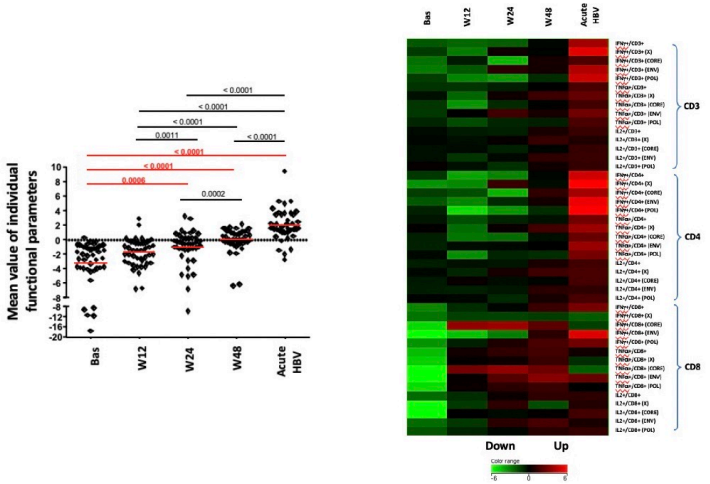
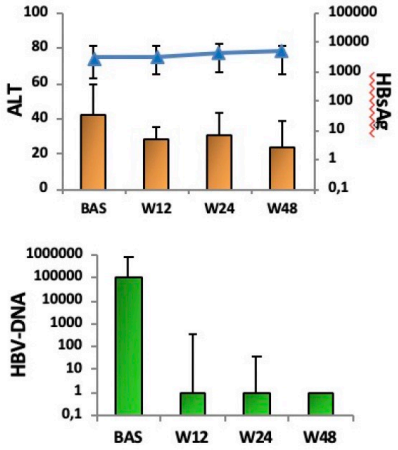
Therapeutic vaccines for chronic HBV infection







T cell responses are improved by vaccination but still remain much lower than after spontaneous resolution of infection

- All patients normalized ALTs, most became HBV-DNA neg
- No patients had HBsAg loss at week 48

Boni C. et al. Gastroenterology 2018

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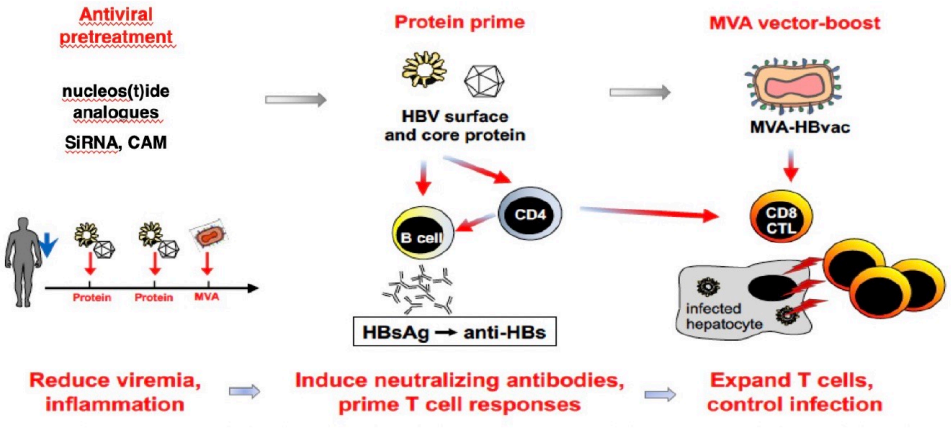
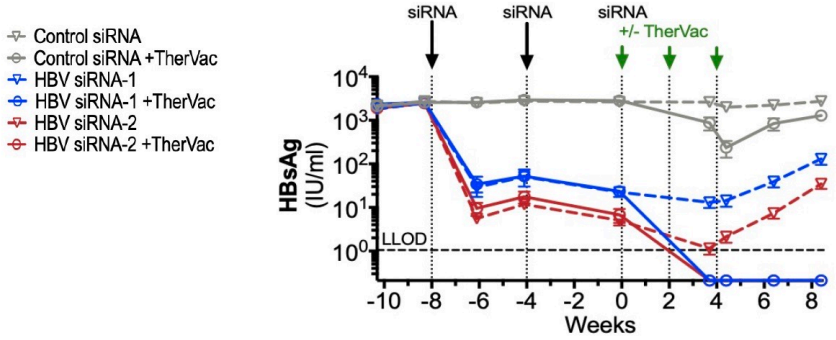
Response to *TherVac* is increased by prior decline of antigen

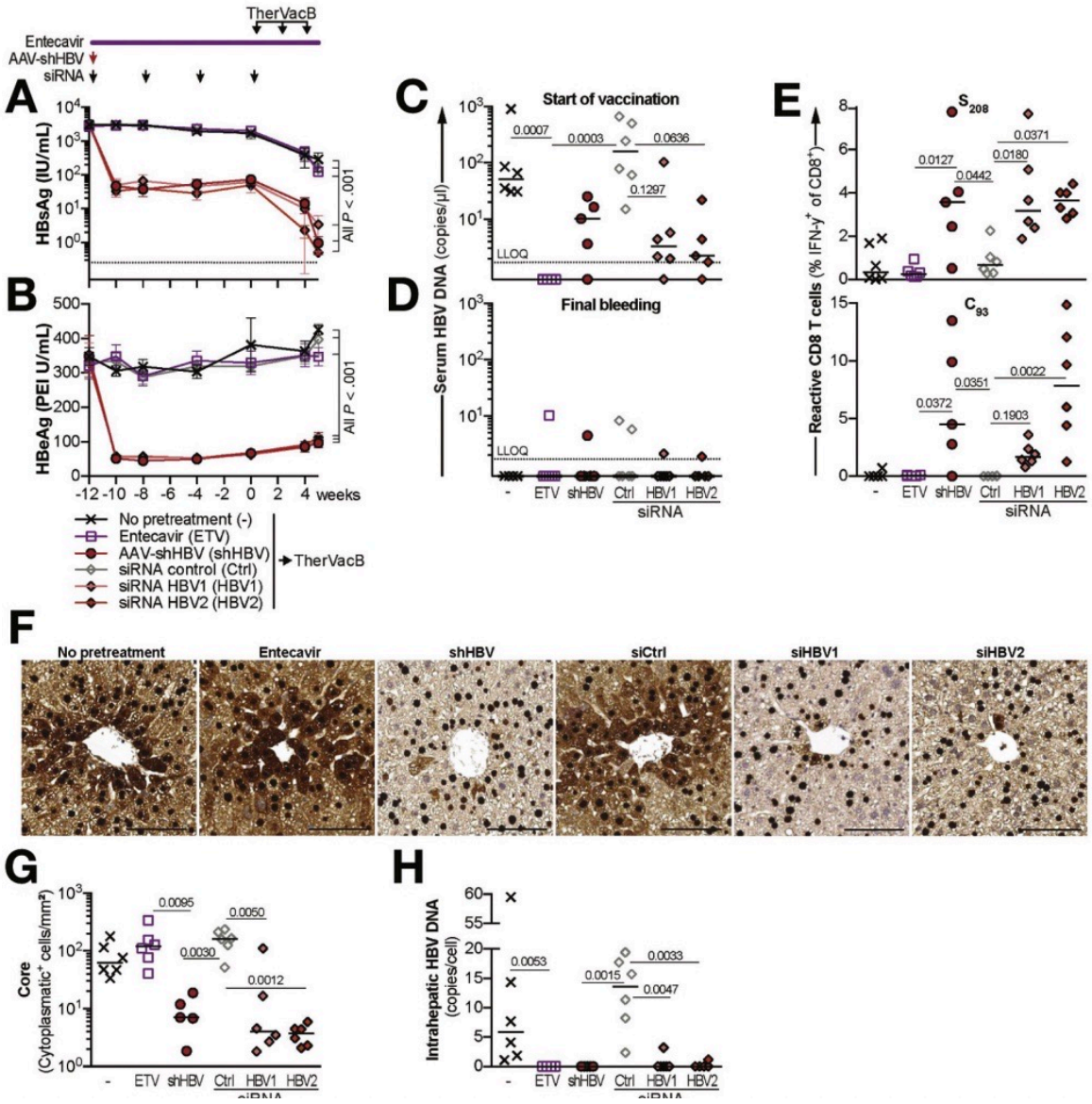
IN MICE!!!





- siRNA pre-treatment and ***TherVacB*** allow to "cure" HBV

Michler T et al Gastroenterology 2020: 158: 1762-1775


TherVacB
Entecavir
AAV-shHBV
siRNA
A
HBsAg (IU/mL)
All P < .001
B
HBeAg (PEI U/mL)
All P < .001
-12 -10 -8 -6 -4 -2 0 2 4 weeks
No pretreatment (-)
Entecavir (ETV)
AAV-shHBV (shHBV)
siRNA control (Ctrl)
siRNA HBV1 (HBV1)
siRNA HBV2 (HBV2)
TherVacB
C
Start of vaccination
Serum HBV DNA (copies/µl)
LLOQ
D
Final bleeding
- ETV shHBV Ctrl HBV1 HBV2
siRNA
E
S208
C93
Reactive CD8 T cells (% IFN-γ+ of CD8+)
0.0007
0.0003
0.0636
0.1297
0.0127
0.0442
0.0371
0.0180
0.0372
0.0351
0.0022
0.1903
F
No pretreatment
Entecavir
shHBV
siCtrl
siHBV1
siHBV2
G
Core
(Cytoplasmatic+ cells/mm²)
0.0095
0.0030
0.0050
0.0012
H
Intrahepatic HBV DNA
(copies/cell)
0.0053
0.0015
0.0033
0.0047

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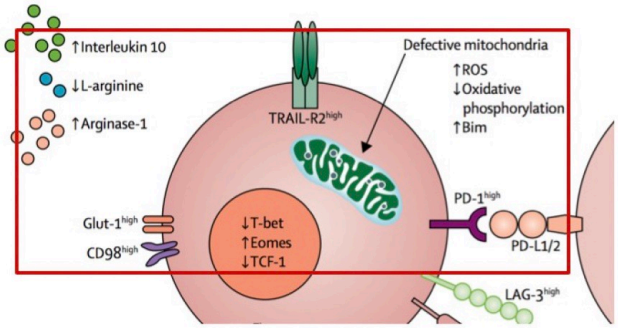
Targeting underlying HBV-specific T cell mitochondrial/metabolic dysfunction

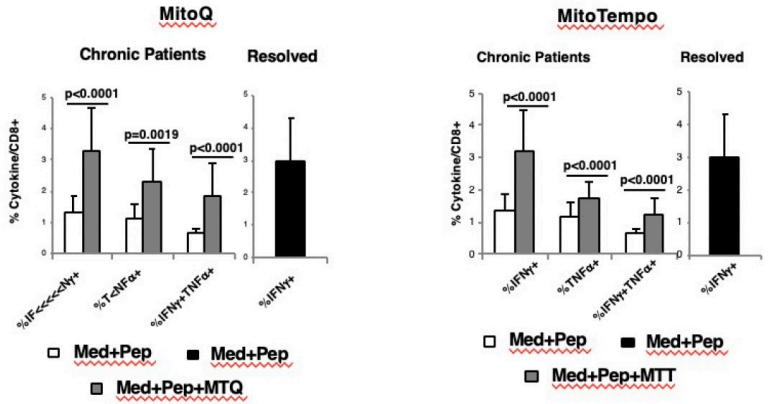


Schurich et al Cell Reports 2016
Fisicaro et al Nat Med 2017

Exhausted CD8 T cells are poorly able to use oxphos to meet their energy demands

MitoQ: Ubiquinone moiety CONJUGATED TO A TPP CATION

MitoTEMPO: Superoxide dismutase mimetic action
Catalase-like action
CONJUGATED TO A TPP CATION



Functional restoration of antiviral effector CD8 responses by mitochondrial targeted anti-oxidant compounds

Adapted from Maini and Pallett, Lancet Gastroenterol Hepatol 2018

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Rapidly progressing area…

Table 1. List of current clinical trials investigating heterologous prime boost therapeutic vaccines against chronic hepatitis B.

Vaccine Candidates	Components	Stage	Reference
GSK3528869A	ChAd155-hIi-HBV HBc-HBs/AS01B-4 MVA-HBV	Phase 1	NCT03866187
VTP-300	ChAdOx1-HBV MVA-HBV Nivolumab	Phase 1/2	NCT04778904
TherVacB	HBs and HBcore antigen MVA-HBV	Phase 1 (in prep)	Available online: https://www.thervacb.eu/ (accessed on 5 October 2021)

(different strategies in play)

Knolle et al Vaccines 2021, 9, 1333. https://doi.org/10.3390/vaccines9111333

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Discussion:

- HBV is a significant disease with burden – pandemic
- Heterogeneity of disease (host/ virus) still poorly understood
- Mutiple focus and extensive novel MOA
- After 3 years we are still lacking a roadmap…
- Immunostimulation is relevant given high Ag burden and immune exhaustion
- Off target effect and safety always a concern
- Therapeutic vaccination has demonstrated enhanced T cell responses / immune responses but yet to translate to significant SAg clearance
- It’s a hot focus area (cf Covid – a syndemic)

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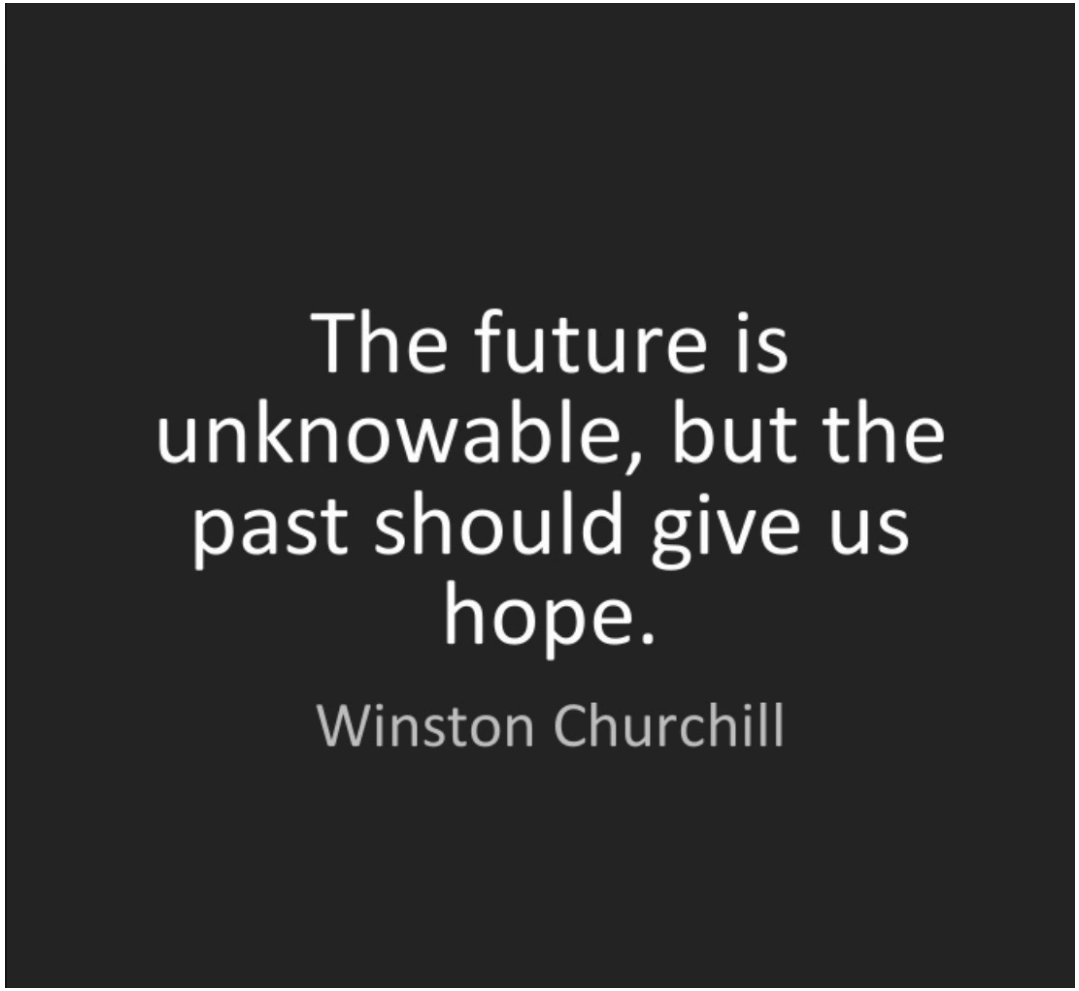
The future is unknowable, but the past should give us hope.
Winston Churchill

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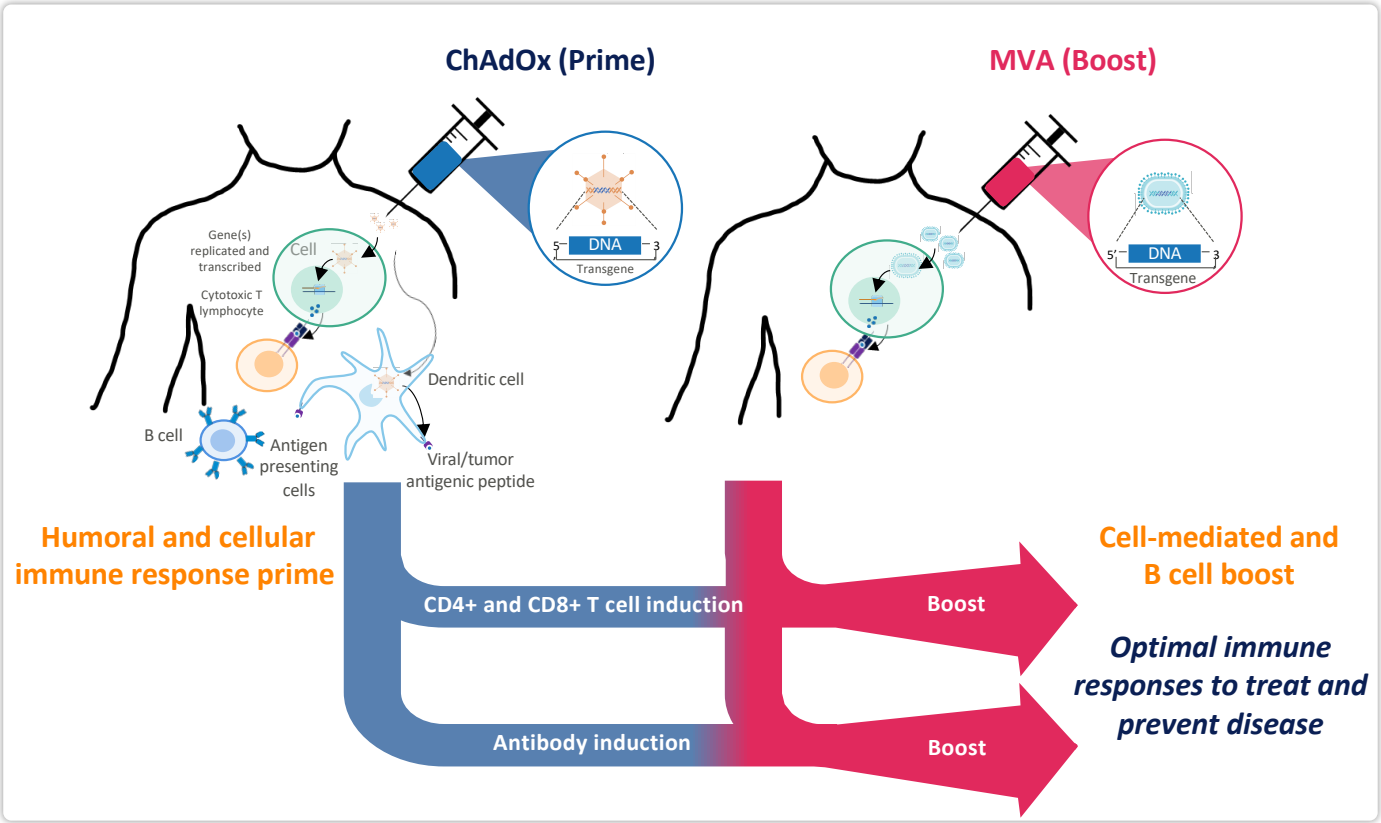
Vaccitech's VTP-300 HBV therapeutic progress and plans

Dr Tom Evans

Overview of the Vaccitech VTP-300 platform

Key Platform Features

- Proprietary ChAdOx ‘Prime’ Vectors
- Modified Vaccinia Ankara (MVA) ‘Boost’ Vector
- Single antigen expressed by Proprietary Promoters and Enhancers
- Bioinformatic Integration for Unique Antigen Selection and Design
- Rapid Vector Generation and Manufacturing
- Excellent Safety



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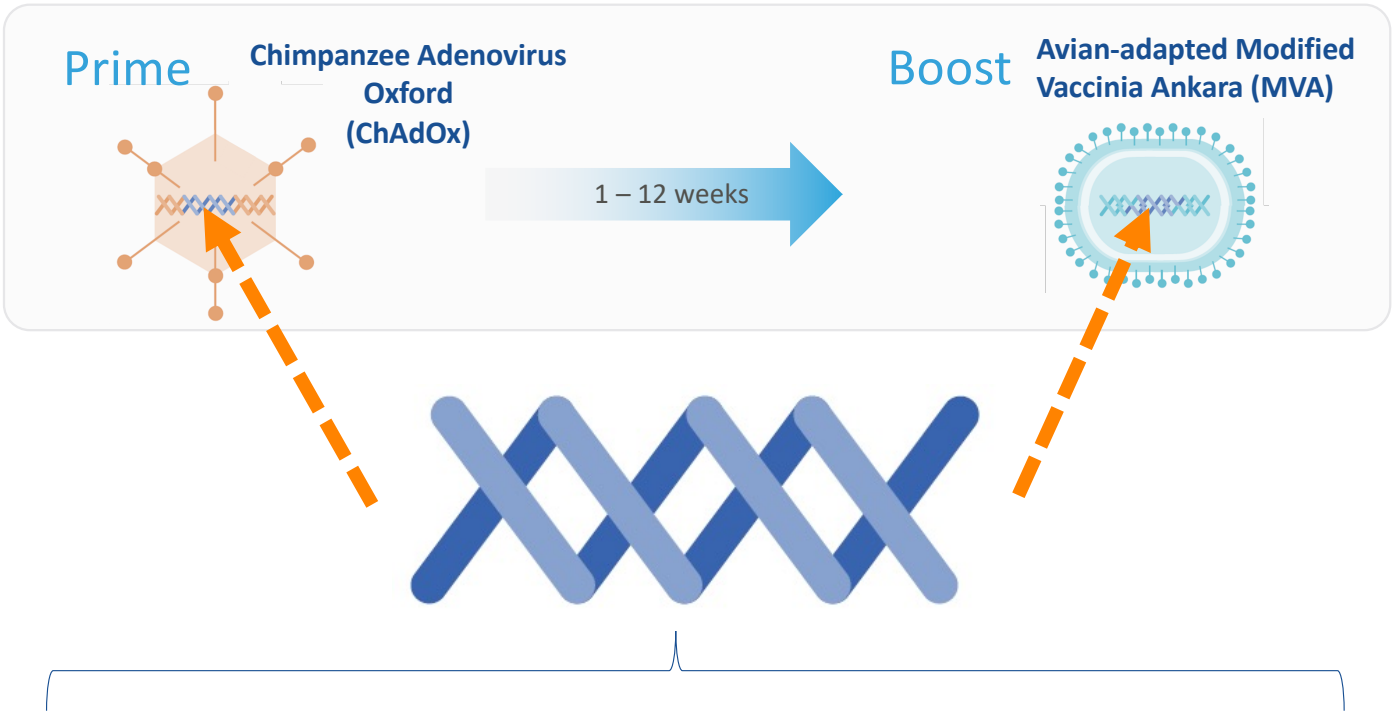
VTP-300

Our immunotherapy design includes a full-length HBV sequence



- Full length surface (including Pre-S1, Pre-S2, modified polymerase, core)
- Consensus genotype C
- Proprietary promoters

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VTP-300

Trials conducted or planned for initiation by end 2022

HBV001- 40 healthy participants and 12 chronic HBV patients administered ChAdOx-HBV as a monotherapy at two different doses

HBV002- 52 chronic HBV patients administered VTP-300 with and without low-dose nivolumab (37 enrolled)

AB-729-202 – 40 chronic HBV patients randomized to VTP-300 or placebo following 6 months of Arbutus 729 siRNA therapy; includes a potential antiviral discontinuation group (to start in 1H 2022)

HBV003- 120 chronic HBV patients to explore boosting regimens and timing of checkpoint inhibition

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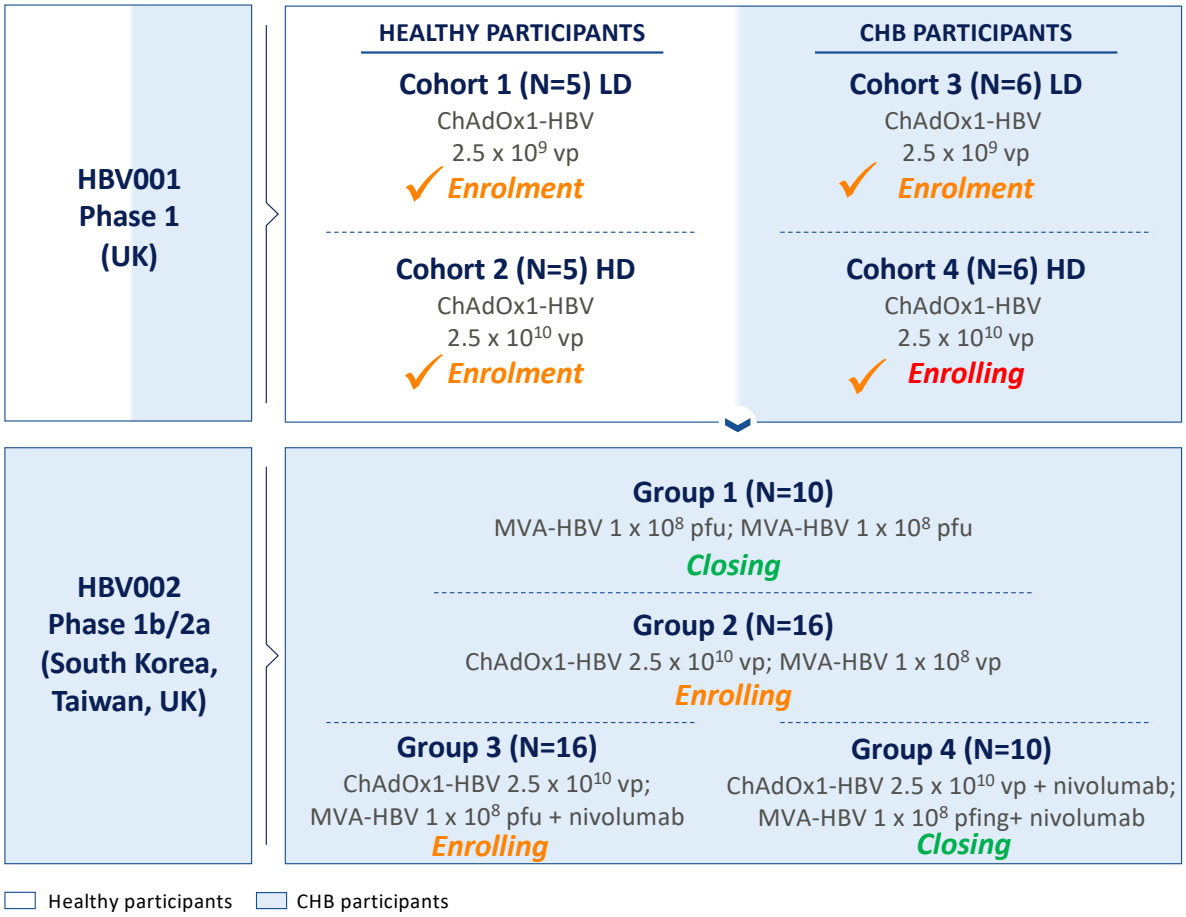
Vaccitech high level trial designs - HBV001 and HBV002



Inclusion Criteria

- HBV DNA <40 copies
- HBsAg <4,000 IU/mL
- On antivirals for 1 year

Study Outputs

- Safety and immunogenicity data from HBV001:
  - Healthy participants (HP) and CHB patients: Q4 2021 ✓
- Interim efficacy data (HBsAg loss) from HBV002: Q4 2021 ✓
- Full efficacy readout: Q4 2022

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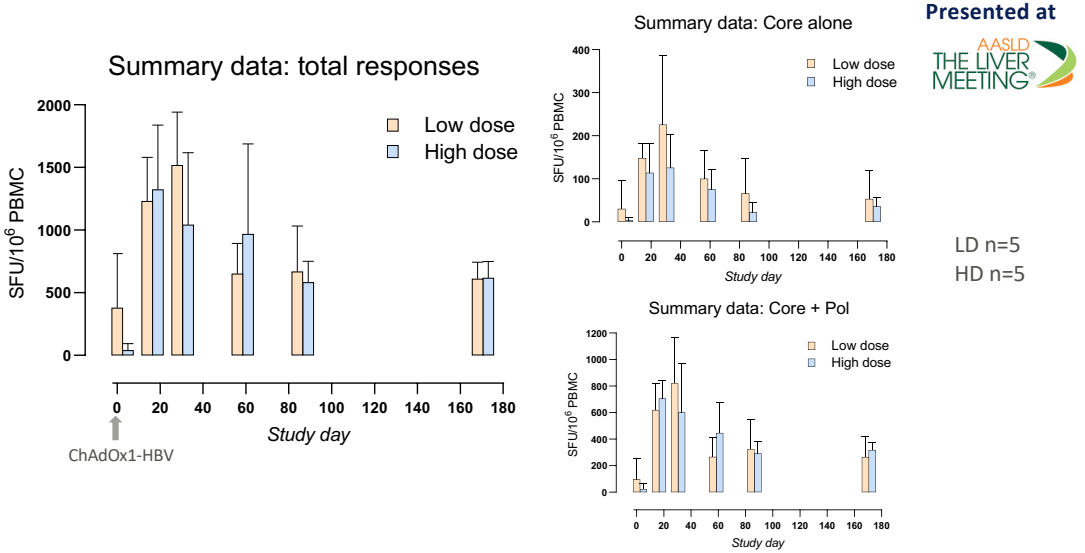
Phase 1 HBV001 T cell data – ChAdOx-HBV **prime only**

*The strongest published T cell responses against HBV-antigens measured in humans – **one shot, no boost***

Ex vivo HBV001 ELISpot* Results – Healthy Participants

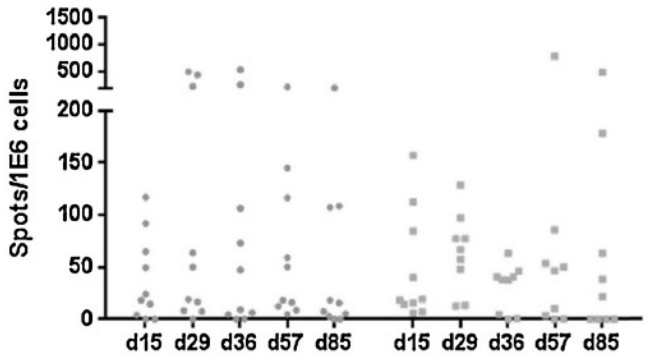
Presented at AASLD THE LIVER MEETING®



LD n=5
HD n=5

- **Single injection** resulted in a peak mean **over 1,000** sfu/million PBMCs in HD group at d28, from an **unstimulated assay**
- Excellent responses to **all HBV genes** incl. Core and Pol

…compared to GS-4774 immunogenicity in Healthy Participants



Gane et al (2019) Journal of Hepatology, 71, 5

- **5 injections 1QW and on d57**
- Highest responses – over 500 sfu/million – **stimulated assay**

*T cell responses were assessed by interferon-gamma (IFNg) ***ex vivo*** ELISpot assays using overlapping peptides,15 amino acids in length, corresponding to the vaccine immunogen.

Cargill et al (2021) AASLD: Interim results of HBV001, a phase 1 study evaluating the safety and tolerability of therapeutic vaccination with ChAdOx1-HBV in healthy volunteers and patients with chronic Hepatitis B infection

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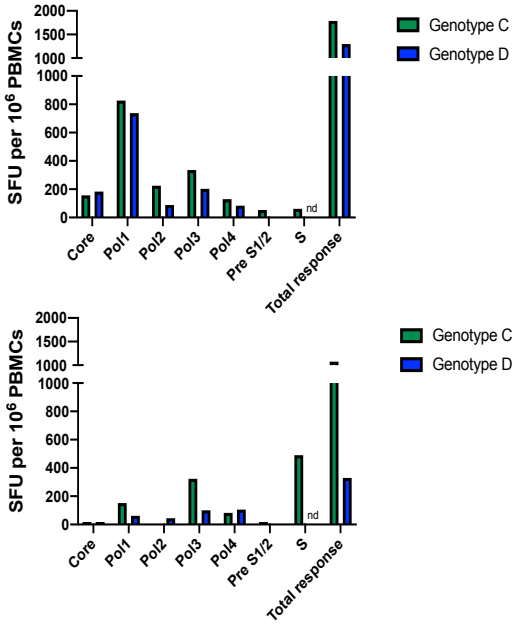
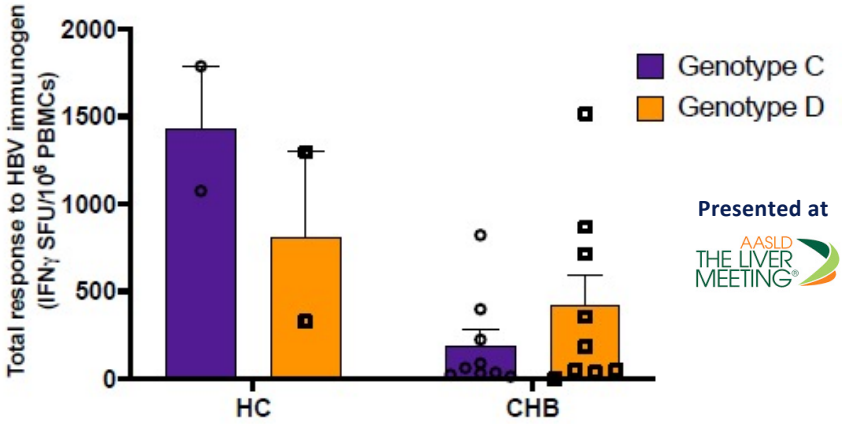
Phase 1 HBV001 T cell data – ChAdOx-HBV **prime only**

*T cells also reactive against HBV Genotype D **not** encoded in construct - Genotype C and D represent >50% HBV infections worldwide*

Cross-HBV genotype immunogenicity in both Healthy and CHB participants



2 Healthy Participants fresh PBMCs Healthy volunteers d28 after high dose ChAdOx1-HBV



Cross-reactive HBV-specific T cell responses in both Healthy Participants and CHB Patients

Cargill et al (2021) AASLD: Interim results of HBV001, a phase 1 study evaluating the safety and tolerability of therapeutic vaccination with ChAdOx1-HBV in healthy volunteers and patients with chronic Hepatitis B infection

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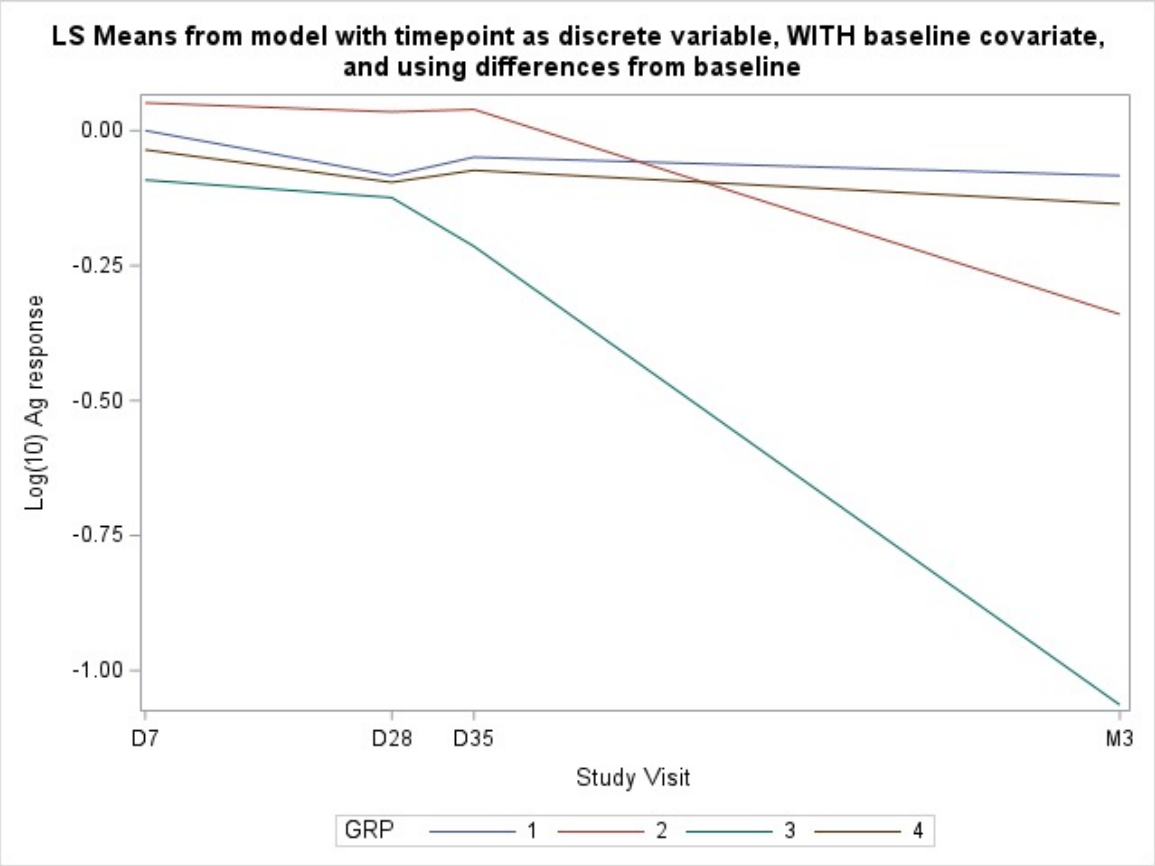
Phase 2a HBV002 HBsAg data



Group 1 – MVA/MVA

Group 2- ChAdOx1/MVA

Group 3- ChAdOx1/MVA+ nivo

Group 4- CHAdOX1 + nivo/MVA = nivo

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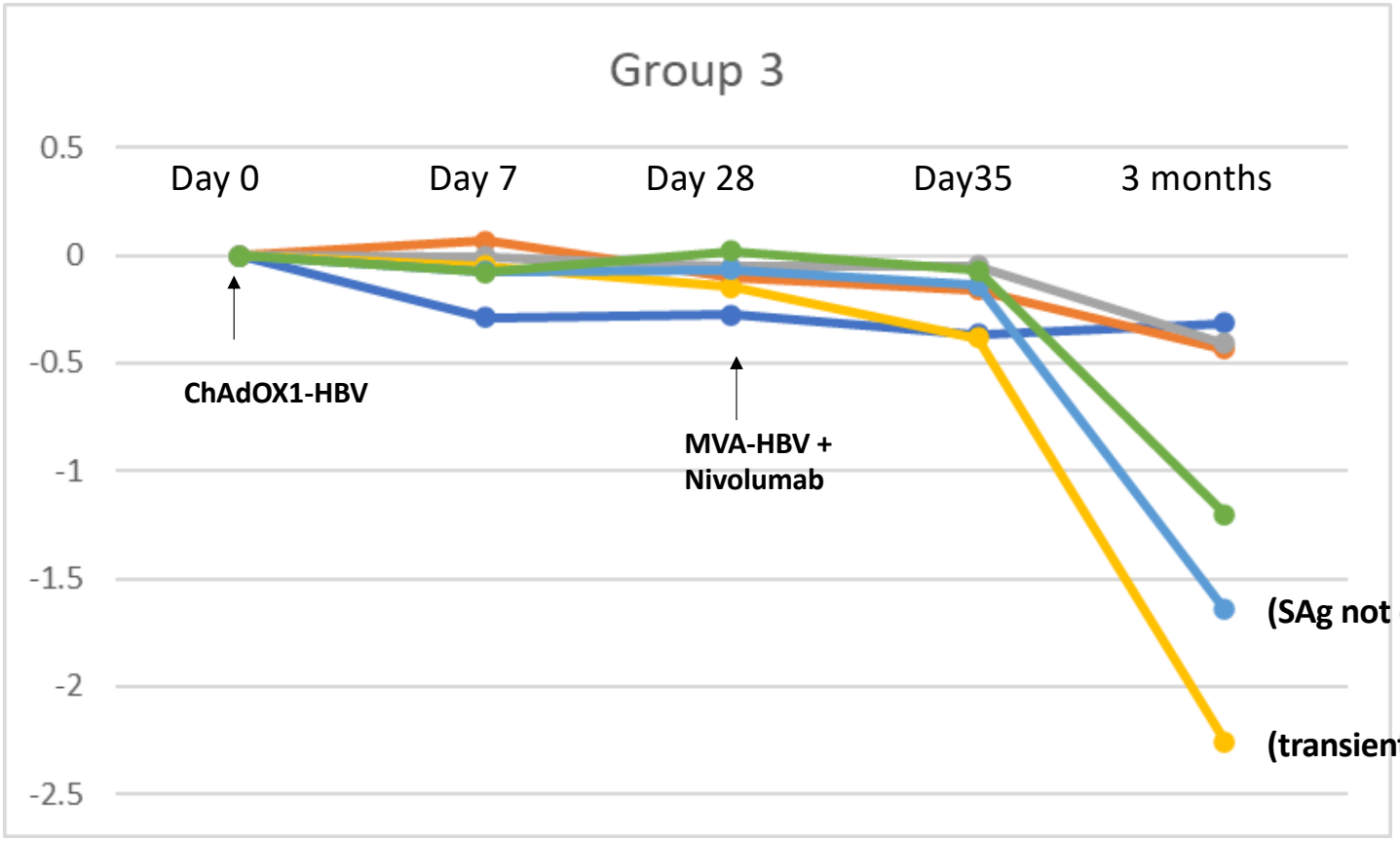
Phase 2a HBV002 HBsAg data- nivolumab at day 28



Mean starting level -441 IU/ml

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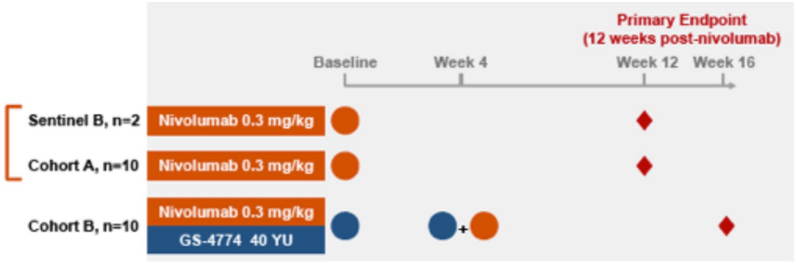
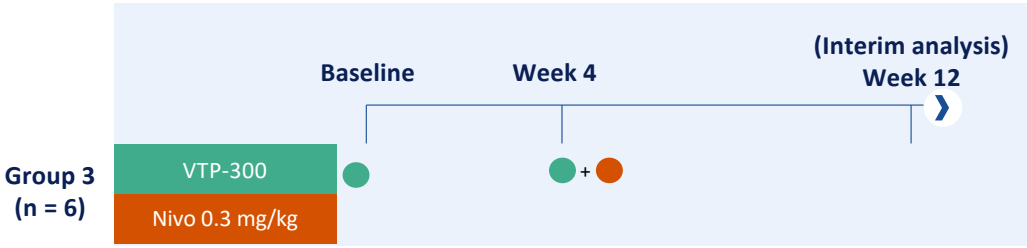
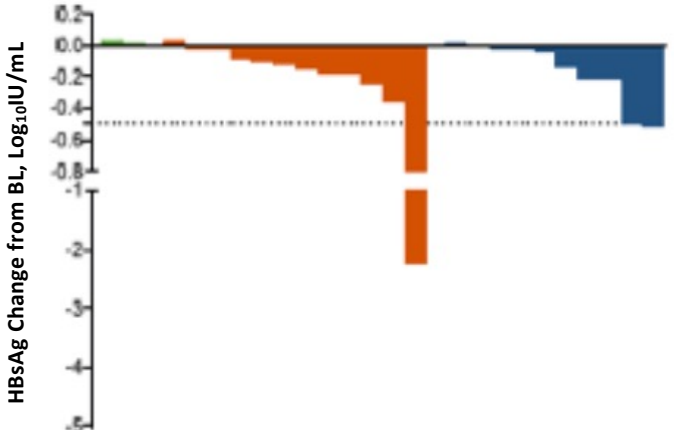
Highly Impressive initial efficacy *vs nivo (+/- GS-4774)*[1]

Our results are the first ever to indicate that inducing high levels of functional HBV-specific T cells is efficacious (by sAg decline)





Week 12 – Gane study

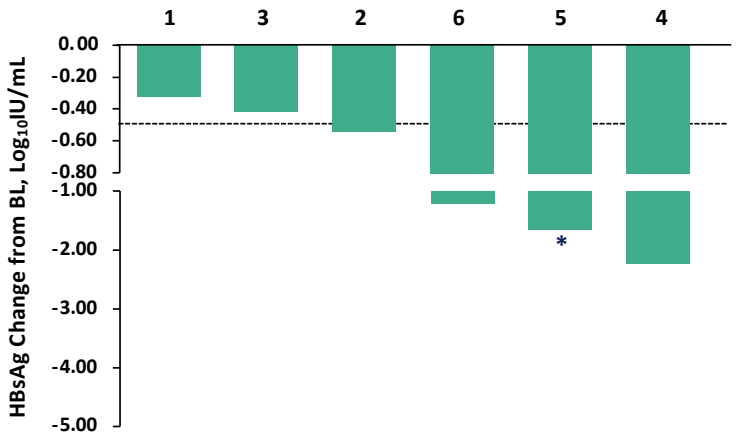


Nivolumab 0.1 mg/kg

Nivolumab 0.3 mg/kg (mean decline -0.3)

Nivolumab 0.3 mg/kg + GS-4774 (mean decline -0.16)

Week 12 – Group 3 – (mean sAg decline -1.04)



***Result undetectable at Week 12**

1) Gane et al (2019) Journal of Hepatology, 71, 5

Vaccitech press release, individual responses unpublished data

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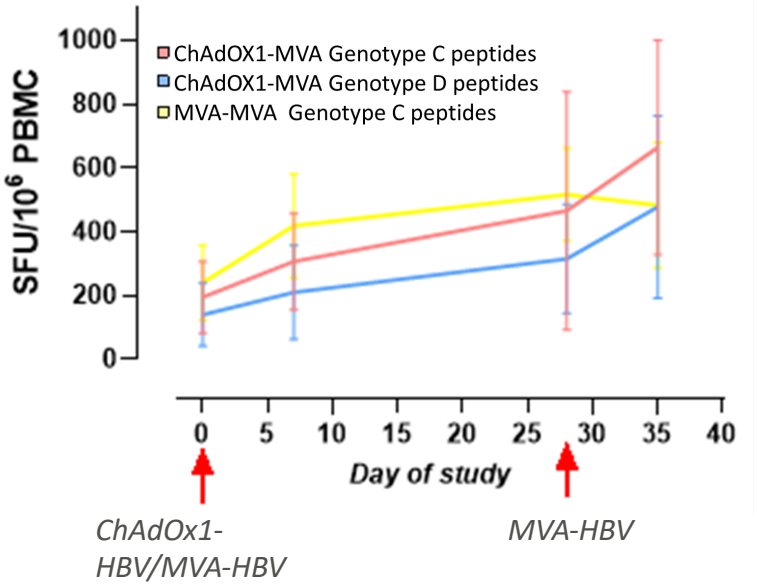
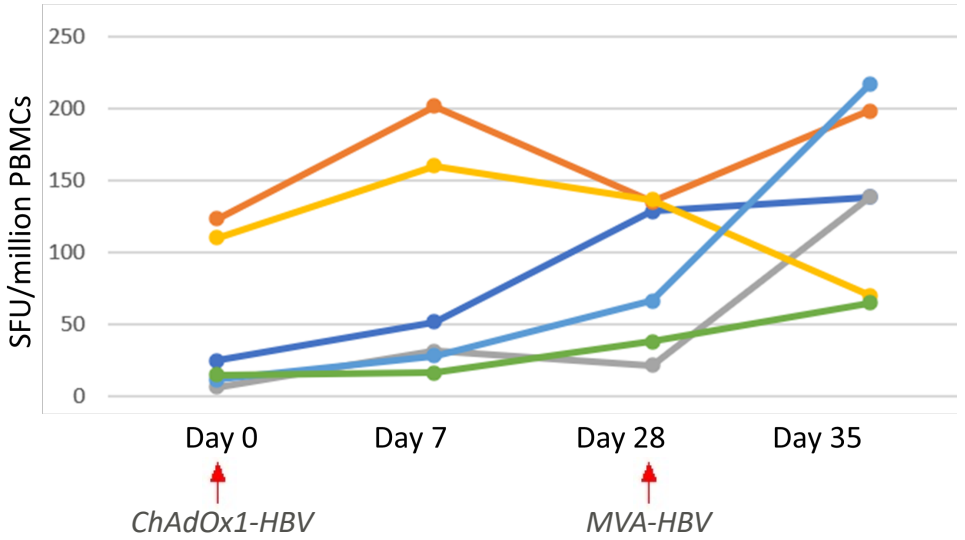
Outstanding immunogenicity and genotype cross-reactivity

Best-in-class *T cell immunogenicity demonstrated in chronically infected HBV patients with ChAdOx prime and MVA boost (VTP-300)*

Groups 1 & 2 – Summed T cell response across peptide pools (Genotype C and D for Group 2)



Group 2 - ChAdOx1 Day 0/MVA Core specific peptide pool responses



HBV patients showed pan-genotypic T cell reactivity to ***all viral genes****, establishing VTP-300's potential as part of a global functional cure regimen*

Evans et al (2021) AASLD: Phase 1b/2a study of heterologous ChAdOx1 HBV/MVA HBV therapeutic vaccination (VTP 300) combined with low dose nivolumab in virally suppressed CHB patients

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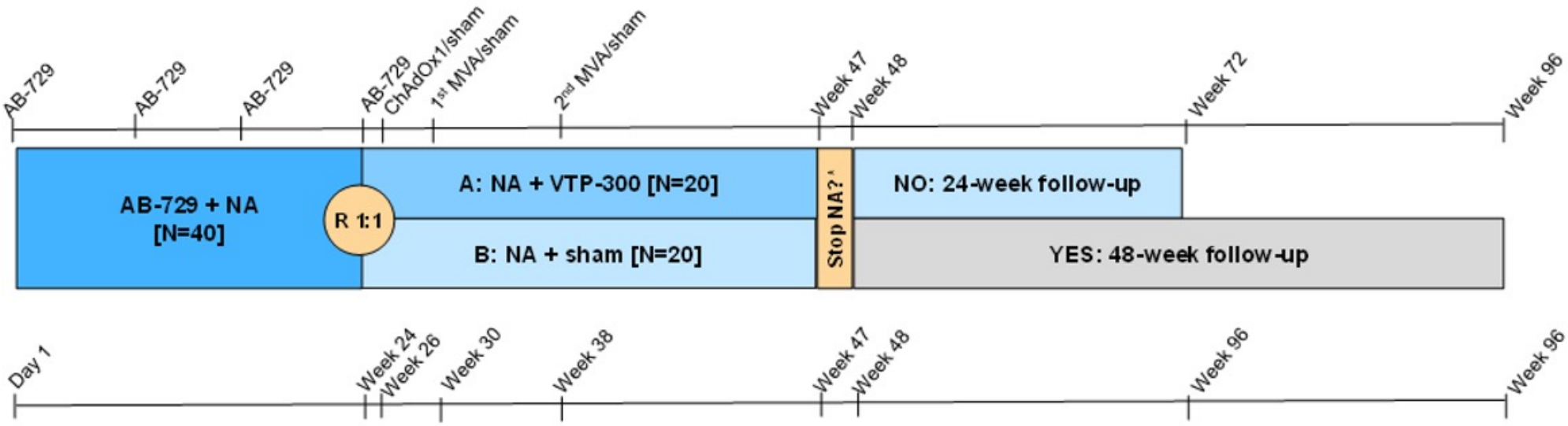
AB-729-202 Study Design



Study documents submitted in 4 countries
Study start 1H 2022

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HBV003 study design- refine regimen and boosts to drive higher efficacy

		Day 0	Day 7	Day 28	Day 35	Day 56	Day 84	
A		ChAdOx1-HBV		MVA-HBV+ LD nivolumab				
B		ChAdOx1-HBV		MVA-HBV+ LD nivolumab			MVA-HBV+ LD nivolumab[1]	
C		ChAdOx1-HBV		MVA-HBV	LD nivolumab	MVA-HBV[1]	MVA-HBV[1]	
D		ChAdOx1-HBV	LD nivolumab	MVA-HBV		MVA-HBV+ LD nivolumab[1]		

- Regulatory submission planned for Q2 2022
- Allows for low level of HBV DNA in patients on chronic antivirals

VTP-300

Progress in validating T cell induction as a new MOA in the fight against CHB

Immunogenicity - best-in-class T cell induction

- ✓ **The highest level of antigen-specific CD8+ and CD4+ T cells** generated by any targeted immunotherapy in HBV patients
- ✓ T cell responses were reproducibly cross-reactive against **both Genotype C and Genotype D** viral peptides, the two most prevalent HBV genotypes circulating globally

Efficacy – unprecedented sAg declines for immunotherapy

- ✓ Patients who received **VTP-300 alone (Group 2)**[1] and in combination with **low-dose nivolumab at the boost timepoint (Group 3)** showed marked efficacy responses over 12 weeks, measured by sAg **(mean -1.04 in Group 3)**
- ✓ Two patients in Group 2 had **significant** sAg reduction at 12 weeks **(reductions of 1.29 and 0.70 respectively)**

Safety - highly reassuring after prime and boost and nivolumab

- ✓ **There have been no VTP-300 associated SAEs to date**. One patient in Group 3 with a sAg decrease experienced a transaminase flare after the MVA boost plus nivolumab that resolved over 3 weeks

1) Vaccitech press release and unpublished data

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