A Phase 2b, Open-label Study to Evaluate the Efficacy, Safety, Tolerability, Immunogenicity and Treatment Regimens of VTP-300 Combined with Low-dose Nivolumab in Chronic Hepatitis B Infection

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BARINTHUS BIOTHERAPEUTICS

Disclosure

- Declaration of Potential Conflict of Interest:
  - Payment of consultancy fees to Dr Dereck Tait by Barinthus Biotherapeutics, formerly Vaccitech

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Introduction

- Current therapies for chronic HBV infection are effective in reducing the progression of liver disease but functional cure is not common
- VTP-300 is being investigated as a potential component of a functional cure therapy

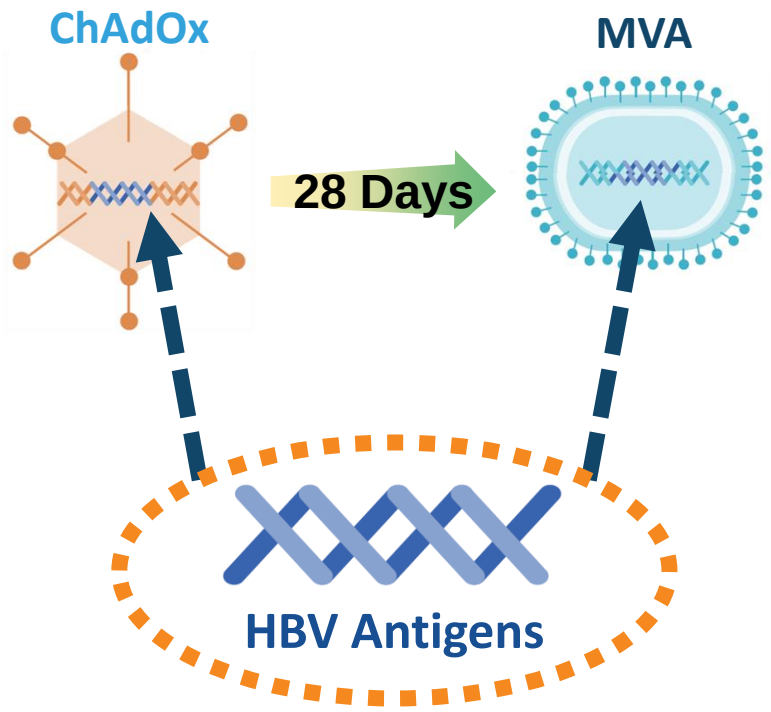
Three potential components to a functional cure

Approved	Investigational	Investigational
Inhibit viral replication	Directly **lower** viral antigen Hepatitis B surface antigen burden (HBsAg)	**Stimulate** host immune system response
NUCs	**RNAi**	**Ag-specific immunotherapies**
Capsid & Entry Inhibitors (*Investigational*)	**Oligonucleotide**	**PD-1 Inhibitors**
	Monoclonal antibodies (mAbs)	**Immunostimulants (TLR agonists)**

This presentation will:

- Recap data from HBV002, a Phase 1b/2a study presented at EASL in June 2023
- Share preliminary safety and efficacy data from the ongoing HBV003 Phase 2b study
- Highlight combination interim data from an ongoing VTP-300 / Imdusiran study (AB-729-202)
  - Poster presentation at AASLD 2023 – LB#5036-C

VTP-300: Targeted Immunotherapy Designed to Stimulate Host Immune System



ChAdOx/MVA Combination Approach: Has yielded higher magnitude, quality and duration of CD8+ T cells, essential for controlling disease in humans

Antigens based on a consensus genotype C include full length surface (S, PreS1, PreS2), modified polymerase, and core

Phase 1b/2a study demonstrated meaningful and sustained reductions in HBsAg when given alone and with checkpoint inhibitor

Ongoing studies evaluating VTP-300 in combination with other therapies as a **component of a functional cure regimen**

ChAdOx: Chimpanzee Adenovirus Oxford
MVA: Avian-adapted Modified Vaccinia Ankara

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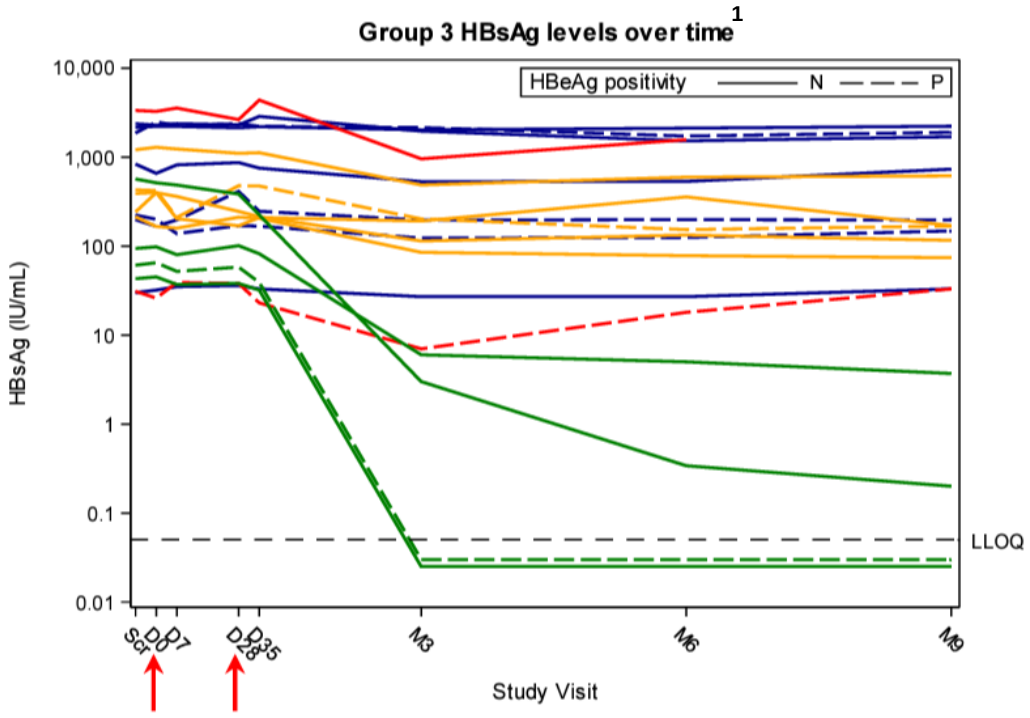
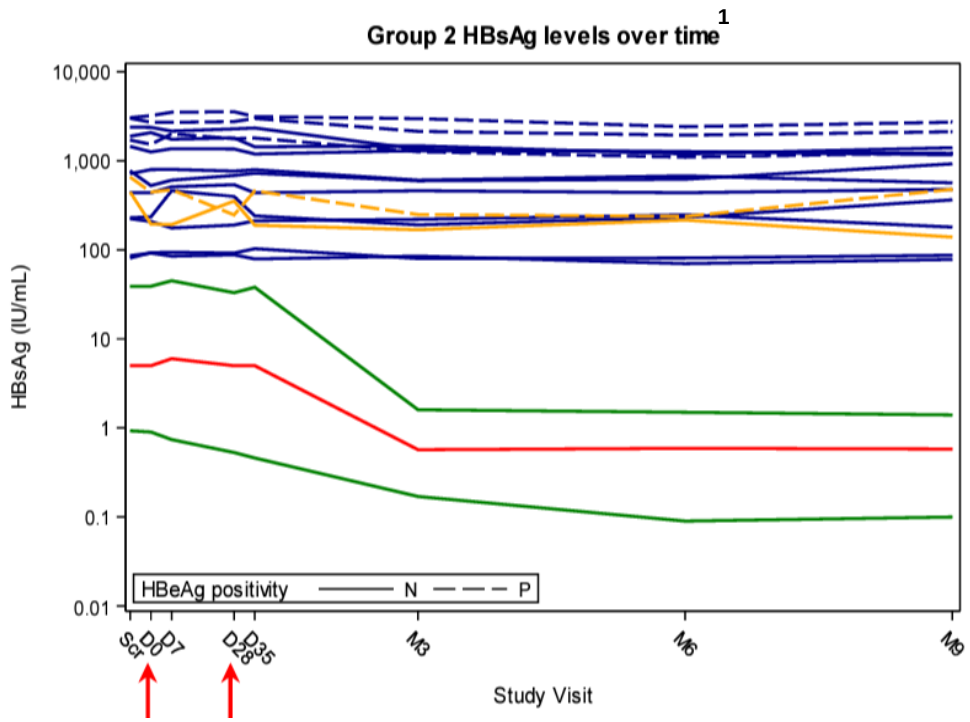
VTP-300 Showed Meaningful, Sustained HBsAg Reductions in a Phase 1b/2a Study[1]





Maximum observed drop in HBsAg

- 0.3 logs or less
- 0.3 to <0.5 logs
- 0.5 to <1.0 logs
- 1.0 log or higher

← **Dosing**

- **Significant, durable reductions of HBsAg were** seen in both VTP-300 monotherapy (Group 2) and VTP-300 + low-dose nivolumab group (Group 3)
  - Reductions in HBsAg were **most prominent in those with lower baseline HBsAg**.
  - **Non-detectable HBsAg** was observed in 2 of 5 Group 3 patients with **baseline HBsAg <100 IU/mL at month 3 through month 9**.

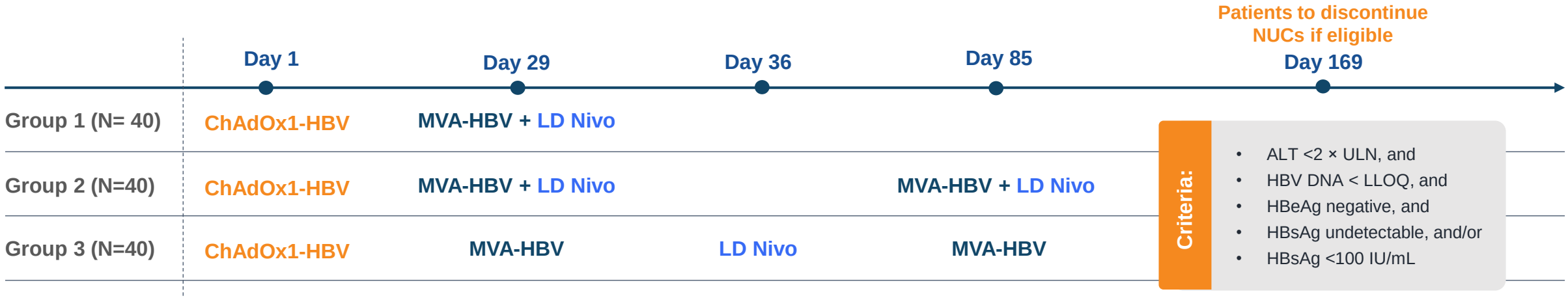
[1] Full data was presented as a poster at EASL, Q2 2023.

HBV003 – Ph 2b Study Designed to Evaluate Additional Dosing and PD-1 inhibition Timing

Enrolment initiated 25/10/2022; 12 sites in Thailand, Hong Kong, and Taiwan

74 of up to 120 participants randomised by 10 October 2023; Data up to Day 113 available for 56 participants (76%)

VTP-300 + Low-Dose Nivolumab (N=120) - Initiated in Q4 2022



Inclusion Criteria

HBV DNA ≤1,000 IU/mL

HBsAg ≥10 to <4,000 IU/mL

On NUCs for ≥6 months

Primary Endpoint

- % participants with a greater than 1 log HBsAg reduction at 6 months after initiation of therapy

Secondary Endpoints

- Safety and reactogenicity: incidence of AEs and SAEs
- T cell response

Presentation will focus on available data to Day 113

56 (76%) of 74 randomized participants; preliminary data from ongoing study

Study Reference: NCT05343481

HBV003 Phase 2b – Preliminary Baseline Data and Available Data by Visit

	Group 1 (N=25)	Group 2 (N=25)	Group 3 (N=24)	Total (N =74)
Age, mean (SD)	49.9 (9.1)	49.0 (8.1)	50.3 (8.5)	49.7 (8.5)
Male, %	80%	68%	71%	73%
Day 1 HBsAg IU/mL **Median (25th, 75th %tile)** **Screening ≤200 IU/mL, %**	 533 (118, 1082) 28%	 554 (181, 1084) 28%	 411 (116, 990) 38%	 490 (118, 1082) 31%
HBeAg positive, %	32%	12%	21%	22%

Numbers of Participants with Available HBsAg Log Change Data by Visit

	Group 1 (N=25)	Group 2 (N=25)	Group 3 (N=24)	Total (N =74)
Day 1	25	25	23	73 (99%)
Day 113	20	19	17	56 (76%)
Day 169	14	16	16	46 (62%)

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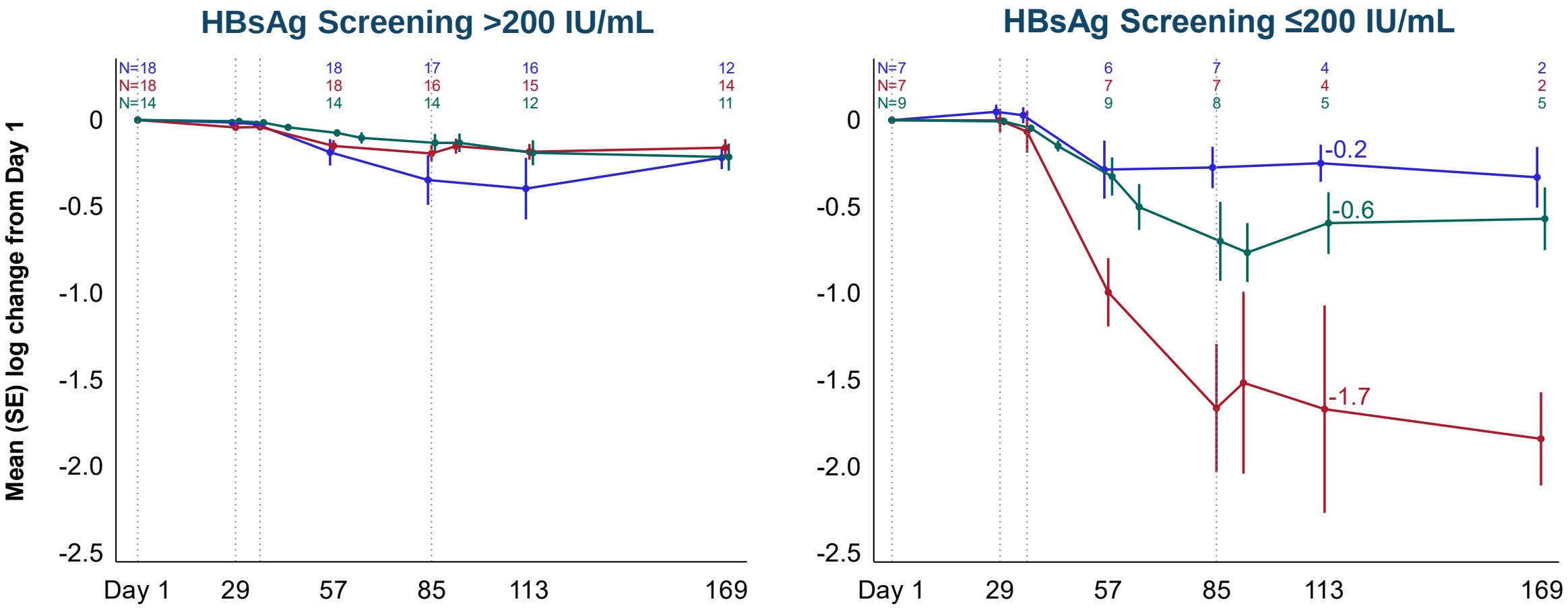
Preliminary Efficacy Data

VTP-300 in Combo with Nivolumab Continues to Show Sustained HBsAg Reductions

Reductions in HBsAg are most prominent in patients with Screening HBsAg levels ≤200 IU/mL



- Group 1: Day 1 ChAdOx1-HBV, Day 29 MVA-HBV+Nivo
- Group 2: Day 1 ChAdOx1-HBV, Day 29 & Day 85 MVA-HBV+Nivo
- Group 3: Day 1 ChAdOx1-HBV, Day 29 MVA-HBV, Day 36 Nivo, Day 85 MVA-HBV

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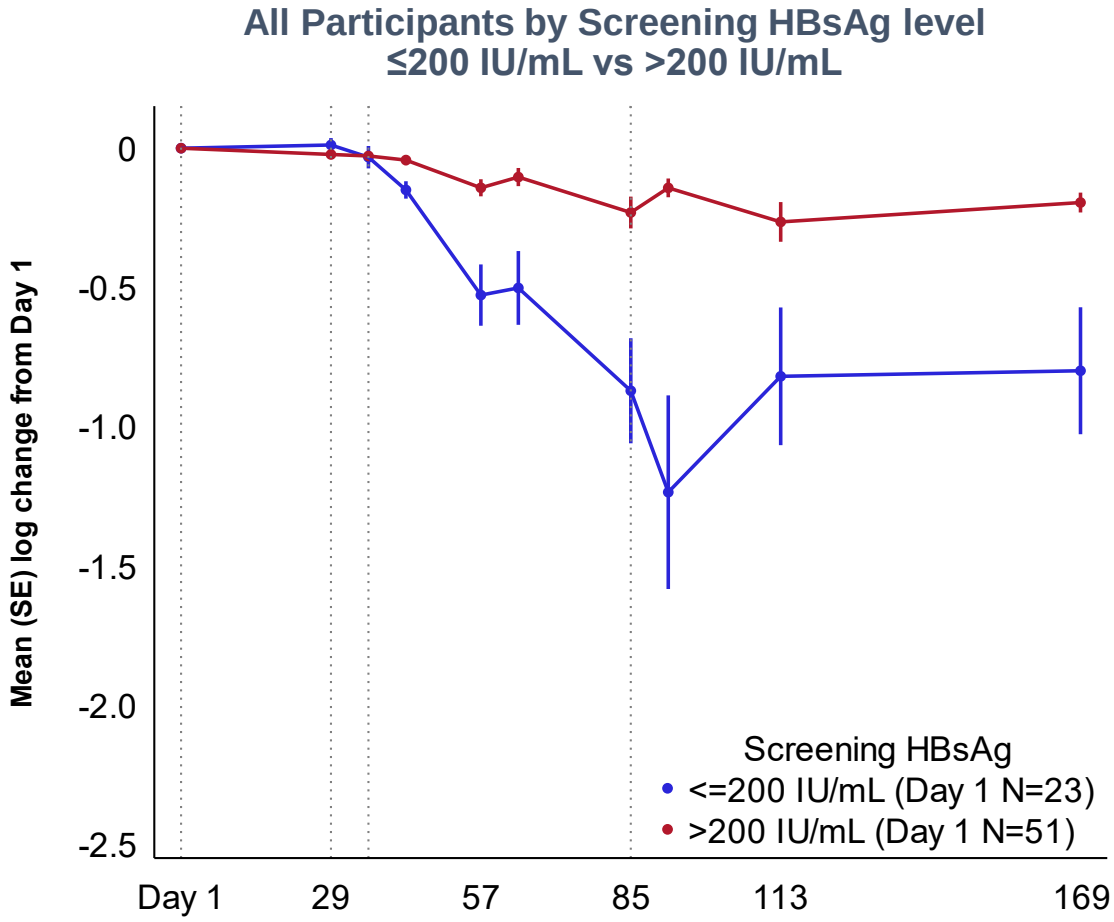
Reductions in HBsAg are most prominent in patients with BL HBsAg ≤200 IU/mL

- **54%** participants with HBsAg **at Screening ≤ 200 IU/mL** had a **>0.5 log decline** from Day 1*
- **31%** of participants with HBsAg **at Screening ≤ 200 IU/mL** had a **>1 log decline** from Day 1*



HBsAg log reductions at Day 113 from Day 1

	n/N (%)
>0.5 log HBsAg reduction	13/56 (23%)
>1 log HBsAg reduction	5/56 (9%)

HBsAg log reductions at Day 113 by Screening level

	>200 IU/mL	≤200 IU/mL
>0.5 log reduction	6/43 (14%)	7/13 (54%)
>1 log reduction	1/43 (2%)	4/13 (31%)

- **Day 113: 4 weeks after last MVA dose**
- **Day 169: possible NUC discontinuation timepoint**

*Of subset of participants with data available at Day 113.

Eligibility criteria met for NUC discontinuation in some participants

- Participants who discontinued NUCs closely followed up post-discontinuation
  - Bi-weekly for 8 weeks; monthly for 4 months; and quarterly for 6 months
  - Strict criteria for reinitiating NUCs
- 7 (15%) of 47 participants who reached Day 169 were eligible for discontinuation*
  - 7 (78%) of 9 participants who reached Day 169 with screening HBsAg below 200 IU/mL were eligible
  - 3 participants have discontinued NUC therapy

	HBsAg (IU/mL)			
Pt #	**Day 1**	**Day 169**	**Day 169 log Δ**	**Status**
1 (Grp 3)	116	22	-0.72	Undetectable HBsAg 16 weeks post-discontinuation
2 (Grp 3)	19	2	-0.98	Restarted NUC after 8 weeks due to DNA ↑ (>20000 IU/mL)
3 (Grp 2)	105	3	-1.57	Restarted NUC after 8 weeks due to DNA ↑ (>20000 IU/mL)

* Discontinuation criteria: ALT <2 × ULN, and HBV DNA < LLOQ, and HBeAg negative, and HBsAg undetectable or <100 IU/mL.

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Preliminary Safety Data

VTP-300 in combination with nivolumab was generally well tolerated

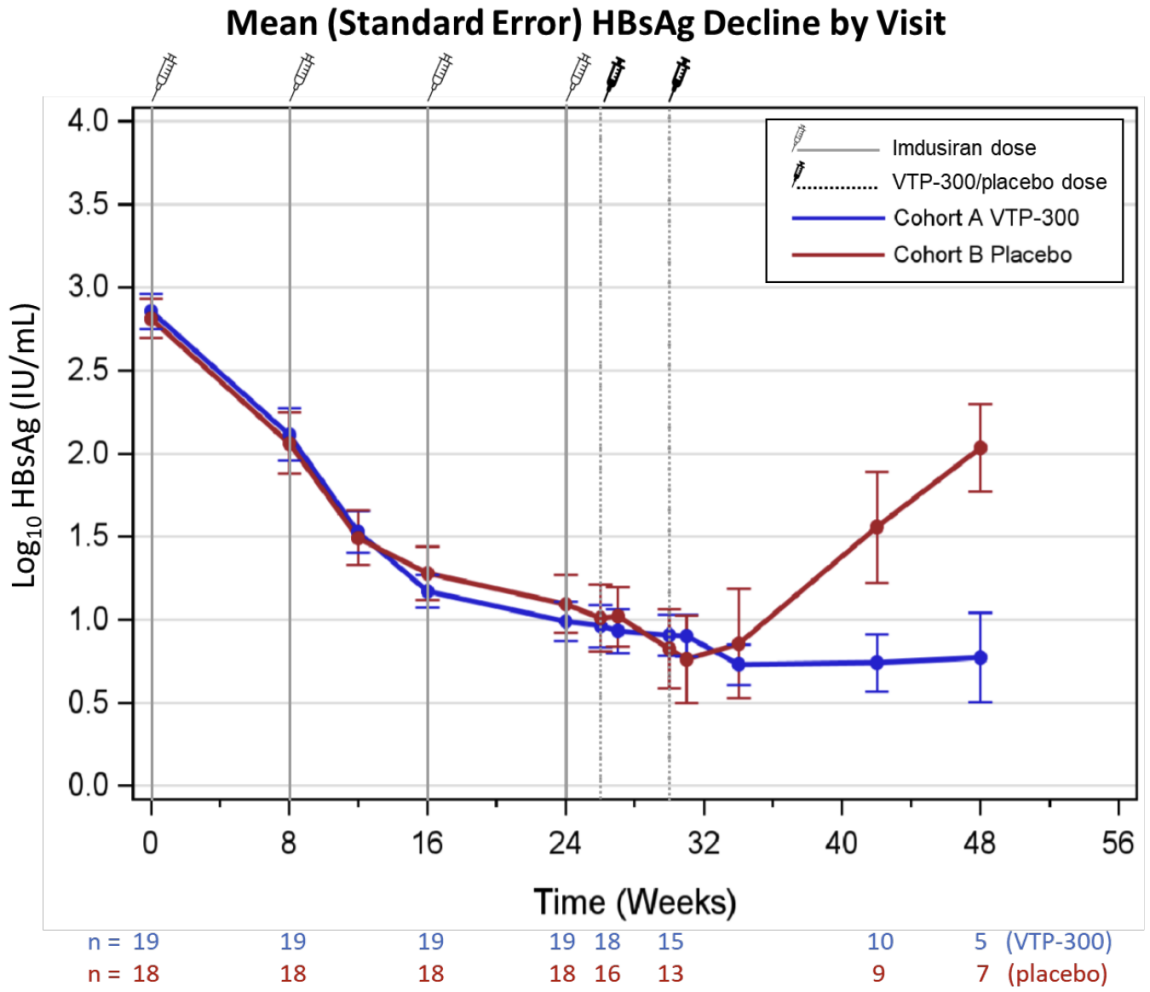
- No study discontinuations
- 1 SAE – urinary tract infection; not related to either study drug as assessed by the investigator
- One treatment discontinuation – participant with Bell's Palsy (did not receive Day 85 MVA-HBV); resolved
- Thyroid dysfunction reported in 7 participants (all groups) attributed to nivolumab; follow-up ongoing
  - 5 asymptomatic; thyroid function laboratory values **returned to within normal range in 4 out of 5 participants**
  - 2 symptomatic; one had anti-thyroid antibodies at screening; one TSH slightly above ULN and one just below ULN at screening
- ALT/AST
  - Through Day 169 follow-up, transaminase elevations above 2xULN (2.05 to 6.7x ULN) occurred in 12 participants; observed in all groups
  - Not reported as clinically significant and transient other than for one participant (Follow-up ongoing)
  - Occur soon after Day 29 MVA-HBV and most revert to <2x ULN by Day 85*

*Data for the 12th participant does not yet exist beyond Day 85

Collaboration Data with Arbutus

AB-729-202

Interim data from AB-729-202 indicate that VTP-300 following 24 weeks of Imdusiran appear to contribute to maintaining low HBsAg levels in early post-treatment period



- Ongoing collaboration with Arbutus:
  - Imdusiran administered for 24 weeks followed by VTP-300.
- **See AASLD poster presentation LB#5036-C for more information.**

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HBV003 Phase 2b

Conclusions

Conclusions

- The data presented are preliminary data from small numbers of participants and the study is still ongoing
- VTP-300 in combination with nivolumab was observed to lead to HBsAg declines in all treatment groups particularly in participants with Screening HBsAg levels ≤200 IU/mL
- Greater mean HBsAg log reductions were observed in Group 2 (with 2 doses of MVA-HBV/Nivo) but insufficient data for definitive conclusion
- 7 participants (15%) have met criteria for NUC discontinuation at Day 169
- Preliminary safety data suggest VTP-300 in combination with nivolumab was generally well tolerated with no treatment related SAEs observed or reported
  - Transient ALT/AST elevations and thyroid function abnormalities observed in all groups
- We believe these early data are encouraging and in combination with interim data from an ongoing study with Imdusiran/VTP-300 suggest that VTP-300 may be an important component of a future functional cure regimen