Rapid HBsAg declines and HBsAb seroconversion observed with a single dose of VRON-0200 plus Tobevibart and Elebsiran: preliminary results of a VRON-0200 combination treatment from a Phase 1b study for functional cure in chronically HBV-infected patients

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LATE-BREAKER LBP-033

BACKGROUND

- VRON-0200 is an immune modulator for functional cure of HBV infection designed to enhance and broaden CD8+ T cells to HBV core & pol[1-3]
  - VRON-0200 dose NOT target HBV Surface antigen
- In chronically HBV-infected patients, VRON-0200 has previously demonstrated[4] [**See EASL 2025 Abstract #1404**]
  - A favorable safety and tolerability profile
  - Immunogenicity
  - Anti-HBV activity (HBsAg declines)
- VRON-0200 P1b study was expanded to add a cohort to evaluate the safety and efficacy of VRON-0200 with the addition of other therapeutic agents

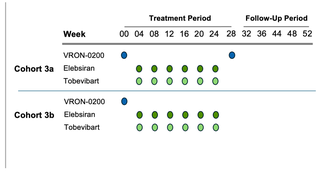
PURPOSE

- **To report the first-ever preliminary safety, immunogenicity, and HBsAg and HBsAb data, for VRON-0200 prime only, plus monthly doses of elebsiran and tobevibart (E/T)**

METHODS

- This is a Phase 1b multi-center, multi-national, open label, clinical trial in chronic-HBV infected, virally suppressed adults between 18 and 55 years of age, with HBsAg levels ≤500 IU/mL (Cohorts 1 & 2; Cohort 3 ≤1,000IU/mL), and no evidence of advanced liver fibrosis or cirrhosis (**NCT06070051**)
  - Cohort 1 and 2 receive VRON-0200 only, prime, or prime and boost dosing (**see EASL 2025 Abstract #1404**)
  - Cohort 3 received VRON-0200 with the addition of elebsiran and tobevibart
- This analysis only includes patients in Cohort 3, who are randomized to receive a prime i.m. injection of VRON-0200 $5x10^{10}$vp (**Figure 1**)
  - Cohort 3a receives 6 monthly subcutaneous doses of elebsiran and tobevibart starting on Day 28 followed by a VRON-0200 boost on Day 196
  - Cohort 3b receive 6 monthly subcutaneous doses of elebsiran and tobevibart starting on Day 28 only
- Patients were evaluated for safety, immunological and virologic measures, at multiple time points
- **This analysis includes all available safety, immunogenicity, HBsAg, and HBsAb data from a data cutoff of March 31, 2025, and PBMC ELISpot data from a data cutoff of January 6, 2025**

Figure 1. Cohort 3 Study Schema



mAb – monoclonal antibody; siRNA – small interfering RNA
* Both elebsiran and tobevibart are part of Vir Biotechnology, Inc.'s clinical-stage portfolio for Hepatitis

RESULTS

PATIENT DEMOGRAPHICS

- Six patients were male (86%), mean age of 51 years, and baseline HBsAg of 125 IU/mL (range: 12-842 IU/mL) (**Table 1**)

Table 1: Patient Demographics (N=7)

	Cohort 3 (N=7)
Median age, yrs (range)	**51 (41 - 55)**
Sex, n (%)	
Male	**6 (86%)**
Female	**1 (14%)**
Race, n (%)	
Asian	**5 (71%)**
Native Hawaiian or Other Pacific Islander	**0 (0%)**
White	**1 (14%)**
Other	**1 (14%)**
BMI (kg/m^2), median (range)	**22.9 (18.6 - 32)**
Baseline HBsAg Levels (IU/mL), median (range)	**125 (12 - 842)**
Baseline HBsAg Levels, n (%)	
>500 IU/mL	**2 (29%)**
200 - ≤500 IU/mL	**1 (14%)**
100 – 199 IU/mL	**1 (14%)**
<100 IU/mL	**3 (43%)**
Baseline ALT (x ULN), n (%)	
<1 x ULN	**7 (100%)**
1 to 1.5x ULN	**0 (0%)**
1.6 x ≤2x ULN	**0 (0%)**
HBsAg Status at Baseline, n (%)	
Negative	**7 (100%)**
Positive	**0 (0%)**

SAFETY AND TOLERABILITY

- There are **821** total patient safety days reported. VRON-0200 plus elebsiran and tobevibart was well tolerated with 25 adverse events being reported in 5 patients (**Table 2**).
  - There were no treatment related serious adverse events, no treatment discontinuations, or treatment related laboratory abnormalities, including liver function tests (not shown)
  - Nine treatment related adverse events (TRAEs) were reported, including 1 - Grade 2 rash; all other TRAEs were Grade 1
  - One patient had a non-treatment related serious adverse event that resulted in a 2-dose treatment interruption of elebsiran and tobevibart

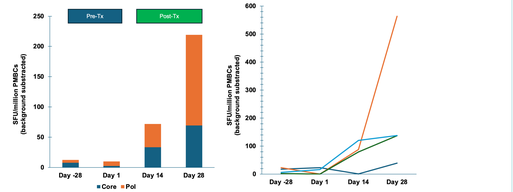
Table 2: Safety & Tolerability (N=7)

	Any AE, n	TRAE, n	TRAEs, n VRON-0200	TRAEs, n VRON-0200 + E/T
Any AE, n	**25**	**9**	**1**	**8**
Grade 1	**20**	**8**	**1**	**7**
Grade 2	**4**	**1**	**0**	**1**
Grade 3 or 4	**1**	**0**	**0**	**0**
SAE, n	**1**	**0**	**0**	**0**
AEs leading to Study Drug Discontinuation, n	**0**	**0**	**0**	**0**
Study Discontinuations, n	**0**	**0**	**0**	**0**
ALT elevations, n	**1**	**0**	**0**	**0**
Grade 1	**0**	**0**	**0**	**0**
Grade 2	**1**	**0**	**0**	**0**

IFNγ ELISpot RESPONSES; PRIME ONLY (N=4)

- Prior to treatment, all 4 patients had IFNγ ELISpot responses below LLOD to both core and pol peptide pools (**Figure 2**)
- At Day 28, post VRON-0200 prime dosing only, all 4 patients had IFNγ ELISpot ELISpot increases when compared to their pre-treatment values

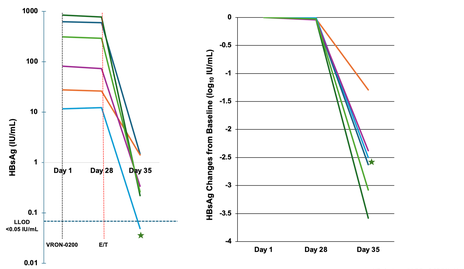
Figure 2. IFN ELISpot Responses, VRON-0200 Prime Only Dosing (n=4)



HBsAg CHANGES OVER TIME

- **Figure 3** shows HBsAg changes following a single VRON-0200 dose on Day 1, followed by a single elebsiran and tobevibart dose on Day 28
  - At Day 28, no HBsAg changes from baseline were observed (note: HBsAg declines begin at Day 28 post VRON-0200 dosing (**See EASL 2025 Abstract #1404**))
  - All patients (n=6) experienced HBsAg declines at Day 35 (7 days after the addition of elebsiran and tobevibart) ranging from -3.6 to -1.3 $\log_{10}$IU/mL
  - At Day 35, one patient achieved HBsAg loss following a -2.4 $\log_{10}$IU/mL decline

Figure 3. Individual HBsAg Changes at Day 35 Following a Single VRON-0200 Prime Dose (Day 1) plus a Single Elebsiran plus Tobevibart (E/T) Dose on Day 28 (n=6)



HBsAg CHANGES OVER TIME

- **Figure 4** shows the absolute HBsAg changes, over time, following a single VRON-0200 dose on Day 1, followed by multiple monthly elebsiran and tobevibart doses starting at Day 28. The $\log_{10}$IU/mL change from baseline is listed for each patient at their last evaluable timepoint
  - One patient achieved HBsAg loss at Day 140 following a -3.8 $\log_{10}$IU/mL decline from baseline
- **Table 3** lists the percentage of patients by absolute HBsAg level category over time
  - At Day 35, all patients had HBsAg levels ≤10 IU/mL (7 days after the first elebsiran and tobevibart dose)
    - Two patients achieved HBsAg loss (≤0.05 IU/mL) through Day 140
- **Figure 5** shows HBsAg declines over time by treatment regimen
  - A VRON-0200 Prime alone, or Prime and Boost dose results in 27% of patients achieving ≥0.4 $\log_{10}$IU/mL HBsAg declines over time (**see EASL 2025 Abstract #1404** for more details)
  - VRON-0200 Prime on Day 1, followed by monthly elebsiran and tobevibart doses beginning on Day 28, resulted in all patients reporting rapid and profound HBsAg declines
    - Two patients achieved HBsAg loss by Week 20
- **Table 4** shows HBsAb status – all six patients seroconverted from HBsAb negative to positive

Figure 4. Individual HBsAg Changes

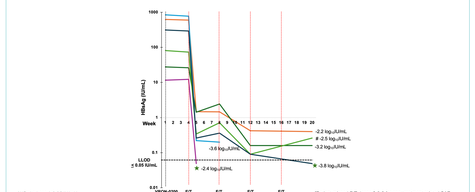


Figure 5. HBsAg Changes by Treatment Regimen

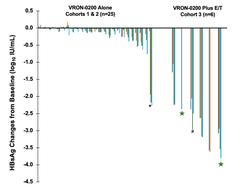


TABLE 3. HBsAg Levels Over Time

HBsAg Levels	Day 1 (n=6)	Day 28 (n=6)	Day 35 (n=6)	Day 56 (n=5)	Day 84 (n=4)	Day 140 (n=4)
≥100 IU/mL	50%	50%	0%	0%	0%	0%
≥10 - <100 IU/mL	50%	50%	0%	0%	0%	0%
≥0.05 - <10 IU/mL	0%	0%	83%	100%	100%	75%
<0.05 IU/mL (LLOD)	0%	0%	17%	0%	0%	25%

TABLE 4. HBsAb Status*,**

HBsAb	Day 1 (n=6)	Day 28 (n=6)	Day 35 (n=6)	Day 56 (n=5)	Day 84 (n=4)	Day 140 (n=4)
Negative	100%	100%	0%	0%	0%	0%
Positive	0%	0%	100%	100%	100%	100%

*As per study protocol, the Elecsys Anti-HBs II assay was utilized for all patients in this study. ≥10mIU/mL is considered positive
**Serum collected for HBsAb testing prior to dosing on Days 1, 28, 56, 84, and 140

METHODS II: Clinical Assessments

Safety

- Physical exams were performed, and serum were collected for clinical laboratory assessments, including liver function tests on all patients (n=7)

Patients who received a VRON-0200 prime dose, and at least one dose of E/T, were included for the following assessments (n=6)

HBsAg (Quantitative)

- ELISA HBsAg II Quant; LLOD: 0.05 IU/mL
- Absolute changes ($\log_{10}$ IU/mL)

HBsAb (Qualitative)

- Elecsys Anti-HBs II (E601/602 v1.0): ≥10mIU/mL is considered positive

Immunologic assessments (PBMC)

- IFNγ ELISpot to core, pol, and surface peptide pools; LLOD < 30 SFU/million PBMCs
- 2 pre-treatment samples were obtained prior to VRON-0200 dosing
- 4 patients had IFNγ ELISpot measurements through Day 28 and are included (Prime only)

CONCLUSIONS

This is the first clinical report of a VRON-0200 combination regimen. To date, following a single VRON-0200 prime dose, the addition of elebsiran and tobevibart:

- Was safe and well-tolerated, with no treatment-related SAEs, treatment discontinuations, or treatment-related clinical laboratory abnormalities
- VRON-0200 HBsAg declines were substantially enhanced with the addition of the combination agents
  - Rapid and profound S-antigen declines were observed within 7 days of the first combination dose
  - All patients achieved HBsAg ≤10 IU/mL by Day 35
  - HBsAb seroconversions were observed in all patients

Given VRON-0200's demonstrated anti-HBV activity, safety profile, and ease of administration, VRON-0200 could be a key component for combination with antiviral agents in future potential HBV cure regimens, thereby possibly replacing PEG-IFN

These data support expediting & expanding clinical development of additional VRON-0200 combinations towards a functional cure

DISCUSSION

- Functional Cure has been limited by an inability to stimulate HBV-specific immune responses
- VRON-0200 is a novel checkpoint modifier containing immune-modulator that has been shown to induce HBV-specific T cell responses, and anti-HBV activity, following a single prime dose (**See EASL 2025 Abstract #1404**)
- In this cohort, with VRON-0200 prime dosing, all patients had rapid, and profound HBsAg declines; these responses have not been previously observed with elebsiran and tobevibart alone, or in combination with PEG-IFN, nor has it been observed with any other PEG-IFN containing regimens[5-7]
- "**Spark and Fan**" proposed model for Functional Cure with VRON-0200 as **the backbone:**
  - "**Spark**" an immune response with a single i.m. VRON-0200 dose
  - "**Fan**" the immune response by the removal of HBV antigens (e.g., Surface) with antiviral agents, thereby improving overall anti-HBV responses
- Potential for new combinations that amplify VRON-0200 induced immune responses to improve the durability of treatment and overall clinical outcomes
  - Can VRON-0200 combination regimens potentially shorten the course of Functional Cure treatment?

ABBREVIATIONS

AE, adverse event; ALT, alanine transaminase; AST, aspartate aminotransferase; ALP, alkaline phosphatase; BMI, body mass index; Core - HBV core enzyme; EOS, end of study; E/T, elebsiran and tobevibart; HBsAg, hepatitis B surface antigen; HBsAb, hepatitis B surface antibody; IM, intramuscular; IU, international units; LLOD, lower limit of detection; PBMC, peripheral blood mononuclear cell; Pol, polymerase; SAE, serious adverse event; SFU, spot-forming unit; TRAE, treatment-related adverse event; Tx, treatment; ULN, upper limit normal; vp, viral particles

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All authors contributed to and approved the poster.

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DISCLOSURES

Ed Gane has served as an advisor and/or speaker for AbbVie, Abbott Diagnostics, Aligos, Arbutus, Arrowhead, Assembly, Dicerna, Gilead Sciences, GlaxoSmithKline, Intellia, Janssen, Merck, Novartis, Precision Biosciences, Genentech-Roche, Tyne, Vaccitech, Vir Biotechnology, and Viron Therapeutics

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