VRON-0200 Induced Broad and Sustained Anti-HBV Immunity in Chronically HBV-Infected Patients

Abstract #587

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BACKGROUND

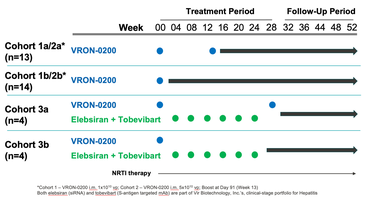
An immune modulator is now considered necessary for HBV functional cure therapies[1,2]. VRON-0200 is a therapeutic vaccine for HBV functional cure (FC) designed to enhance and broaden immune responses: 1) it targets HBV core and pol, but not S-antigen[3]; 2) it contains a novel checkpoint modifier (HSV glycoprotein D; gD), which acts to lower the T cell activation threshold*, and 3) is delivered by a chimpanzee adenoviral vector.

In chronically HBV-infected (CHB) patients, VRON-0200 has demonstrated a favorable safety/tolerability profile, immunogenicity, and HBV-specific immune-activation and restoration in the majority of patients (e.g., HBsAg declines) with sustained and/or deepened responses up to 360 days after end of VRON-0200 only treatment[4,5].

PURPOSE

To report safety, immunogenicity, and HBsAg changes in chronically HBV-infected patients, who received VRON-0200 alone, or with an investigational antiviral combination, when added to standard of care nucleos(t)ide therapy: 1) VRON-0200 alone, out to EOS (360 days after VRON-0200 prime dose), and; 2) VRON-0200 plus an investigational antiviral combination, up to Day 196 (28 days after last combination dose).

STUDY SCHEMA



DESIGN

- P1b, open label, randomized, multi-center study

KEY INCLUSION CRITERIA

- Adults 18 to 55 years of age
- BMI 18 to 32 kg/mg^2
- Documented chronic HBV
- HBsAg
  - Cohorts 1 & 2: ≤ 500 IU/mL
  - Cohort 3: ≤ 1000 IU/mL
- On stable NUC therapy > 12 months
- Normal liver function; no cirrhosis

IMMUNOLOGIC ASSESSMENTS (PBMC)^

- IFNγ ELISpot to core and pol; LLOD < 30 SFU/million PBMCs
- Day 28 immunologic "responder": Defined as 2 consecutive core + pol ELISpot measurements at Day 28 > average of the 2 pre-treatment timepoints, and above the LLOD

SAFETY ASSESSMENTS^

- Adverse events (AEs) and SAEs (CTCAE) and labs, including LFTs, vital signs, and PEs

VIROLOGIC ASSESSMENTS (HBsAg)^

- ELISA HBsAg II Quant; LLOD 0.05 IU/mL

^Data Cut-off for immunologic assessments was July 7, 2025, and for safety and virologic assessments, December 19, 2025.

A single VRON-0200 dose was able to "spark" and re-awaken durable HBV-specific immunity, with HBsAg declines sustained or deepened through Day 360; profound synergy was observed when these responses were "fanned" with antigen lowering antivirals

PATIENT DEMOGRAPHICS (N = 35)

	Cohort 1 (n=13)	Cohort 2 (n=14)	Cohort 3# (n=8)
Median age, yrs (range)	45 (37-54)	46 (41-55)	51 (41-55)
Sex, n (%)			
Male	12 (92%)	10 (71%)	6 (75%)
Race, n (%)			
Asian	11 (85%)	13 (93%)	6 (75%)
Other	2 (15%)	1 (7%)	2 (25%)
BMI (kg/m^2), median (range)	26.3 (20.2-32)	25.9 (19.7-31.6)	21.7 (18.6-32)
Baseline HBsAg Levels (IU/mL), median (range)*	179 (16-623)	149 (10-563)	469 (12-1169)
Baseline HBsAg Levels, n (%)			
≥500 IU/mL	1 (8%)	1 (7%)	4 (50%)
200 to <500 IU/mL	6 (46%)	4 (29%)	1 (13%)
100 to <200 IU/mL	2 (15%)	6 (43%)	0 (0%)
<100 IU/mL	4 (31%)	3 (21%)	3 (38%)
Baseline ALT (x ULN), n (%)			
1.5 to ≤2x ULN	1 (8%)	0 (0%)	0 (0%)
1 to <1.5x ULN	0 (0%)	1 (7%)	0 (0%)
<1 x ULN	12 (92%)	13 (93%)	8 (100%)
HBeAg Status at Baseline, n (%)			
Negative	12 (92%)	14 (100%)	8 (100%)

1 pt withdrew consent at D28 (Cohort 3), and is included in demographics and baseline characteristics, and safety, but excluded from Clinical Data (not evaluable)
*As per protocol, participants had prior HBsAg at screening ≤500 IU/mL in Groups 1 and 2, and ≤1000 IU/mL in Cohort 3.

ADVERSE EVENTS

	Cohort 1 (n=13)	Cohort 2 (n=14)	Cohort 3 (n=8)
Any AE, n	16	29	44
Grade 1	13	19	35
Grade 2	3	10	8
Grade 3 or 4	0	0	1
SAE, n	0	0	1*
TRAEs, n	5	16	17
AEs leading to Study Drug Discontinuation, n	0	0	0
Study Discontinuations, n	0	0	1**
ALT elevations, n	0	0	1
Grade 1	0	0	0
Grade 2	0	0	1

Safety data as of December 19, 2025; 32 of 35 reached EOS.
* 1 pt in Cohort 3 had a non-treatment-related significant adverse event that resulted in a 2-dose elebsiran+tobevibart treatment interruption.
** Pt withdrew consent at D28 - included in demographics, baseline characteristics, and safety, but excluded from Clinical Data (not evaluable).

12,073 Patient Safety Days; No serious TRAEs, treatment-related discontinuations or clinical laboratory abnormalities
89 AEs in 24 patients; 38 TRAEs included 4 - Grade 2: eczema, myalgia, headache, injection site reaction, all others Grade 1

HBsAg DECLINES (COHORTS 1 & 2; VRON-0200 ONLY)

VRON-0200 DOES NOT TARGET HBsAg

Pt #	Day 1	Day 14	Day 28	Day 60	Day 91	Day 104	Day 118	Day 154	Day 360
1	622.9					NA			406.9
2	562.6								39.8
3	441.9								297.7
4	389.9								105.9
5	322.2								184.8
6	319.2								323.7
7	273.4								195.5
8	271.0								127.9
9	265.4								271.2
10	226.0								101.1
11	225.3								187.4
12	221.8								197.9
13	178.9								141.2
14	177.1								155.3
15	150.2								67.0
16	148.3					NA			127.0
17	124.8		NA					NA	22.0
18	112.8								81.9
19	103.1								47.0
20	101.3								77.5
21	94.2								56.3
22	43.2								20.1
23	28.6								22.9
24	25.4								0.7
25	17.1								1.8*
26	16.4				NA				0.1
27	9.7								3.8

Log_{10} Change from BL
≤ –0.06
–0.07 to –0.49
–0.50 to –0.99
≥ –1.00

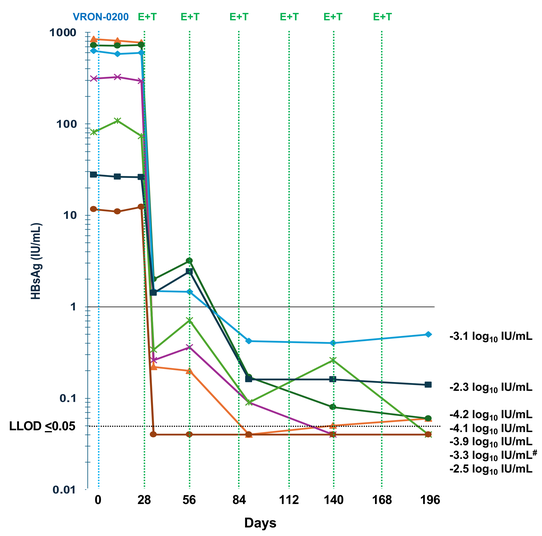
Boost D91

D28 IFNγ "Responder"

*-0.97 log_{10} IU/mL decline; NA – not available; EOT - Day 1 for Prime Only: 6 mos post-tx (D180); EOT - Day 91 for Prime and Boost: 6 mos post-tx (D271)

- HBsAg declines begin around Day 28
- Day 91 boost does not appear to improve HBsAg declines
- Day 28 IFNγ ELISpot responses not associated with HBsAg declines
- At Day 360:
  - **23/27 (85%)** pts with sustained control and/or continued declines
  - **4 pts** with **≥ 1 log_{10} IU/mL** decline*
  - HBsAg **declines independent of BL levels**
  - 12/23 **(52%)** had **> 50% declines**
  - **6 pts** with BL HBsAg > 100 IU/mL **below 100 IU/mL at Day 360** (decreased HCC risk)

HBsAg DECLINES (COMBINATION COHORT 3)

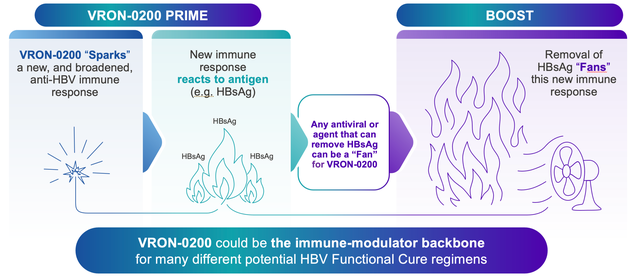


Patient missed E+T Doses 2 & 3 for non-treatment related AE

E+T – elebsiran plus tobevibart; Both elebsiran and tobevibart are part of Vir Biotechnology, Inc.'s, clinical-stage portfolio for Hepatitis

- Rapid and profound HBsAg declines within 7 days of first E+T dose
- At Day 196 (28 days after last E+T dose):
  - **100% ≤ 1 IU/mL**
  - **5/7 ≤ 0.06 IU/mL**
  - **3/7 below LLOD**
  - **Responses independent of BL HBsAg levels**

"SPARK AND FAN" MODEL FOR CHB



CONCLUSIONS

VRON-0200, which does NOT target HBsAg:

- Was safe & well tolerated, when given alone, and in combination with investigational antivirals
- Activated & restored HBV-immunity in the majority of VRON-0200-only treated pts:
  - HBsAg declines were sustained and/or deepened up to 360 days
  - Neither Day 28 IFNγ ELISpot responses, or a boost dose at Day 91, were associated with these declines
- In combination with investigational antivirals, resulted in rapid & profound HBsAg declines in all pts - these declines were sustained & continued 1-month post-antiviral treatment

This novel approach, where anti-HBV immunity is "sparked" (i.e., primed) with VRON-0200, and then "fanned" (i.e., boosted) by HBV removal, support VRON-0200 as a potential foundational backbone agent for future HBV Functional Cure regimens

- A long-term study has been implemented to follow pts
- A phase 2B SPARK-B study is in development
- Studies in HIV/HBV and HDV/HBV co-infected pts are being discussed

POTENTIAL IMPLICATIONS FOR CHB & OTHER CHRONIC VIRAL DISEASES

- **Benefits of Novel Checkpoint Modification (CPM) MOA**
  - Locally acting, thereby minimizing the risk for serious "off target" adverse events
  - Clinically validated to restore and stimulate immunity in chronically infected pts
- **VRON-0200 Implications for CHB**
  - First new HBV immune-modulator since PEG-IFN
  - Sustained and/or improving immune responses may prevent the need for rescue medications after HBV treatment discontinuation
  - VRON-0200 combination treatments might improve overall FC rates
  - Potential to shorten treatment durations and expand pt populations to higher BL HBsAg (e.g., >3,000 IU/mL) and co-infected pts (e.g., HIV/HBV, HDV/HBV)
- **VRON-0200 Global Implications**
  - Administration, dosing, and safety profile ideal for global public health
  - Designed to be easily scalable and widely accessible
- **Implications for Other Viral Diseases and Their Complications**
  - CPM has the potential for HDV, HIV Cure, HSV-2, EBV, among others
  - Immune restoration, with improved viral control, may lower cancer risk(s)

REFERENCES

1. Wong, et al. J Hepatol. 2022, 76: 1249-62.; 2. Mak & Lok, Antiviral Res. 2026, #245; 3. Ertl H, et al. EASL 2023: TOP107; 4. Gane E, et al. EASL 2025: Abstract #1404; 5. Wong et al, AASLD 2025, #OP0196.

DISCLOSURES

Sue (SL) Currie is an employee of Virion Therapeutics and owns shares in the company.

FOR MORE INFORMATION

*More information about VRON-0200 is also available at www.VirionTx.com
Contact Dr Sue Currie at scurrie@virionTx.com for permission to reprint and/or distribute.

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