Anti-vector neutralizing antibody responses observed and sustained following prime-vaccination with VRON-0200 chimpanzee adenoviral vectors in adults with chronic HBV(CHB) infection on nucleos(t)ide therapy: exploratory analysis from a phase 1b study

Abstract # 3374

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INTRODUCTION

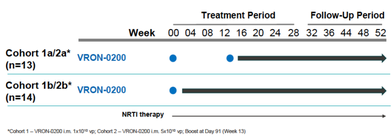
VRON-0200 is a therapeutic vaccine designed to restore broad HBV-specific T cell immunity in patients with chronic hepatitis B (CHB) on nucleos(t)ide therapy. Delivered using replication-incompetent chimpanzee adenoviral vectors (AdC6 or AdC7), it encodes HBV core and polymerase antigens together with glycoprotein D (gD), a novel checkpoint modifier that lowers the T cell activation threshold.

AdC6 and AdC7 were selected for their low seroprevalence in humans and minimal cross-reactivity. This exploratory analysis assessed the prevalence of pre-existing neutralizing antibodies (NAbs) to AdC6 and AdC7 and characterized the post-vaccination anti-vector humoral response in participants of the ongoing VRON-0200 Phase 1B trial (**NCT06070051**).

PURPOSE

To assess the prevalence and kinetics of anti-AdC6 and anti-AdC7 neutralizing antibodies after a single prime dose of VRON-0200 in 12 CHB patients, and to determine the magnitude and durability of these responses through Day 91.

CLINICAL TRIAL STUDY SCHEMA

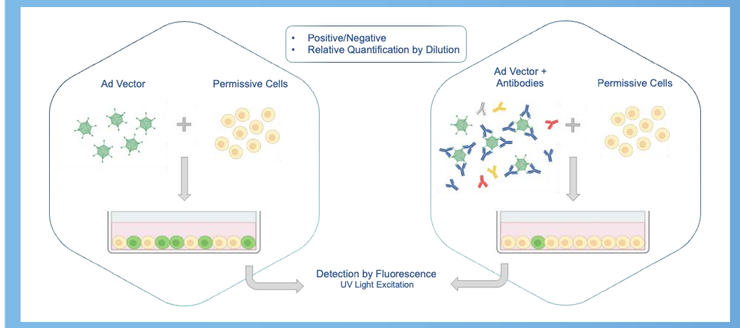


PATIENT SELECTION CRITERIA

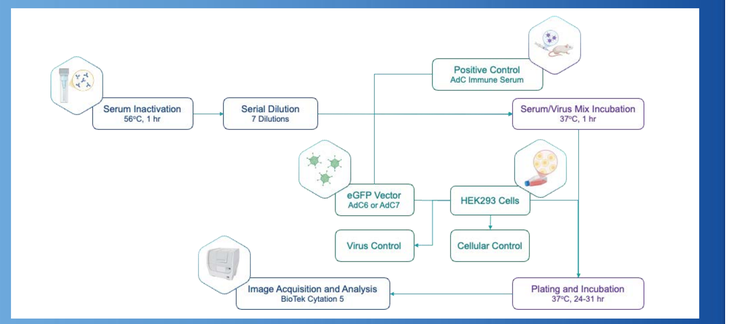
- VRON-0200 Phase 1B Study virally suppressed CHB patients on nucleos(t)ide therapy *(inclusion and exclusion criteria and baseline demographics available, Gane et al, Wong et al),* who received a single i.m. prime dose of VRON-0200
- Serum samples available for Days 1, 28, and 91
- Representation from all participating sites (Hong Kong and New Zealand)
- Included Cohorts 1 & 2 patients

A single VRON-0200 prime dose induced robust and durable anti-vector neutralizing antibody responses in 92% of patients, with responses observed regardless of pre-existing immunity and sustained through Day 91.

NEUTRALIZATION ASSAY RATIONALE



NEUTRALIZATION ASSAY OVERVIEW



METHODS

- Sera from 12 patients were collected at baseline (Day 1), Day 28, and Day 91
- Neutralization assays used replication-incompetent AdC6 or AdC7 vectors expressing eGFP. Sera were serially diluted & incubated with virus prior to infection of permissive cells
- Following incubation, cultures were examined for eGFP expression as a measure of viral infection. Neutralization titers were determined by comparing serum-treated cultures with virus-only control cultures, thereby assessing the neutralizing capacity of each serum sample. A hyperimmune serum positive control was included in each plate. Titers greater than 20 were classified as positive for the presence of serotype-specific neutralizing antibodies

RESULTS

KEY FINDINGS: ANTI-VECTOR IMMUNITY

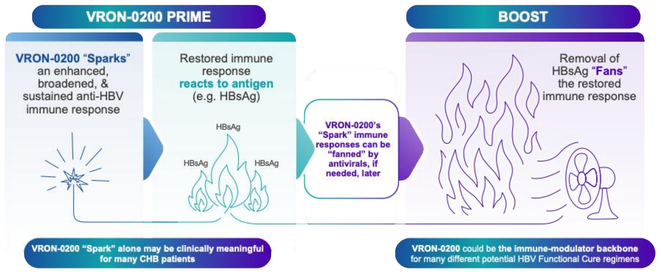
- 36 samples were analyzed, across 3 time points, from 12 patients
- Pre-existing immunity to the prime vector detected in **2/12** patients
  - Prime vaccination with **VRON-0200** significantly boosted anti-vector antibody responses despite pre-existing immunity
- Neutralizing antibody (NAb) responses against the prime vector observed in **11/12** (**92%**) of patients
  - NAb responses were induced, **regardless of cohort vector or pre-existing immunity**
  - Responses sustained from **Day 28 through Day 91**

PARTICIPANT NEUTRALIZING ANTIBODY TITERS (N=12)

Cohort	Pt	Visit D1 Baseline (pre-treatment)	Visit D28	Visit D91
1A	1	120	3240	3240
	2	<10	40	20
	3	<10	40	20
1B	4	<10	360	360
	5	<10	360	360
	6	<10	120	40
2A	7	40	120	40
	8	<10	10	10
	9	<10	40	40
2B	10	<10[1]	20	25[1]
	11	<20[2]	20	40
	12	<10	1080	360

1: Average of two assay runs.
2: Due to sample volume, sample plating started at 1:20 dilution. The starting dilution was negative for neutralization.

”SPARK AND FAN” MODEL FOR CHB



CONCLUSIONS

- Pre-existing NAbs or anti-adenovirus T cell immunity were infrequent (observed in only 2/12 patients)
- A single prime dose of VRON-0200 induced robust neutralizing antibody responses in 92% (11/12) of patients
- These responses were durable (sustained through Day 91) and occurred regardless of baseline immunity

POTENTIAL IMPLICATIONS

- These findings indicate that pre-existing immunity did not appear to compromise anti-vector responses to VRON-0200
- These NAb response data support a prime dose clinical development strategy
- Studies are underway to further explore other markers associated with VRON-0200’s anti-HBV clinical activity (e.g., T-Cell cross reactivity)
- VRON-0200 SPARK-B Phase 2B Study planning is underway

VRON-0200 Implications for CHB

- First new HBV immune-modulator since PEG-IFN
- Administration, dosing, and safety profile ideal for global public health
- VRON-0200 alone, or in combination treatments, might improve overall FC rates
- Immune restoration, with improved viral control, may lower cancer risk(s)

Implications for Other Viral Diseases

- Checkpoint Modifier Platform has potential for HDV, HIV Cure, HSV-2, EBV, & others

REFERENCES

1. Haut, et al. J Infect Dis. 2011, Apr 15;203(8):1073-81; 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; 6. Currie et al, APASL 2026, Abstract # 1344.

DISCLOSURES

Paula MacDonald woks for Virion Therapeutics and owns shares in the company.

FOR MORE INFORMATION

Contact Paula MacDonald at pmacdonald@viriontx.com for permission to reprint and/or distribute.

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