Medicines Control Authority of Zimbabwe

Clinical Trials Registry

PUBLIC TITLE/ACRONYM	GRAdHIVNE1 Vaccine Trial
Scientific Title	A Phase 1 Randomized Double Blinded Placebo Controlled, Dose Ranging Trial, of a Gorilla Adenovirus Vectored Networked Epitopes Vaccine (GRAdHIVNE1 Vaccine), Administered to Healthy Adults Living without HIV and Living with HIV, in Southern Africa

Primary Sponsor Details

Sponsors *	International AIDS Vaccine Initiative (IAVI)

Secondary Sponsor Details

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Countries of Recruitment *

Zimbabwe

South Africa

Source of Funds	Bill and Melinda Gates Foundation
Health Condition(s) or Problem(s) Studied *	HIV prevention and treatment
Medicine Name *	GRAdHIVNE1 Vaccine
Quantity of medicine required *	120

7.0 PRINCIPAL INCLUSION CRITERIA *

1. At least 18 years of age on the day of screening and has not reached his or her 51st birthday on the day of signing the Informed Consent Document.

2. Willing to comply with the requirements of the protocol and available for follow-up for the

planned duration of the study.

3. In the opinion of the Principal Investigator or designee and based on Assessment of

Informed Consent Understanding results, has understood the information provided and

potential impact and/or risks linked to administration of the investigational product; written

informed consent will be obtained from the participant before any study-related procedures

are performed.

4. All sexually active female participants capable of becoming pregnant must commit to use

an effective method of contraception from 21 days prior to receiving the IP until 4 months

following the last IP administration, including:

a. Intrauterine device, or contraceptive implant

b. Hormonal contraception

c. Successful vasectomy in the male partner (considered successful if a woman reports

that a male partner has [1] documentation of azoospermia by microscopy (< 1 year

ago), or [2] a vasectomy more than 2 years ago with no resultant pregnancy despite

sexual activity post-vasectomy)

5. Women who have undergone a hysterectomy, bilateral oophorectomy, or tubal ligation, as

well as those who are postmenopausal (>45 years of age with amenorrhea for at least 2

years, or any age with amenorrhea for at least 6 months and a serum follicle stimulating

hormone [FSH] level >40 IU/L) will not be required to use contraceptives.

6. Willing to forgo donations of blood, or any other tissues during the study.

Additional Inclusion criteria for PLWH (Part B only):

7. Confirmed HIV infection (HIV Ab+ or HIV RNA+) by documentation in the medical records or in-clinic HIV testing on screening visit.

8. CD4 ≥ 500 cells/µl at screening.

9. Currently on ART, and documentation of continuous combination ART (cART) for at least 12 months with suppression of plasma HIV-1 viral load < 50 copies / ml for greater than 6 months prior to trial entry, measured on at least 2 independent occasions that can include the screening viral load. cART is defined as a regimen including ≥ 2 compounds, e.g., 2 nucleoside reverse transcriptase inhibitors plus either non-nucleoside reverse transcriptase inhibitor or protease inhibitor or integrase inhibitor.

10. Viral load < 50 copies / ml at time of screening (within 28 days prior to IP administration).

11. Must commit to adhering to a suppressive ART regimen for the duration of the study

Eligibility Criteria Specific to PLWoH (Part A)

People living without HIV(PLWoH) at screening, must be deemed to be at low risk of HIV

infection and willing to maintain low-risk behavior for the duration of the trial per the guidelines

for determining low likelihood of acquiring HIV.

The following guidelines should be applied by the investigator to identify potential vaccine trial

participants with a low likelihood of acquiring HIV. These guidelines are based on behavior within

the last 12 months prior to enrollment. Some participants may not be appropriate for enrollment

even if they meet these guidelines, and more stringent criteria may be applied based on the site

Principal Investigator's (PI) discretion. These guidelines should be supplemented and interpreted

with local epidemiological information about HIV prevalence. The site PI may review with the

Medical Monitor and/or the Protocol Safety Review Team (PSRT) a participant's likelihood of

acquiring HIV.

For participants not on stable pre-exposure prophylaxis (PrEP)

o Consider for inclusion in the trial if in the 12 months prior to enrollment, the person:

• Abstained from vaginal and anal intercourse, OR

• Was in a mutually monogamous relationship with a partner known to be living

without HIV, OR

• Had 2 or fewer partners known or believed to be living without HIV, with whom

they regularly used condoms for vaginal or anal intercourse, OR

• Had 2 or fewer partners living with HIV who are known to be virally suppressed,

as assessed by the investigator

o Exclude the participant if in the past 12 months they:

• Have a history of injecting drugs or other substances without a prescription

• Used cocaine, methamphetamine, or excessive alcohol in such a way that, in the

investigator's judgment, rendered the participant at a greater-than-low likelihood

of acquiring HIV

• Gave or received money, drugs, gifts, or services in exchange for vaginal or anal

sex that, in the opinion of the investigator, increases the likelihood of HIV

acquisition

• Has a history of newly acquired syphilis; gonorrhoea (rectal, vaginal, urethral/urine); chlamydia (rectal, vaginal, urethral/urine); trichomoniasis; active herpes simplex virus type 2 (HSV-2) lesions; chancroid; genital warts of the labia minora, vagina, or cervix; or any other symptomatic genital warts. For participants on pre-exposure prophylaxis (PrEP): o PrEP Assessment Reports 6 months (180 days) or more of protective PrEP using any combination of the following: • For daily oral PrEP use in persons assigned male sex at birth (AMAB) who have sex with AMAB persons: Reports equal to or greater than 70% when asked the following: "Thinking about the past 4 weeks, what percent of the time were you able to take all your PrEP medications?" • For daily oral PrEP use in persons having receptive vaginal sex: Reports equal to or greater than 90% when asked the following: "Thinking about the past 4 weeks, what percent of the time were you able to take all your PrEP medications?" • For event-driven (on-demand or "2-1-1") PrEP use in AMAB persons who have sex with AMAB persons: - For individuals with frequent use (> 15 pills per month): At least 80% of condomless sex acts are covered with on-demand PrEP at the recommended dose schedule - For individuals with less frequent use (≤ 15 pills per month): 👇 A past history of high adherence (> 90%) 👇 Commitment to use on-demand PrEP for all condomless sex acts at the recommended dose schedule

• For injectable PrEP such as cabotegravir; must have received at least 2 doses, and

is currently on a schedule consistent with product label

• PrEP medications other than FTC/TAF or FTC/TDF, or injectable cabotegravir

may be appropriate based on national recommendations

• Commits to maintaining protective PrEP use throughout trial

o Sexual Behaviour

• Persons stably taking PrEP as prescribed above for 6 months or longer are

considered to have a low likelihood of acquiring HIV, regardless of any sexual

behaviour that might otherwise be associated with a high likelihood of HIV

exposure.

o Nonsexual Behaviour

• In the last 12 months, did not inject drugs or other substances without a prescription

7.1 PRINCIPAL EXCLUSION CRITERIA *

1. Any clinically significant acute or chronic medical condition, other than HIV infection (in Part B only), that is considered progressive or in the opinion of the investigator makes the participant unsuitable for participation in the study.

2. For the PLWH (Part B), history of AIDS-defining illness or CD4 < 200 cells/µl.

3. If female, pregnant, lactating or planning a pregnancy during the period of screening through completion of the study.

4. In the past 6 months a history of alcohol or substance use, judged by the Investigator to potentially interfere with participant study compliance.

5. Bleeding disorder that was diagnosed by a physician (e.g., Factor deficiency, coagulopathy or platelet disorder that requires special precautions). Note: A participant who states that he or she has easy bruising or bleeding but does not have a formal diagnosis and has intramuscular injections and blood draws without any adverse experience, is eligible.

6. History of a splenectomy.

7. Previous receipt of an adenovirus vectored vaccine.

8. Receipt of live attenuated vaccine or other vaccine within the previous 60 days or planned receipt within 180 days after administration of IP. Receipt of blood transfusion or bloodderived products within the previous 3 months.

9. Participation in another clinical trial of an investigational product currently, within the previous 3 months or expected participation during this study.

10. Prior receipt of an investigational HIV vaccine candidate, monoclonal antibody or polyclonal immunoglobulin (note: receipt of placebo in a previous HIV vaccine or monoclonal antibody trial will not exclude a participant from participation if documentation is available and the Medical Monitor gives approval).

11. History of severe local or systemic reactogenicity to vaccines (e.g., anaphylaxis, respiratory difficulties, angioedema).

12. Psychiatric condition that compromises safety of the participant and precludes compliance with the protocol. Specifically excluded are persons with history of psychoses within the past 3 years, ongoing risk for suicide, or history of suicide attempt or gesture within the past 3 years.

13. If, in the opinion of the Principal Investigator or designee, it is not in the best interest of the participant to participate in the trial.

14. Seizure disorder: a participant who has had a seizure in the last 3 years is excluded. (Not excluded: a participant with a history of seizures who has neither required medications nor had a seizure for 3 years.)

15. Infectious disease: chronic hepatitis B infection (HbsAg positive), current hepatitis C infection (HCV Ab positive and/ or HCV RNA) or treatment for hepatitis C infection in the past year, or active syphilis (RPR confirmed by TPHA).

16. A history of malignancy within the past 5 years (prior to screening) or ongoing malignancy.

17. Active, serious infections (other than HIV infection in PLWH) requiring parenteral antibiotic, antiviral or antifungal therapy within 30 days prior to enrollment.

18. Any of the following abnormal laboratory parameters at screening: a. Haematology i. Haemoglobin <10.5 g/dL in females; haemoglobin <11.0 g/dL in males ii. Absolute Neutrophil Count (ANC): ≤1000/mm3 iii. Absolute Lymphocyte Count (ALC): < 650/mm3 iv. Platelets: < 125,000 mm3 or ≥ 550,000/mm3 b. Chemistry i. Creatinine ≥1.1 x ULN ii. AST ≥1.25 x ULN iii. ALT ≥1.25 x ULN iv. Total bilirubin ≥1.25 x ULN v. Alkaline phosphatase ≥1.25 x ULN vi. Albumin ≤ 3.0 g/dL or ≤ 30 g/L c. Urinalysis

i. Clinically significant abnormal dipstick confirmed by microscopy

ii. Protein = 1+ or more

iii. Blood = 1+ or more (not due to menses)

19. Any clinically relevant abnormality on history or examination including history of immunodeficiency or autoimmune disease, other than HIV among the PLWH; use of systemic corticosteroids, immunosuppressive, anticancer, or other

7.2 PRIMARY END POINTS *

Safety and Tolerability:

1. Proportion of participants with each type of reactogenicity event classified by severity of the events from initial administration through 7 days following completion of each dose of the investigational product.
2. Proportion of participants reporting unsolicited adverse events (AEs), including safety laboratory (biochemical, haematological) parameters, classified by severity and causality, from initial administration through 28 days following completion of each dose of the investigational product.
3. Proportion of participants reporting serious adverse events (SAEs) throughout the study period, classified by causality.

9.0 DESIGN OF THE TRIAL

Type of trial *	Controlled

If controlled

Randomised	Yes
Single Blind	
Double Blind	Yes
Parallel group	
Cross over	
Other	
If yes to other, specify	
If controlled, specify the comparator	Normal saline
Other medicinal product(s)	No
Placebo	Yes
Other	
If yes to other, specify	
Other	

Expected Number of participants in Zimbabwe *	40
Total enrolment in each site: (if competitive enrolment, state minimum and maximum number per site.) *	40, however this is competitive enrollment as such the numbers in Zimbabwe could be lower or higher than 40. There are 3 sites and no site minimums or maximums.
Total participants worldwide *	120

Time period for the trial *	March 2025 to December 2027