abstract #427

Safety and Viral Dynamics During Temporary Treatment Interruption (TTI) in the RV630 HIV Cure Trial

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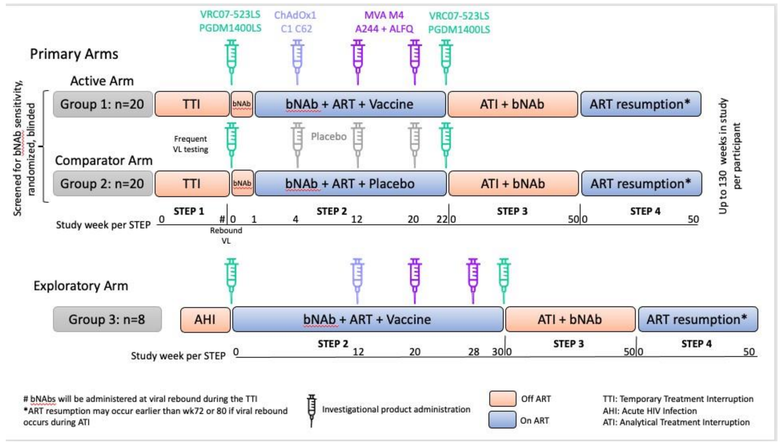
Background

- Temporary treatment interruption (TTI) is a novel clinical trial strategy in which antiretroviral therapy (ART) is stopped to allow viral reactivation and transient viremia under close monitoring.
- In HIV cure trials that include broadly neutralizing antibodies (bNAbs) or therapeutic vaccines, TTI allows formation of antigen-antibody immune complexes and primes B and T cells with participant-specific antigen exposure prior to vaccination, which may then enable ART-free HIV remission.

Methods

- RV630/DELIVER-01 (NCT06484335) is an ongoing study recruiting clinically stable and virally suppressed adult participants from the RV254 acute HIV infection (AHI) cohort in Bangkok, Thailand.
- Participants in Groups 1 and 2 undergo TTI up to 8 weeks at study entry. Viral load (VL) and clinical exam with review of symptoms for acute retroviral syndrome (ARS) are done at least weekly.
- When VL>1,000 copies/mL is confirmed, two bNAbs (VRC07-523LS 40 mg/kg, PGDM1400LS 5 mg/kg) are given IV and ART is restarted one week later.
- Group 3 enrolls during acute HIV infection, does not undergo TTI
- The study intervention also includes a vaccine regimen (ChAdOx1.tHIVconsv1, ChAdOx1.tHIVconsv62, MVA.tHIVconsv4 and A244d11gp120/ALFQ) or placebo and a second dose of bNAbs administered over the following 22 weeks.
- Participants then undergo analytic treatment interruption (ATI) for up to 50 weeks to evaluate efficacy of the intervention.

Figure 1: Study Schema



TTI is a non-pharmacologic method to reactivate T-cells with latent HIV infection.

TTI was safe and well tolerated in participants who initiated ART during acute HIV infection.

Results

- Sixteen participants have been enrolled in Groups 1 and 2 since September 2025. All were male with a median (IQR) age of 36 (33-39) years. Six participants were enrolled in Group 3.
- 15/16 met criteria to receive bNAbs while 1 maintained viral suppression through 8 weeks.
- VL dropped quickly at 1 week post bNAb infusion without ART (Table 2)
- The study is ongoing; no participants have reached the ATI stage yet.

Figure 2: Time to viral rebound

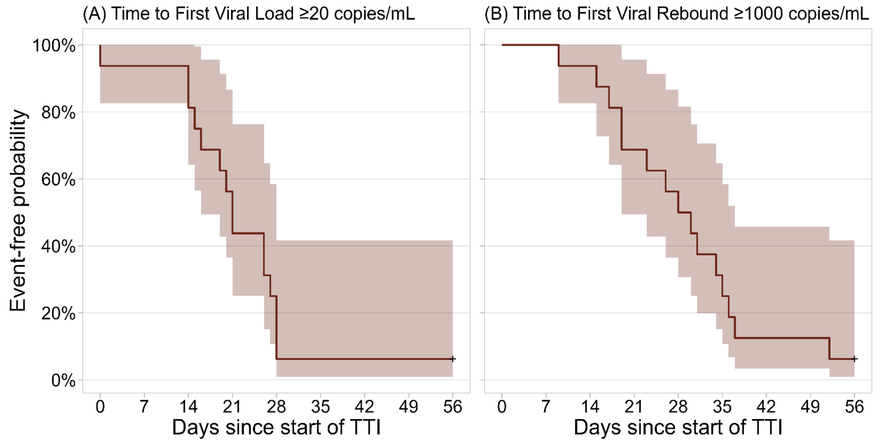


Table 1: Median days (95% CI) of TTI to:

VL>20 copies/mL	VL>1,000copies/mL	bNAb infusion
21 (16-28)	29 (19-37)	33 (24-41)

Table 2: VL change after TTI (median (IQR) copies/mL)

VL @ bNAb infusion	VL after 1 week
11,100 (6,328 - 32,750)	1,183 (1,300 -3,525)

TTI was safe and well tolerated (Table 3)

- Four adverse events (pharyngitis, diarrhea, and two headaches) were reported during the TTI prior to viral rebound (n=3) or during low-level viremia (41-94 copies/mL) and were deemed unrelated to the study.
- No signs or symptoms of ARS were reported during periods of viremia.
- All participants remained in the study post-TTI.

Table 3: Prevalence of ARS symptoms during TTI (n=15)

ARS (Acute Retroviral Syndrome) signs/symptoms	n	(%)
Fatigue	1	6.2%
Pharyngitis	1	6.2%
Headache	2	12.5%
Myalgia	1	6.2%
Anorexia	0	0%
Diarrhea	1	6.2%
Morbilliform rash	0	0%
Arthralgia	0	0%
Mucocutaneous ulceration	0	0%
Nausea/vomiting	0	0%
Lymphadenopathy	0	0%
Leukopenia	0	0%
Thrombocytopenia	0	0%
Oral/vaginal candidiasis	0	0%
Meningismus/aseptic meningitis	0	0%

Conclusions

- TTI was safe and well tolerated in this cohort of participants who initiated ART during AHI.
- Active surveillance observed no signs or symptoms of ARS during the brief period of viremia.
- bNAb infusions at peak viremia induced a median 1 log reduction in VL without ART.

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Material has been reviewed by the Walter Reed Army Institute of Research. There is no objection to its presentation and/or publication. The opinions or assertions contained herein are the private views of the author, and are not to be construed as official, or as reflecting true views of the Department of the Army or the Department of Defense. The study protocol was approved by the WRAIR Institutional Review Board in compliance with all applicable Federal regulations governing the protection of human subjects. The investigators have adhered to the policies for protection of human participants as prescribed in AR 70–25.