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Lessons Learned From Conducting the First HIV Cure Interventional Trial in Africa With Collaboration Between Academia, Government, and Industry

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The Females Rising through Education, Support, and Health (FRESH) cohort was established in 2012 in Durban, South Africa

A Story of **Collaboration, Community Engagement, Resilience, and Agility**



Durban, South Africa

The FRESH program facilitates detection of hyperacute HIV infection in young women, combined with an intensive life skills and job readiness curriculum



FRESH

Longitudinal follow-up of high-risk women included frequent (twice-weekly) HIV-RNA testing by finger-prick blood test
Participants began treatment within a median of 1 day after HIV detection

HIV infection

Viral load with early antiretroviral therapy (ART) initiation



- The FRESH study focuses exclusively on young women because of the higher rate of HIV infection in this age group compared with men and the relative paucity of data on HIV pathogenesis in women
- This population bears a disproportionate burden of the global epidemic but remains underrepresented in clinical trials
- *An innovative approach was used to establish this cohort, which integrated scientific research with social support, addressing participants' holistic needs. This strategy, featuring an empowerment curriculum, has fostered exceptional retention, adherence, and engagement among participants and community stakeholders, while advancing critical HIV research*

Twenty women from the FRESH cohort participated in an ATI-inclusive HIV cure trial evaluating the safety and efficacy of 2 bNAb's combined with vesatolimod

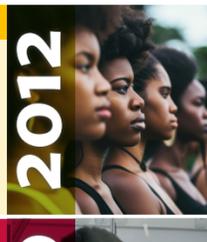
PHASE 2a TRIAL: June 2022 - January 2025



ART, antiretroviral therapy; ATI, analytical treatment interruption; bNAb, broadly neutralizing antibody; IV, intravenous.

- Phase 2a, open-label trial evaluated the safety and efficacy of 2 anti-HIV envelope broadly neutralizing antibodies (bNAb's), VRC07-523LS and CAP256V2LS, combined with a Toll-like receptor 7 agonist, vesatolimod (VES) (GS-US-382-5445; NCT05281510)
- Participants: Unique population of early-treated women with clade C HIV-1 recruited from FRESH cohort, who had been virally suppressed on ART for ≥ 12 months
- Complex HIV cure trials ask a lot of participants and staff
 - *Frequent safety monitoring, extended observation after study drug dosing, biweekly and weekly visits, intensive safety and tissue sampling, and longitudinal assessment of participant experiences*

The study weathered several disruptive external events, including the COVID-19 pandemic, political unrest, and natural disasters



FRESH BEGINS

- Having an established cohort and a trusting relationship with the site staff facilitated recruitment, likely increased willingness to participate, participant retention, uptake of optional sampling, and adherence to an intensive study protocol



COVID-19; DISRUPTION: ALL FACILITIES CLOSED

- All clinical trial sites in South Africa were required to close
- All research facilities/universities in South Africa were required to close
- FRESH team mobilized additional resources for ART delivery and launched ART home delivery to maintain viral suppression



POLITICAL UNREST

- FRESH clinical site decimated; all equipment, furnishings, and supplies destroyed or stolen
- Study team moved to a temporary location at the nearby hospital
- Took 3 months to rebuild the site
- Despite delays and challenges, Gilead successfully launched clinical trial training

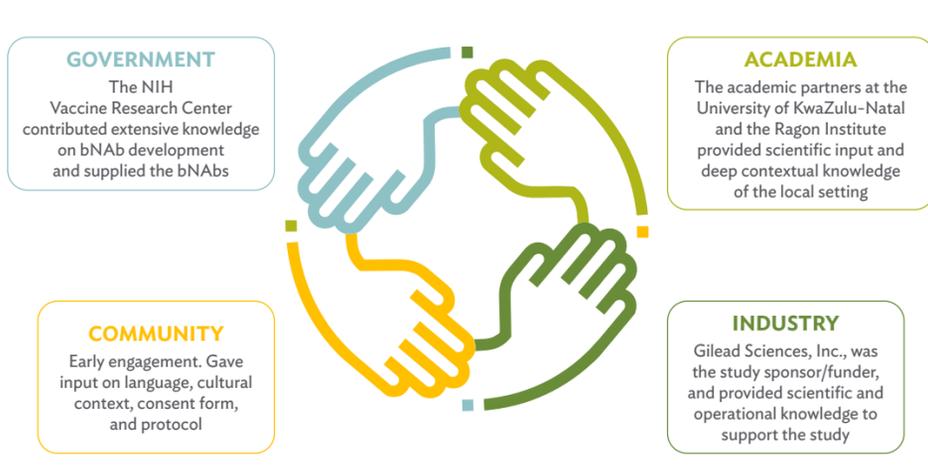


CATASTROPHIC FLOODING, ROAD CLOSURES AND DAMAGE

- Roads to the site washed away, no access by car; participants and study team walked to site
- No water or electricity for weeks
- No missed days of monitoring for acute HIV infection
- Mobilized additional resources to rebuild and restore the site and finally launched first trial participant's first VES dose

Overcoming multiple challenges required **unwavering commitment, enthusiasm, and support** to make the trial a reality

This trial was a culmination of a productive partnership between academia, government, community, and industry



This trial demonstrated the feasibility of conducting complex HIV cure trials in Africa, which has the highest prevalence of HIV globally



FRESH:

Females Rising through Education, Support, and Health

A unique platform for HIV prevention and cure research

Gilead Sciences sponsored the trial and worked closely with key collaborators:

- Department of Health Province of KwaZulu-Natal
- Health Systems Trust - South Africa
- Witten Family Foundation
- Mass General Brigham
- University of KwaZulu-Natal
- HIV Pathogenesis Programme
- ITEACH, NPC
- Ragon Institute of Mass General Brigham, MIT, and Harvard
- US National Institute of Allergy and Infectious Diseases

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