Overview of the Current Landscape of HIV Cure-Related Research
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Treatment Action Group

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The need for an HIV cure
The ways that HIV persists

- HIV primarily persists by hiding out in long-lived immune system cells (primarily CD4 T cells)
- Some persisting HIV is intact, capable of replicating but asleep (latent) during ART and invisible to the immune system (latent reservoir)
- Some persisting is HIV intact, capable of replicating and persistently or intermittently producing infectious HIV that’s blocked from infecting other cells by ART (active reservoir)
- A large amount of persisting HIV is defective and incapable of replicating, but in some cases able to produce partial virus components
- Some persisting HIV appears to be intact but trapped inside cells and unlikely to be able to emerge and replicate
Leading ideas for curing HIV

• Wake up latent HIV so it’s visible to the immune system
• Promote clearance of the HIV that persists in the body despite ART
• Increase the ability of the immune system to control HIV when ART is stopped
• Protect vulnerable cells from HIV infection
HIV cure-related clinical research

• Since 2014, Treatment Action Group (TAG) has maintained a listing of HIV cure-related clinical trials and observational studies:
  https://www.treatmentactiongroup.org/cure/trials/

• Information mainly drawn from clinical trial registries:
  https://clinicaltrials.gov/ and others internationally
  (https://www.hhs.gov/ohrp/international/clinical-trial-registries/index.html)
# Research Toward a Cure February 15, 2023

## Table 1. Current Clinical Trials

<table>
<thead>
<tr>
<th>Trial</th>
<th>Trial Registry Identifier(s)</th>
<th>Sponsor(s)</th>
<th>Phase</th>
<th>Estimated End Date/Interim Results</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ADOPTIVE IMMUNOTHERAPY</strong></td>
<td></td>
<td></td>
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<tr>
<td>AutoRESIST: HIV antigen-specific T-cells targeting conserved epitopes for treatment of HIV-associated lymphoma</td>
<td>NCT04975698</td>
<td>Catherine Bollard, Children's Research Institute</td>
<td>Phase II</td>
<td>June 2026</td>
</tr>
<tr>
<td><strong>AllocRESIST</strong>: Evaluate the safety, immunologic, and virologic responses of donor derived HIV-specific T-cells in HIV+ individuals following allogeneic bone marrow transplantation</td>
<td>NCT04248192</td>
<td>Catherine Bollard, Children's Research Institute</td>
<td>Phase I</td>
<td>April 2024</td>
</tr>
<tr>
<td><strong>HST-NEETs</strong>: HIV-1 specific T-cells for HIV+ individuals</td>
<td>NCT03485963 (closed to enrollment)</td>
<td>Children's Research Institute</td>
<td>Phase I</td>
<td>December 2023</td>
</tr>
<tr>
<td><strong>ANALYTICAL TREATMENT INTERRUPTION</strong></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Assessment of HIV remission in early treated individuals with the MHC B35/53Bw4TTC2 genotype</td>
<td>NCT05482854 (not yet open for enrollment)</td>
<td>ANRS</td>
<td>N/A</td>
<td>April 2025</td>
</tr>
<tr>
<td>SCOPE-ATI</td>
<td>NCT04359166</td>
<td>UCSF</td>
<td>N/A</td>
<td>June 2024</td>
</tr>
<tr>
<td>Imaging and biopsy of individuals undergoing ATI</td>
<td>NCT05419024</td>
<td>National Cancer Institute (NCI)</td>
<td>Phase II</td>
<td>August 2026</td>
</tr>
<tr>
<td><strong>ANTIBODIES</strong></td>
<td></td>
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</tr>
<tr>
<td>VRC01 (analytical treatment interruption in HVTN 703/HPTN 081 AMP trial participants)</td>
<td>NCT04860323</td>
<td>HIV Vaccine Trials Network</td>
<td>N/A</td>
<td>August 2023</td>
</tr>
<tr>
<td>VRC01 (analytical treatment interruption in HVTN 704/HPTN 085 AMP trial participants)</td>
<td>NCT04801758</td>
<td>HIV Vaccine Trials Network</td>
<td>N/A</td>
<td>January 2030</td>
</tr>
<tr>
<td>GSK3810109A (broadly neutralizing antibody formerly named N6-LS)</td>
<td>NCT04871113 (closed to enrollment)</td>
<td>ViIV Healthcare</td>
<td>Phase Ila</td>
<td>September 2023</td>
</tr>
</tbody>
</table>

Entries shaded in light grey include analytical treatment interruptions (ATIs); in some cases, ATIs are only initiated if certain outcomes are achieved. For the most up-to-date version, visit: [http://www.treatmentactiongroup.org/cure/trials](http://www.treatmentactiongroup.org/cure/trials). Please send updates, corrections, or suggestions to Richard Jefferys at richard.jefferys@treatmentactiongroup.org.
HIV cure-related studies, February 2023

- Interventional
  - 93 trials (90 adult, 3 pediatric)
    - 38 phase I, 12 phase I/II, 30 phase II, 2 phase II/III (metformin, early infant ART in Botswana), 2 phase III (dolutegravir + lamivudine simplification, acute infection treatment)

- Observational (no interventions given)
  - 38 studies (37 adult, 1 pediatric)
  - 34 studies involve analytical treatment interruptions (ATIs)
    - In some cases, ATIs only initiated if certain parameters are met
Types of interventions

- Adoptive immunotherapy
- Antibodies
- Anti-CMV therapy
- Anti-inflammatory therapy
- Bcl-2 antagonists
- Cannabinoids
- Combinations
- Cytokines
- DART molecules
- Gene therapies
- Gene therapies for PWPHIV and cancers
- Gonadotropin-releasing hormone (GnRH) agonists
- Immune checkpoint inhibitors
- Imaging studies
- Immunosuppressors
- Latency reversing agents
- mTOR inhibitors
- Stem cell transplantation
- T-cell receptor-based bispecifics
- Stimulants
- Therapeutic receptor agonists
- Toll-like receptor/early treatment
- Treatment intensification
- Tyrosine kinase inhibitors
Types of interventions

- Adoptive immunotherapy – 3
- Analytical treatment interruption – 3
- Antibodies – 13 *(7 w/ATI)*
- Anti-CMV therapy – 1
- Anti-inflammatory – 1
- Antiretroviral therapy – 1
- Bcl-2 antagonists – 1
- Cannabinoids – 1
- Combinations – 17 *(11 w/ATI)*
- Cytokines – 1
- Dual-affinity re-targeting (DART) molecules – 1
- Gene therapies – 12 *(6 w/ATI)*
- Gene therapies for PWHIV & cancers – 3 *(2 w/ATI)*
- Gonadotropin-releasing hormone agonists – 1
- Imaging studies – 2
- Immune checkpoint inhibitors – 6 *(2 w/ATI)*
- Immunomodulators – 1
- Latency-reversing agents – 5
- mTOR inhibitors – 1
- Stem cell transplantation – 2
- Stimulants – 1
- T-cell receptor-based bispecifics – 1
- Therapeutic vaccines – 6 *(1 w/ATI)*
- Toll-like receptor agonists – 1
- Treatment intensification/early treatment – 4
- Tyrosine kinase inhibitors – 1
Promote clearance of the HIV that persists in the body despite ART

- Adoptive immunotherapy
- Broadly neutralizing antibodies (bNAbs)
- Bcl-2 antagonists
- Cytokines
- Dual-affinity re-targeting (DART) molecules
- Gene therapies (CAR T cells)
- Immune checkpoint inhibitors
- T-cell receptor-based bispecifics
- Therapeutic vaccines

Increase the ability of the immune system to control HIV when ART is stopped

- Adoptive immunotherapy
- Broadly neutralizing antibodies (bNAbs)
- Cytokines
- Dual-affinity re-targeting (DART) molecules
- Gene therapies
- Immune checkpoint inhibitors
- T-cell receptor-based bispecifics
- Therapeutic vaccines

Wake up latent HIV so it’s visible to the immune system

- Cytokines
- Immune checkpoint inhibitors
- Latency-reversing agents
- Therapeutic vaccines
- Toll-like receptor agonists

Protect vulnerable cells from HIV infection

- Gene therapies
- Stem cell transplantation (for HIV+ people with cancers)
- Tyrosine kinase inhibitors
Relatively few studies with ATIs in the Majority World

- Two studies enrolling people who acquired HIV during the Antibody-Mediated Prevention (AMP) trials with sites in:
  - Botswana, Malawi, South Africa, Zimbabwe
  - Brazil, Peru (+ United States)

- New ACTG study of long-acting broadly neutralizing antibodies (bNAbs) with sites in Brazil and Peru

- Gilead-sponsored study of bNAbs + toll-like receptor agonist in the FRESH cohort of young women in South Africa

- IMPAACT P1115 study in newborns with potential for ATI
  - Argentina, Brazil, Haiti, Kenya, Malawi, South Africa, Tanzania, Thailand, Uganda, United States, Zambia, Zimbabwe
Pediatric studies

- IMPAACT P1115 v2.0: Very early intensive treatment of HIV-infected infants to achieve HIV remission (ART +/- VRC01)
  - Newborns (up to 10 days old)
- HVRRICANE: HIVIS DNA + MVA-CMDR vaccines +/- TLR4 agonist
  - 9 Years and older
- EIT: Early infant HIV treatment in Botswana
  - 0 Days to 3 Years
- Long-term clinical, immunologic, and virologic profiles of children who received early treatment for HIV (observational)
  - Children living with HIV who received early treatment in IMPAACT network studies or other research studies sponsored by the US National Institutes of Health (NIH)
Industry-sponsored

- AbbVie - 2
- Aelix Therapeutics - 1
- American Gene Technologies International Inc. - 1
- Ascletis Pharmaceuticals Co., Ltd. - 1
- Excision BioTherapeutics - 1
- Frontier Biotechnologies Inc. - 1
- Gilead Sciences – 3
- Immune System Regulation AB - 1
- Immunocore - 1
- MacroGenics - 1
- UBP Greater China (Shanghai) Co., Ltd - 3
- ViiV Healthcare - 1
African research institutions

- Latent HIV-1, Viral Suppress and Hope for HIV Cure
  (observational study)

- https://clinicaltrials.gov/ct2/show/NCT04938518

- Primary sponsor: Kenya Medical Research Institute
  - Support from the European and Developing Countries Clinical Trials Partnership (EDCTP)
Summary

- United States remains the most common site of HIV cure-related clinical studies
- US National Institutes of Health the major source of funding support
- Studies involving ATIs potentially beginning to occur more frequently in the Majority World
- Minority of studies primarily sponsored by industry (~18%)
- Majority of studies primarily sponsored by research institutions based in US & Europe