
2023
COMMUNITY
HIV CURE RESEARCH
WORKSHOP
Overview of the Current Landscape
of HIV Cure-Related Research

# Overview of the Current Landscape of HIV Cure-Related Research

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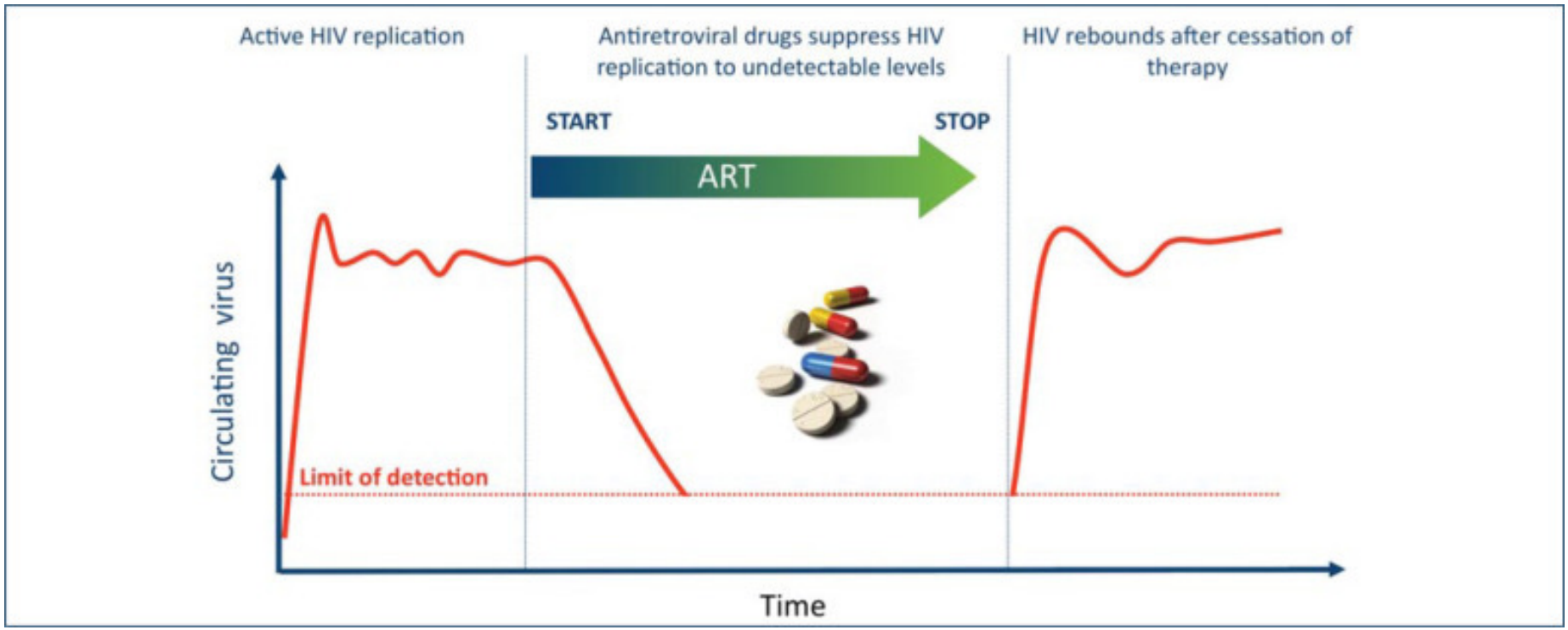
Treatment Action Group

# 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)

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# Research Toward a Cure February 15, 2023

**Table 1. Current Clinical Trials**

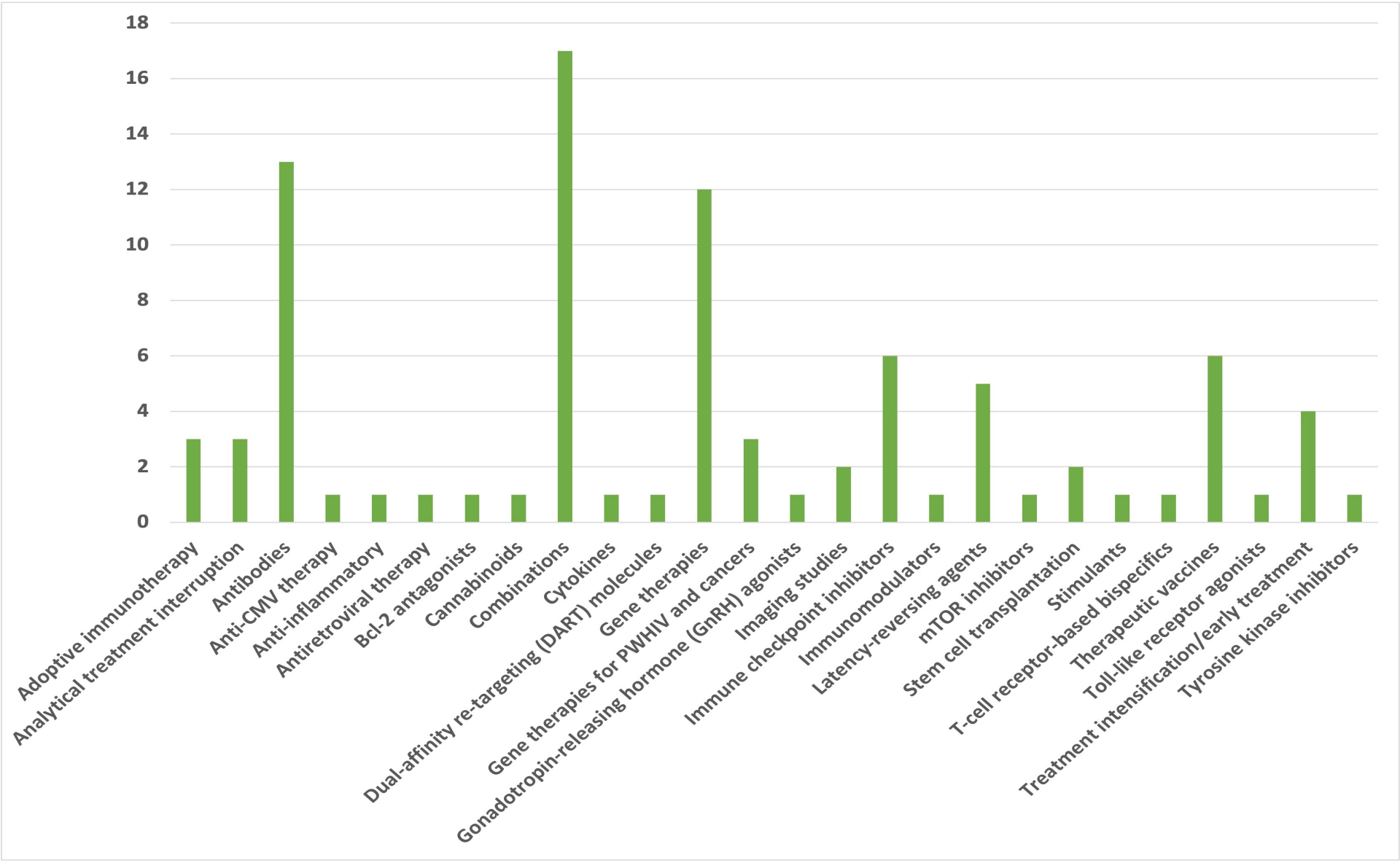
| Trial | Trial Registry Identifier(s) | Sponsor(s) | Phase | Estimated End Date/Interim Results |
|---|---|---|---|---|
| **ADOPTIVE IMMUNOTHERAPY** | | | | |
| **AutoRESIST**: HIV antigen-specific T-cells targeting conserved epitopes for treatment of HIV-associated lymphoma | NCT04975698 | Catherine Bollard, Children's Research Institute | Phase II | June 2026 |
| **AlloRESIST**: Evaluate the safety, immunologic, and virologic responses of donor derived HIV-specific T-cells in HIV+ individuals following allogeneic bone marrow transplantation | NCT04248192 | Catherine Bollard, Children's Research Institute | Phase I | April 2024 |
| **HST-NEETs**: HIV-1 specific T-cells for HIV+ individuals | NCT03485963 (closed to enrollment) | Children's Research Institute | Phase I | December 2023 |
| **ANALYTICAL TREATMENT INTERRUPTION** | | | | |
| Assessment of HIV remission in early treated individuals with the MHC B35/53Bw4TTC2 genotype | NCT05482854 (not yet open for enrollment) | ANRS | N/A | April 2025 |
| **SCOPE-ATI** | NCT04359186 | UCSF | N/A | June 2024 |
| Imaging and biopsy of individuals undergoing ATI | NCT05419024 | National Cancer Institute (NCI) | Phase II | August 2026 Front Med. 2022 Aug 22;9:979756. |
| **ANTIBODIES** | | | | |
| **VRC01** (analytical treatment interruption in HVTN 703/HPTN 081 AMP trial participants) | NCT04860323 | HIV Vaccine Trials Network | N/A | August 2023 |
| **VRC01** (analytical treatment interruption in HVTN 704/HPTN 085 AMP trial participants) | NCT04801758 | HIV Vaccine Trials Network | N/A | January 2030 |
| **GSK3810109A** (broadly neutralizing antibody formerly named N6-LS) | NCT04871113 (closed to enrollment) | ViiV Healthcare | Phase IIa | September 2023 HIV Glasgow 2022, Abstract O34 |

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. 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



# 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

## 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

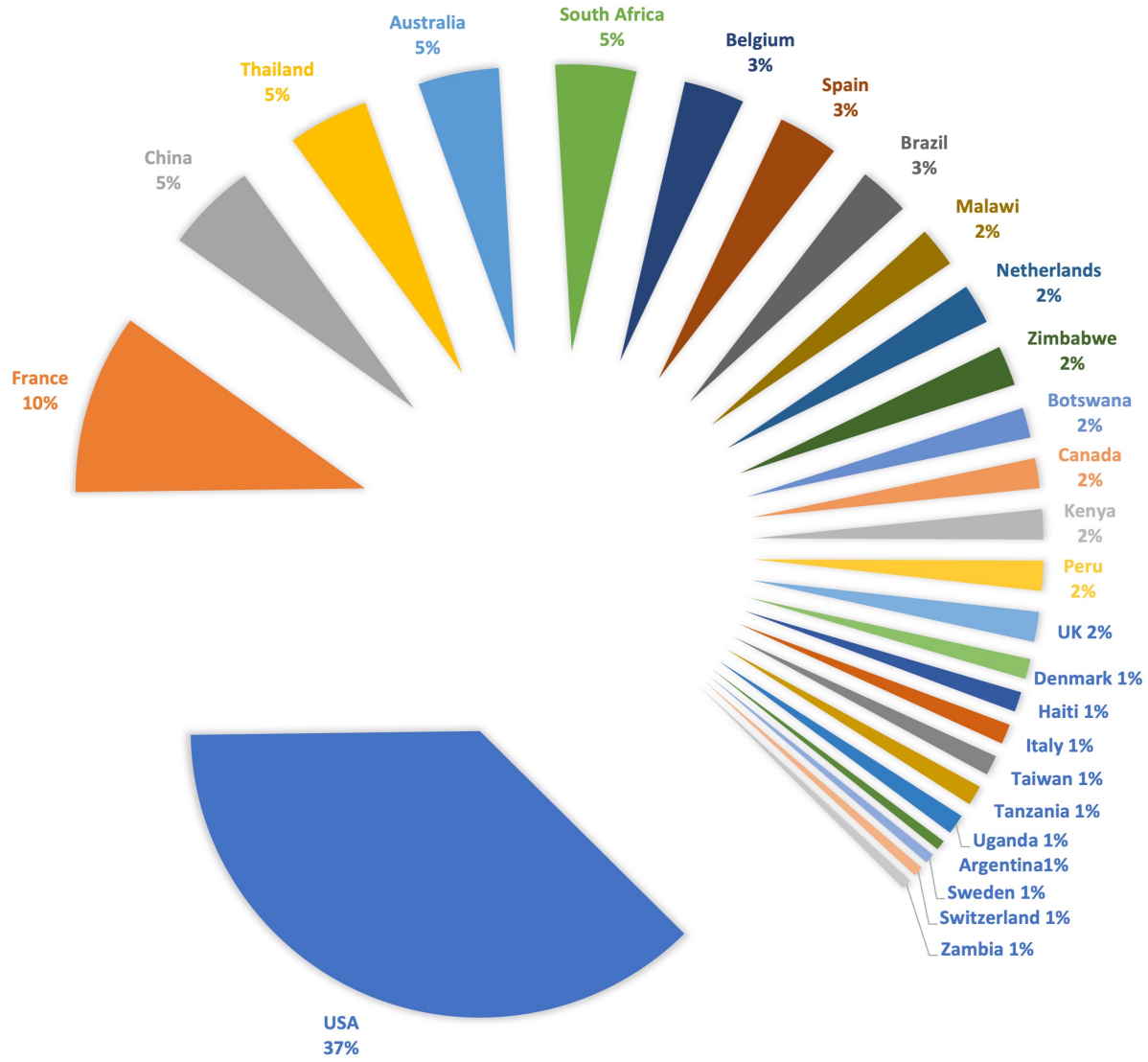
## Increase the ability of the immune system to control HIV when ART is stopped

- 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

## Protect vulnerable cells from HIV infection

- Gene therapies
- Stem cell transplantation (for HIV+ people with cancers)
- Tyrosine kinase inhibitors

# Study site locations, February 2023



# 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)
  - Investigation of the Impact of Inducible, Replication-competent Latent HIV-1 as an Impediment to HIV/AIDS Cure in the Context of Sustained Viral Suppression
  - 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
  - See: Global Investment in HIV Cure Research and Development in 2020 – AVAC, International AIDS Society
- 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