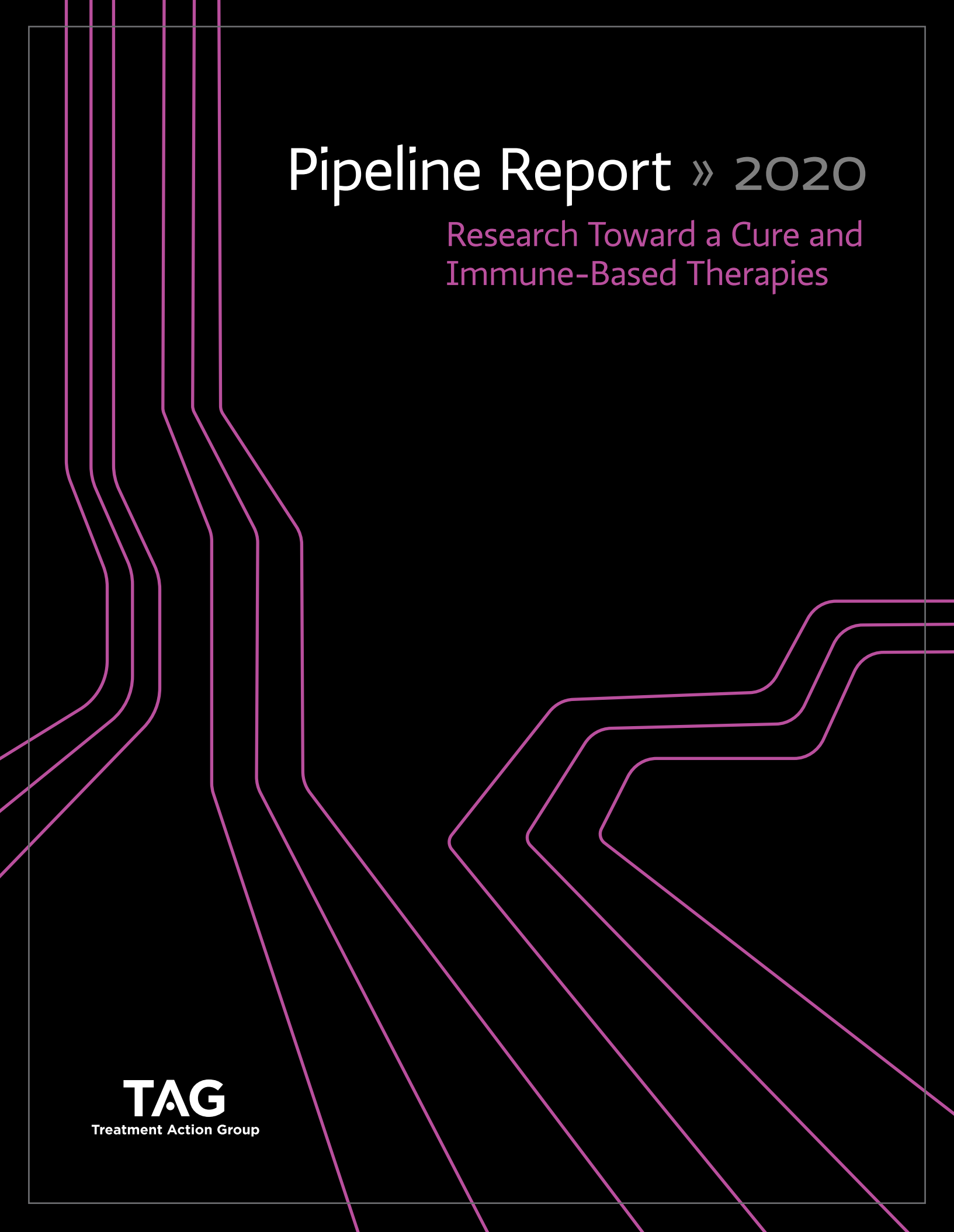
Pipeline Report » 2020

Research Toward a Cure and Immune-Based Therapies



TAG
Treatment Action Group

Research Toward a Cure and Immune-Based Therapies Pipeline 2020

By Richard Jefferys

Introduction

The scientific pursuit of a cure for HIV infection continues to make progress, with much being learned about the nature of the viral reservoir that persists in people on antiretroviral therapy (ART).[1,2] Efforts to translate this improved knowledge into practical therapies remain at an early stage, and no candidates in the current pipeline are thought likely to be curative—the hope is to achieve results that will take researchers closer to this goal.

Updates over the past year suggest that two additional people may have been cured of HIV in similar circumstances to those experienced by Timothy Ray Brown. For more than a decade, Brown had been considered the lone example of a successful HIV cure after receiving stem cell transplants from a donor homozygous for the CCR5Δ32 mutation as part of a series of treatments for a life-threatening cancer.[3] The stem cell transplants essentially created a new, largely HIV-resistant immune system, and Brown was able to discontinue ART without viral load rebound. Unfortunately, the approach is not a practical means to a cure—stem cell transplants carry a high risk of mortality and are thus only appropriate for people with HIV who require them to treat serious cancers.

What Brown's case has provided is a sliver of evidence—and a beacon of hope—that a cure for HIV is possible. Researchers have sought to bolster this evidence by providing stem cell transplants from donors homozygous for the CCR5Δ32 mutation to other people with HIV and cancer diagnoses. Many early attempts were stymied by complications of the procedures or progression of the cancers,[4] but there's now cause for optimism that Brown's outcome has been recapitulated in two more people, one in London and the other in Düsseldorf, Germany.

The London patient has been off ART for over 2.5 years posttransplant, and in a detailed follow-up paper published in *Lancet HIV* in March[5] the researchers involved in the case state: "We propose that these findings represent HIV-1 cure." The person also courageously identified himself as Adam Castillejo in an article by Apoorva Mandavilli for the *New York Times*, outlining his aim to become an "ambassador of hope."[6] The person in Düsseldorf is at an earlier stage of follow-up, approaching 1.5 years since stopping ART.[7]

Researchers have occasionally detected low-level fragments of HIV genetic material in Brown, Castillejo, and the Düsseldorf patient, but there's no sign of any intact replication-competent virus. Antibody responses to HIV have waned in all three cases.

Scientists Jennifer Zerbato and Sharon Lewin authored a commentary to accompany the *Lancet HIV* paper, noting that based on these findings "a cure for HIV might be better defined as no intact virus, rather than no detectable virus."[8] They also offer the caution that the potential for delayed reemergence of HIV is not well understood: "We will need more than a handful of patients cured of HIV to really understand the duration of follow-up needed and the likelihood of an unexpected late rebound in virus replication." But so far, so good for these three examples of possible HIV cures, and their existence offers encouragement to the broader research field.

In June 2019 the researchers Xinzhu Wei and Rasmus Nielsen published a study suggesting that people who are homozygous for the CCR5Δ32 mutation may have shorter lifespans, on average, compared with those who lack the mutation or inherit it from only one parent (CCR5Δ32 heterozygotes).[9] The results raised concerns about the safety of stem cell transplants from CCR5Δ32 homozygote donors and gene therapy strategies that aim to block HIV infection by abrogating expression of the CCR5 coreceptor on vulnerable cells. These concerns have since been ameliorated by the discovery that the results were skewed by a technical artifact,[10] and the original paper has been retracted.[11]

Over the past year news emerged of a possible HIV cure case unrelated to stem cell transplants. In a presentation at the 10th International AIDS Society Conference on HIV Science (IAS 2019), Xu Yu described "the San Francisco patient," a person whose immune system has suppressed viral replication to undetectable levels for decades, obviating the need for treatment and placing them in the category of elite controller.[12] Yu reported that only borderline levels of fragmentary HIV genetic material could be detected in their samples, with no intact virus evident by any measure. Yu suggested that all the intact HIV that was capable of replicating may have been eliminated over time by the person's immune system. The study appears to add to the evidence that the absence of intact HIV may be key to defining a cure.

The findings have led to the coining of a term, "exceptional elite controller," and Yu is working with other researchers to establish a cohort of similar cases that will allow further exploration of the phenomenon. The goal is to identify factors that might be translated into therapies for the majority of people with HIV, whose immune systems do not naturally control viral replication.

The term San Francisco patient was later revealed to be a misnomer when Sacramento resident Loreen Willenberg—a longtime advocate for elite controller research and participant in many studies—identified herself as the person in question.[13]

The increased appreciation for the importance of distinguishing intact HIV from fragmentary, defective viruses has led to the development of the intact proviral DNA assay (IPDA),[14] which is increasingly being used to measure the viral reservoir in research studies, although refinements may be needed to avoid missing some variants.[15]

In June 2020, the landscape of cure-related clinical research includes 97 interventional trials and 41 observational studies (see Table 1). A survey-based analysis conducted by

TAG in September 2019 suggests that over 13,000 people are likely to participate in this research.[16] The primary location remains the United States, but there is also work ongoing across the globe, particularly in Europe, Australia, and Asia. The number of studies on the African continent remains limited but will expand if plans are realized for interventional research in the FRESH cohort of young South African women.[17]

Women remain underrepresented in HIV cure research, with respondents to TAG's survey reporting 16.7% of enrollees as female based on sex at birth and very few transgender participants (1.4%). A review of results presented over the past two years indicated that 14% of study participants were female.[16] Efforts are ongoing to address the issue, with the importance underscored by evidence for sex differences in HIV persistence that are likely to be highly relevant to cure research.[18]

Analytical treatment interruptions (ATIs)

An emerging concern about the use of ATIs (temporary ART interruptions) in cure-related research is the increased risk of HIV transmission that accompanies viral load rebounds. Two cases of HIV transmission from study participants during ATIs have been described in the scientific literature.[19,20] This has prompted a collaboration between researchers and community members to generate guidance for addressing and reducing the risk.[21] There are 33 studies listed in Table 1 that include the possibility of an ATI (in some cases only if certain criteria are met).

There is relatively little activity in the realm of immune-based therapy development as an adjunct to ART (see Table 2). Evidence suggests that therapies capable of reducing residual inflammation and/or promoting immune reconstitution in people with suboptimal CD4+ T cell recovery on ART might produce clinical benefits.[22,23,24] The difficulty lies in proving the benefit: In order to demonstrate a significant reduction in the increased risk of morbidity and mortality associated with low CD4+ T cell gains and elevated inflammatory biomarkers, very large trial sample sizes would be required. Researchers at the U.S. Food and Drug Administration (FDA) analyzed data from ART trials to assess if there might be less serious clinical events that could be included to create a composite endpoint that would allow for smaller trials, but the effort was not successful.[25]

Results are pending from the largest trial of a drug with potential anti-inflammatory activity: The Randomized Trial to Prevent Vascular Events in HIV (REPRIEVE) study has enrolled 7,557 participants to evaluate whether pitavastatin calcium (Livalo) can reduce the incidence of heart disease in people with HIV, with overall morbidity and mortality included as secondary endpoints. Substudies will assess changes in inflammatory biomarkers and any associations with clinical outcomes.

An overarching concern for all the research listed in this report is the impact of the COVID-19 pandemic. Currently most trials are likely to be delayed or paused, but hopefully the situation will soon improve. To ascertain the status of a study, check with the contacts listed in the trial registry entry.

Table 1. Research Toward a Cure 2020

Trial	Additional description	Trial registry identifier(s)	Manufacturer/ sponsor(s)	Location(s)	Phase
ADOPTIVE IMMUNOTHERAPY					
alloRESIST: Evaluate the safety, immunologic, and virologic responses of donor derived HIV-specific T cells in HIV+ individuals following allogeneic bone marrow transplantation		NCT04248192 (not yet open for enrollment)	Children's Research Institute	USA	Phase I
HIV-1 specific T cells for HIV-infected individuals	HIV-specific T cells with non-escaped epitope targeting (HST-NEETs)	NCT03485963	Children's Research Institute	USA	Phase I
ANTIBODIES					
10-1074-LS + 3BNC117-LS	Long-acting broadly neutralizing antibodies in primary infection, **ATI**	NCT04319367 (not yet open for enrollment)	Imperial College London	UK	Phase II
UB-421	Antibody inhibitor of HIV binding to CD4 receptors	NCT03743376	United BioPharma	Taiwan	Phase II
vedolizumab	Anti-$\alpha_4\beta_7$ integrin antibody, **ATI**	NCT03577782	Hospitales Universitarios Virgen del Rocío	Spain	Phase II
vedolizumab	Anti-$\alpha_4\beta_7$ integrin antibody, **ATI**	NCT03147859	Ottawa Hospital Research Institute	Canada	Phase II
PGT121 + VRC07-523LS +/- PGDM1400	Broadly neutralizing antibody + long-acting broadly neutralizing antibody	NCT03721510	International AIDS Vaccine Initiative	USA	Phase I/IIa
VRC01	Broadly neutralizing antibody in infants	NCT03208231 (closed to enrollment)	National Institute of Allergy and Infectious Diseases (NIAID)	Botswana, Brazil, Malawi, Zimbabwe	Phase I/II
VRC01LS + 10-1074	Long-acting broadly neutralizing antibody + broadly neutralizing antibody in early-treated children, **ATI**	NCT03707977	NIAID	Botswana	Phase I/II
10-1074-LS +/- 3BNC117-LS	Long-acting broadly neutralizing antibodies	NCT03554408 (closed to enrollment)	Rockefeller University	USA	Phase I
3BNC117 + 10-1074	Broadly neutralizing antibodies, **ATI**	NCT03571204	NIAID	USA	Phase I
3BNC117 + 10-1074	Broadly neutralizing antibodies, **ATI**	NCT03526848	Rockefeller University	USA	Phase I
3BNC117-LS	Long-acting broadly neutralizing antibody	NCT03254277 (closed to enrollment)	Rockefeller University	USA	Phase I

Trial	Additional description	Trial registry identifier(s)	Manufacturer/ sponsor(s)	Location(s)	Phase
3BNC117-LS + 10-1074-LS	Long-acting broadly neutralizing antibodies in viremic individuals	NCT04250636 (not yet open for enrollment)	Rockefeller University	USA	Phase I
AAV8-VRC07	Broadly neutralizing antibody delivered by adeno-associated virus (AAV) vector	NCT03374202	NIAID	USA	Phase I
elipovimab (formerly GS-9722)	PGT121-derived broadly neutralizing antibody	GS-US-420-3902 Not listed in clinicaltrials.gov	Gilead Sciences	USA	Phase I
PGDM1400 +/- PGT121 +/- VRC07-523LS	Broadly neutralizing antibodies	NCT03205917 (closed to enrollment)	International AIDS Vaccine Initiative	USA	Phase I
SAR441236	Tri-specific broadly neutralizing antibody	NCT03705169 (closed to enrollment)	NIAID	USA	Phase I
VRC01 + 10-1074	Broadly neutralizing antibodies, **ATI**	NCT03831945	NIAID	USA	Phase I
VRC01	Broadly neutralizing antibody in acute HIV infection	NCT02591420	NIAID	Kenya, Tanzania, Thailand, Uganda	Phase I
ANTI-INFLAMMATORY					
canakinumab	IL-1β inhibitor	NCT02272946	University of California, San Francisco (UCSF)	USA	Phase II
CD24Fc	Human CD24 extracellular domain and human IgG1 Fc fusion protein	NCT03960541	OncoImmune	USA	Phase II
ANTI-PROLIFERATIVE					
mycophenolate mofetil (MMF)	Inosine-5′-monophosphate dehydrogenase inhibitor	NCT03262441 (closed to enrollment)	Fred Hutchinson Cancer Research Center	USA	Phase II
ANTIRETROVIRAL THERAPY					
doravirine concentrations and antiviral activity in cerebrospinal fluid	Non-nucleoside reverse transcriptase inhibitor	NCT04079452 (not yet open for enrollment)	Fundació Lluita Contra la SIDA	Spain	Phase III
IDOLTIB: Impact of dolutegravir + lamivudine simplification on HIV-1 reservoirs	Integrase inhibitor + nucleoside reverse transcriptase inhibitor	NCT04034862 (not yet open for enrollment)	University of Liège	Belgium	Phase III

Trial	Additional description	Trial registry identifier(s)	Manufacturer/ sponsor(s)	Location(s)	Phase
CANNABINOIDS					
TN-CT11LM, TN-TC19LM	Oral capsules containing Δ9-tetrahydrocannabinol and cannabidiol in two different ratios	NCT03550352 (not yet open for enrollment)	McGill University Health Center	Canada	Phase II
COMBINATIONS					
maraviroc, dolutegravir, dendritic cell vaccine, auranofin, nicotinamide	CCR5 inhibitor, integrase inhibitor, therapeutic vaccine, anti-proliferative + HDAC inhibitor, **ATI**	NCT02961829 (closed to enrollment)	Federal University of São Paulo	Brazil	Not listed
Perturbing of HIV reservoir with immune stimulation: Fluarix, Pneumovax vaccines	Influenza and pneumococcus vaccines	NCT02707692	University of California, San Diego (UCSD)	USA	Not listed
MVA.HTI + ChAdOx1.HTI +/- vesatolimod	Therapeutic vaccines + TLR7 agonist, **ATI**	NCT04364035	Aelix Therapeutics	Spain	Phase IIa
ROADMAP: romidepsin +/- 3BNC117	HDAC inhibitor + broadly neutralizing antibody, **ATI**	NCT02850016 (closed to enrollment)	Rockefeller University	Denmark, Germany, USA	Phase IIa
TITAN: lefitolimod +/- 3BNC117 + 10-1074	TLR9 agonist +/- broadly neutralizing antibodies, **ATI**	NCT03837756	Aarhus University	Australia, Denmark, USA	Phase IIa
eCLEAR: romidepsin + 3BNC117	HDAC inhibitor + broadly neutralizing antibody	NCT03041012	Aarhus University Hospital	Denmark, UK	Phase II
MVA HIV-B +/- vedolizumab	Viral vector vaccine +/- anti-$\alpha_4\beta_7$ integrin antibody, **ATIs**	NCT04120415 (not yet open for enrollment)	French National Agency for Research on AIDS and Viral Hepatitis (Inserm/ANRS)	France, Germany, Italy, Netherlands, Spain, Switzerland, UK	Phase II
Research in viral eradication of HIV reservoirs (RIVER): ART, ChAdV63.HIVconsv and MVA.HIVconsv vaccines, vorinostat	Therapeutic vaccines + HDAC inhibitor	NCT02336074 UK CPMS18010 (closed to enrollment)	Imperial College London	UK	Phase II
vorinostat +/- tamoxifen in postmenopausal women	HDAC inhibitor + estrogen receptor modulator	NCT03382834 (closed to enrollment)	NIAID	USA	Phase II
HIVARNA01.3, MVA vector HIV vaccine, 10-1074, romidepsin, HIVACAR01	Therapeutic vaccines, broadly neutralizing antibody, HDAC inhibitor, **ATI**	NCT03619278 (not yet open for enrollment)	David Garcia Cinca	Spain	Phase I/IIa

Trial	Additional description	Trial registry identifier(s)	Manufacturer/ sponsor(s)	Location(s)	Phase
IMPAACT P1115 v2.0: very early intensive treatment of HIV-infected infants to achieve HIV remission (ART +/- VRC01)	Combination antiretroviral therapy, VRC01 broadly neutralizing antibody, **ATI**	NCT02140255	IMPAACT/NIAID/ NICHD	Argentina, Brazil, Haiti, Kenya, Malawi, South Africa, Tanzania, Thailand, Uganda, USA, Zambia, Zimbabwe	Phase I/II
panobinostat + pegylated interferon-alpha2a	HDAC inhibitor + cytokine	NCT02471430	Massachusetts General Hospital	USA	Phase I/II
IL-12 adjuvanted p24CE DNA vaccine, MVA/HIV62B vaccine, lefitolimod, VRC07-523LS, 10-1074	Therapeutic conserved element DNA vaccine, MVA vaccine boost, TLR9 agonist, broadly neutralizing antibodies, **ATI**	NCT04357821 (not yet open for enrollment)	UCSF	USA	Phase I/II
haploidentical NK cells + N-803	Adoptive transfer of haploidentical natural killer cells + recombinant human superagonist interleukin-15 complex	NCT03899480	University of Minnesota - Clinical and Translational Science Institute	USA	Phase I
CD4-ZETA +/- interleukin-2 (IL-2)	Gene-modified T cells + cytokine	NCT01013415 (closed to enrollment)	University of Pennsylvania	USA	Phase I
chidamide + CAR T or TCR T cell therapy	HDAC inhibitor + chimeric antigen or T cell receptor T cell therapy	NCT03980691	Guangzhou 8th People's Hospital	China	Phase I
HVRRICANE: HIVIS DNA + MVA-CMDR vaccines +/- Cervarix (TLR4 agonist)	Therapeutic vaccines + TLR4 agonist	NCT04301154 (not yet open for enrollment)	PENTA Foundation	Italy, South Africa, Thailand	Phase I
N-803 +/- VRC07-523LS + 10-1074	Recombinant human super agonist interleukin-15 complex, broadly neutralizing antibodies, **ATI**	NCT04340596 (not yet open for enrollment)	NIAID	USA	Phase I
peginterferon alfa-2b + 3BNC117 + 10-1074	Cytokine, broadly neutralizing antibodies, **ATI**	NCT03588715 (suspended due to COVID-19)	Wistar Institute	USA	Phase I
VRC07-523LS + vorinostat	Broadly neutralizing antibody, HDAC inhibitor	NCT03803605 (closed to enrollment)	University of North Carolina, Chapel Hill	USA	Phase I
vorinostat + HXTC: HIV-1 antigen expanded specific T cell therapy	HDAC inhibitor + adoptive immunotherapy	NCT03212989	University of North Carolina, Chapel Hill	USA	Phase I

Trial	Additional description	Trial registry identifier(s)	Manufacturer/ sponsor(s)	Location(s)	Phase
CYTOKINES					
interleukin-2 (IL-2)	Cytokine	NCT03308786	Case Western Reserve University	USA	Phase II
DUAL-AFFINITY RE-TARGETING (DART) MOLECULES					
MGD014	Bispecific DART molecule targeting the HIV Env protein and CD3-expressing T cells	NCT03570918	MacroGenics	USA	Phase I
GENE THERAPIES					
Cal-1: dual anti-HIV gene transfer construct	Lentiviral vector encoding a short hairpin RNA that inhibits expression of CCR5 and a fusion inhibitor (C46)	NCT02390297 (long-term safety phase; closed to enrollment)	Calimmune	USA	Phase I/II
SB-728-T	Autologous CD4+ T cells modified to inhibit CCR5 expression	NCT03666871	Case Western Reserve University	USA	Phase I/II
CD4 CAR + SB-728mR modified T cells	Autologous CD4+ T cells gene-modified to inhibit CCR5 expression and chimeric antigen receptor (CAR) T cells, **ATI**	NCT03617198 (closed to enrollment)	University of Pennsylvania	USA	Phase I
Chimeric antigen receptor (CAR) T cell therapy	Autologous T cells gene-modified to express a chimeric antigen receptor targeting HIV	NCT03240328	Guangzhou 8th People's Hospital	China	Phase I
Long-term follow-up of HIV+ participants exposed to SB-728-T or SB-728mR-T	Autologous CD4+ T cells gene-modified to inhibit CCR5 expression	NCT04201782 (enrolling by invitation only)	Sangamo Therapeutics	USA	Phase I
SB-728mR-HSPC	Autologous hematopoietic stem/ progenitor cells gene-modified to inhibit CCR5 expression, **ATI**	NCT02500849 (closed to enrollment)	City of Hope Medical Center	USA	Phase I
shRNA-modified CD34+ cells	Infusion of autologous CD34+ cells transduced with short hairpin RNAs targeting CCR5 and the HIV genome	NCT03517631	Shanghai Public Health Clinical Center	China	Phase I
anti-gp120 CAR T cells	Autologous T cells gene-modified to express a chimeric antigen receptor targeting HIV gp120	ChiCTR-OPN-17013068 (not yet open for enrollment)	Jinyintan Hospital of Wuhan	China	Phase 0

Trial	Additional description	Trial registry identifier(s)	Manufacturer/ sponsor(s)	Location(s)	Phase
GENE THERAPIES FOR HIV-POSITIVE PEOPLE WITH CANCERS					
Safety of transplantation of CRISPR CCR5 modified CD34+ cells in HIV-infected subjects with hematological malignances	Stem cells gene-modified to abrogate CCR5 expression using CRISPR technology, **ATI**	NCT03164135	307 Hospital of PLA (Affiliated Hospital of Academy to Military Medical Sciences)	China	Not listed
Stem cells gene-modified with Cal-1 in HIV-1-related high-risk lymphoma	Lentiviral vector encoding a short hairpin RNA that inhibits expression of CCR5 and a fusion inhibitor (C46), **ATI**	NCT03593187	Assistance Publique - Hôpitaux de Paris	France	Phase I/II
Gene therapy in treating patients with HIV-related lymphoma receiving stem cell transplant	Stem cells gene-modified with CCR5 shRNA/ TRIM5alpha/TAR decoy	NCT02797470	AIDS Malignancy Consortium	USA	Phase I/II
Gene therapy and combination chemotherapy in treating patients with AIDS-related non-Hodgkin's lymphoma	Stem cells gene-modified with a lentivirus vector encoding three forms of anti-HIV RNA (rHIV7-shI-TAR-CCR5RZ), **ATI**	NCT02337985 (closed to enrollment)	City of Hope Medical Center	USA	Phase I
Busulfan and gene therapy after frontline chemotherapy in patients with AIDS-related non-Hodgkin's lymphoma	Stem cells gene-modified with a lentivirus vector encoding three forms of anti-HIV RNA (rHIV7-shI-TAR-CCR5RZ) + cyclophosphamide conditioning, **ATI**	NCT01961063 (closed to enrollment)	City of Hope Medical Center	USA	Phase I
GONADOTROPIN-RELEASING HORMONE (GnRH) AGONISTS					
triptorelin acetate depot		NCT03536234	Immune System Regulation AB	Sweden	Phase II
HORMONES					
somatotropin	Human growth hormone	NCT03091374	McGill University Health Center	Canada	Phase II
IMAGING STUDIES					
Imaging immune activation in HIV by PET-MR		NCT03684655	UCSF	USA	Phase I
3BNC117 + Copper-64 radio isotope followed by MRI/PET scanning to detect HIV in vivo	Radiolabeled broadly neutralizing antibody	NCT03063788	Bayside Health	Australia	Phase I
Radiolabeled VRC01	Radiolabeled broadly neutralizing antibody	NCT03729752	UCSF	USA	Phase I

Trial	Additional description	Trial registry identifier(s)	Manufacturer/ sponsor(s)	Location(s)	Phase
IMMUNE CHECKPOINT INHIBITORS					
durvalumab in solid tumors	Anti-PD-L1 antibody	NCT03094286 (closed to enrollment)	Spanish Lung Cancer Group	Spain	Phase II
cemiplimab	Anti-PD-1 antibody	NCT03787095 (closed to enrollment)	NIAID	USA	Phase I/II
budigalimab	Anti-PD-1 antibody, **ATI**	NCT04223804	AbbVie	Australia, Canada, France, USA	Phase Ib
nivolumab + ipilimumab	Anti-PD-1 antibody + anti-CTLA-4 antibody in people with advanced HIV-associated solid tumors	NCT02408861 (suspended due to COVID-19)	National Cancer Institute	Australia, USA	Phase I
pembrolizumab	Anti-PD-1 antibody in people with HIV and relapsed, refractory, or disseminated malignant neoplasms	NCT02595866	National Cancer Institute	USA	Phase I
pembrolizumab	Anti-PD-1 antibody, single dose	NCT03239899	National Institute of Neurological Disorders and Stroke	USA	Phase I
LATENCY-REVERSING AGENTS					
valproic acid + pyrimethamine	HDAC inhibitor, BAF inhibitor	NCT03525730	Erasmus Medical Center	Netherlands	Phase I/II
arsenic trioxide	Chemotherapy	NCT03980665	Guangzhou 8th People's Hospital	China	Phase I
kansui	Traditional Chinese medicine containing ingenols	NCT02531295	UCSF	USA	Phase I
OBSERVATIONAL STUDIES					
2000 HIV Human Functional Genomics Partnership Program (2000HIV)		NCT03994835 (not yet open for enrollment)	Radboud University	Netherlands	N/A
Accurate staging of immuno-virological dynamics during acute HIV infection (ACS)		NCT03449706	University Hospital, Ghent	Belgium	N/A
Analytic treatment interruption (ATI) to assess HIV cure	**ATI**	NCT02437526 (enrolling by invitation only)	Mayo Clinic	USA	N/A
ANRS CO24 OncoVIHAC: immune checkpoint inhibitors in HIV+ individuals with cancers		NCT03354936	Inserm-ANRS	France	N/A

Trial	Additional description	Trial registry identifier(s)	Manufacturer/ sponsor(s)	Location(s)	Phase
ANRS EP63: a chronological study of the formation of HIV cellular reservoirs through the expression of surface markers on CD4+ T lymphocytes, including CD32a		NCT03298360	Inserm-ANRS	France	N/A
ATGALIG-HIV: study of autophagy and the effects of GALIG gene products in HIV-1+ patients on antiretroviral therapy since primary infection, chronic phase, or never treated		NCT04160455	Centre Hospitalier Régional d'Orléans	France	N/A
ACTG A5345: biomarkers to predict time to plasma HIV RNA rebound	**ATI**	NCT03001128	AIDS Clinical Trials Group	USA	N/A
CLEAC: comparison of late versus early antiretroviral therapy in HIV-infected children		NCT02674867 (closed to enrollment)	Inserm-ANRS	France	N/A
CODEX (the 'Extreme' cohort)	Long-term non-progressors and HIV controllers	NCT01520844	Inserm-ANRS	France	N/A
Developing a functional cure for HIV disease: clinical specimen collection from HIV+ individuals	Determination of levels of HIV-reactive CD4+ T cells, possible leukapheresis	NCT03215004	American Gene Technologies International	USA	N/A
DOLUVOIR: cartography of virologic reservoir related to antiretroviral concentrations in people with HIV on first line treatment containing dolutegravir and nucleoside/nucleotide reverse transcriptase inhibitors		NCT04133012 (not yet open for enrollment)	Inserm-ANRS	France	N/A
Establish and characterize an acute HIV infection cohort in a high-risk population		NCT00796146	South East Asia Research Collaboration with Hawaii	Thailand	N/A
Evaluation of the role of HIV-1 Tat protein and anti-Tat immune response in HIV reservoir (ISS OBS T-005)		NCT04263207	Barbara Ensoli, MD, PhD, Istituto Superiore di Sanità	Italy	N/A

Trial	Additional description	Trial registry identifier(s)	Manufacturer/ sponsor(s)	Location(s)	Phase
FRESH (females rising through education, support, and health)	Early diagnosis, treatment and support for women at high risk for HIV infection	No clinicaltrials.gov entry	Ragon Institute of MGH, MIT and Harvard	South Africa	N/A
FXReservoir: study of the effects of farnesoid X receptor (FXR) ligands on the reactivation of latent provirus		NCT03618862 (not yet open for enrollment)	Hospices Civils de Lyon	France	N/A
Genotyping FcγRs genes		NCT03130296	University Hospital, Strasbourg	France	N/A
HEATHER: HIV reservoir targeting with early antiretroviral therapy		UK CPMS17589	University of Oxford/Medical Research Council/British HIV Association	UK	N/A
HIV-Mercuri: HIV study on measuring the reservoir on cellular level to cure infection		NCT04305665 (not yet open for enrollment)	University Hospital, Ghent	Belgium	N/A
HIV-PRADA: HIV persistence in lymph node and peripheral blood		NCT03426189 (closed to enrollment)	University of Melbourne	Australia	N/A
Host and viral factors associated with HIV elite control		UK CPMS16146	University College London Hospitals NHS Foundation Trust	UK	N/A
HSCT-HIV: Allogeneic hematopoietic stem cell transplantation in HIV-1-infected patients		NCT02732457	Kirby Institute	Australia	N/A
HUSH restriction in HIV+ patients		NCT04172480	Inserm-ANRS	France	N/A
iCHIP: effect of immune checkpoint inhibitors on HIV persistence		No clinicaltrials.gov entry	University of Melbourne	Australia	N/A
IciStem: collaborative project to guide and investigate the potential for HIV cure in HIV+ patients requiring allogeneic stem cell transplantation for hematological disorders	**ATI**	No clinicaltrials.gov entry	amfAR	International	N/A
Identification and quantification of HIV CNS latency biomarkers		NCT02989285	St Vincent's Hospital, Sydney	Australia	N/A

Trial	Additional description	Trial registry identifier(s)	Manufacturer/ sponsor(s)	Location(s)	Phase
IMPAACT 2015: evaluation of the HIV-1 reservoir in the CNS of perinatally infected youth and young adults with cognitive impairment		NCT03416790 (closed to enrollment)	IMPAACT	USA	N/A
Impact of ART adherence on HIV persistence and inflammation		NCT02797093 (closed to enrollment)	University of Colorado, Denver	USA	N/A
Long-term effects of ART in acute HIV infection		ChiCTR1800015006 (not yet open for enrollment)	Key Laboratory of AIDS Immunology of National Health and Family Planning Commission, Department of Laboratory Medicine, The First Affiliated Hospital, China Medical University	China	N/A
Measurement for viral reservoir and immune function in HIV-1-infected patients under antiretroviral therapy		NCT04068441	National Taiwan University Hospital	Taiwan	N/A
PITCH: prospective interruption of therapy towards a cure for HIV pilot study	**ATI**	No clinicaltrials.gov entry	University of Oxford	UK	N/A
Post-analytic treatment interruption study		NCT02761200	South East Asia Research Collaboration with Hawaii	Thailand	N/A
Primary infection cohort (PRIMO)		NCT03148964	Inserm-ANRS	France	N/A
Quantitative measurement and correlates of the latent HIV reservoir in virally suppressed Ugandans		NCT02154035 (closed to enrollment)	NIAID	Uganda	N/A
RESERVIH32: bioclinical evaluation of two biomarkers of aviremic HIV-1 in CD4+ T cells of adults undergoing treatment		NCT03940521 (not yet open for enrollment)	Centre Hospitalier Universitaire de Nīmes	France	N/A

Trial	Additional description	Trial registry identifier(s)	Manufacturer/ sponsor(s)	Location(s)	Phase
Role of the IL-33/ amphiregulin pathway as a potential therapeutic target in HIV infection		NCT03622177 (not yet open for enrollment)	Inserm-ANRS	France	N/A
SCOPE-ATI: SCOPE analytic treatment interruption protocol	**ATI**	NCT04359186 (not yet open for enrollment)	UCSF	USA	N/A
TESOVIR	Tracking and exploring the source of viral rebound after **ATI**	NCT03117985	Centre Hospitalier Régional d'Orléans	France	N/A
The Last Gift Study (for people with HIV and less than 6 months life expectancy due to terminal illness)		No clinicaltrials.gov entry	UCSD	USA	N/A
The use of leukapheresis to support HIV pathogenesis studies		NCT01161199	UCSF	USA	N/A
Thinking and memory problems in people with HIV		NCT01875588	National Institute of Neurological Disorders and Stroke	USA	N/A
TRESAX: T follicular helper reservoir in axillary lymph nodes study		No clinicaltrials.gov entry	Kirby Institute	Australia	N/A
PROTEASOME INHIBITORS					
ixazomib		NCT02946047 (closed to enrollment)	Mayo Clinic	USA	Phase I
STEM CELL TRANSPLANTATION					
HIVECT: HIV eradication through cord-blood transplantation	**ATI**	NCT02923076	Puerta de Hierro University Hospital	Spain	N/A
IMPAACT P1107	Cord blood transplantation using CCR5Δ32 donor cells for the treatment of HIV and underlying disease	NCT02140944	IMPAACT/ NIAID/Eunice Kennedy Shriver National Institute of Child Health and Human Development	USA	N/A
Cord blood transplant with OTS for the treatment of HIV+ hematologic cancers		NCT04083170 (not yet open for enrollment)	Fred Hutchinson Cancer Research Center	USA	Phase II
HLA-mismatched unrelated donor bone marrow transplantation		NCT02793544 (closed to enrollment)	Center for International Blood and Marrow Transplant Research	USA	Phase II

Trial	Additional description	Trial registry identifier(s)	Manufacturer/ sponsor(s)	Location(s)	Phase
STIMULANTS					
EMRLHD: effect of methamphetamine on residual latent HIV disease study		NCT03825536	UCSF	USA	Phase IV
THERAPEUTIC VACCINES					
p24CE1/2 + p55^gag conserved-element DNA vaccines	DNA vaccines	NCT03560258 (closed to enrollment)	NIAID	USA	Phase I/II
PENNVAX-GP or INO-6145 + IL-12 DNA adjuvant (INO-9012)	DNA vaccine + DNA adjuvant	NCT03606213	Steven Deeks, UCSF	USA	Phase I/II
Ad26.Mos4.HIV + MVA-Mosaic or clade C gp140 + mosaic gp140	Adenovirus and modified Vaccinia Ankara strain vectors encoding mosaic HIV antigens + Env protein boosts	NCT03307915	Janssen Vaccines & Prevention B.V.	USA	Phase I
DC-HIV04: a1DC + inactivated whole autologous HIV, a1DC + conserved HIV peptides	Autologous dendritic cell vaccine variants loaded with either autologous inactivated HIV or conserved HIV peptides	NCT03758625	Sharon Riddler, University of Pittsburgh	USA	Phase I
DNA.HTI + MVA.HTI + ChAdOx1.HTI	DNA + viral vector vaccines, ATI extension	NCT04385875 (not yet open for enrollment)	Fundació Lluita Contra la SIDA	Spain	Phase I
DNA.HTI + MVA.HTI	DNA + modified Vaccinia Ankara strain vector vaccines, **ATI**	NCT03204617 (closed to enrollment)	Aelix Therapeutics	Spain	Phase I
MVA.tHIVconsv3 +/- MVA.tHIVconsv4	Viral vector vaccines	NCT03844386 (closed to enrollment)	University of North Carolina, Chapel Hill	USA	Phase I
TREATMENT INTENSIFICATION/EARLY TREATMENT					
P25-INACTION: implication for strategies of long-term control of viral replication in patients with primary HIV infection	Combination antiretroviral therapy	NCT04225325	Adriano Lazzarin, MD	Italy	Phase IV
LEOPARD: latency and early neonatal provision of antiretroviral drugs clinical trial	Combination antiretroviral therapy	NCT02431975 (closed to enrollment)	Columbia University	South Africa	Phase IV
Antiretroviral regime for viral eradication in newborns	Combination antiretroviral therapy	NCT02712801	National Center for Women and Children's Health, China CDC	China	Phase IV

Trial	Additional description	Trial registry identifier(s)	Manufacturer/ sponsor(s)	Location(s)	Phase
DGVTAF: immediate initiation of antiretroviral therapy during 'hyperacute' HIV infection	Combination antiretroviral therapy	NCT02656511	UCSF	USA	Phase IV
AAHIV: antiretroviral therapy for acute HIV infection	Combination antiretroviral therapy	NCT00796263	South East Asia Research Collaboration with Hawaii	Thailand	Phase III
tenofovir/emtricitabine + dolutegravir or tenofovir/ emtricitabine + darunavir/ cobicistat	Combination antiretroviral therapy	NCT02987530 (closed to enrollment)	Inserm-ANRS	France	Phase III
EIT: early infant HIV treatment in Botswana	Combination antiretroviral therapy	NCT02369406	Harvard School of Public Health	Botswana	Phase II/III
EARLIER: early ART to limit infection and establishment of reservoir	Combination antiretroviral therapy	NCT02859558 (closed to enrollment)	AIDS Clinical Trials Group	Brazil, Malawi, Peru, South Africa, Thailand, USA, Zimbabwe	Phase II

ATI = analytical treatment interruption. In some cases (particularly in trials of gene therapies for HIV-positive people with cancers), ATIs will be conducted only if study participants meet certain criteria.

Shaded entries represent additions since the 2019 Pipeline Report.

For the complete listing, including completed trials related to cure research, with links to published and presented results where available, see TAG's Research Toward a Cure clinical trials web page at: http://www.treatmentactiongroup.org/cure/trials.

Combinations

Investigations into combination approaches represent the largest proportion of cure-related interventional trials, with 21 currently listed. The most prominent strategy is "kick and kill," where the aim is to use agents to kick dormant, latent HIV into revealing itself so the cells that contain the virus are visible to the immune system. These agents are combined with candidates designed to enhance the ability of the immune response to recognize and destroy the HIV-infected cells. The ultimate goal is to reduce the size of the latent HIV reservoir.

A pending trial being conducted under the aegis of the BELIEVE Collaboratory (one of six HIV cure research collaborations funded by the U.S. National Institutes of Health) will evaluate N-803, a modified version of the cytokine interleukin-15 (IL-15) designed to have increased and prolonged biological activity, in combination with two broadly neutralizing antibodies (bNAbs), VRC07-523LS and 10-1074. N-803 has been reported to have both latency-reversing and immune-enhancing activities in preclinical studies,[26,27] and it proved

safe and showed some evidence of activity in a phase I human trial conducted by Timothy Schacker and colleagues at the University of Minnesota.[28] The rationale for including bNAbs is that they can both directly inhibit HIV and promote the killing of virus-infected cells via effector mechanisms (antibody-mediated cellular cytotoxicity or antibody-mediated cellular phagocytosis).[29] At CROI 2020, James Whitney presented promising results obtained with N-803 plus dual bNAbs in SHIV-infected macaques.[30] The majority of the animals that received the combination displayed sustained control of viral replication after an ART interruption. The human trial will also include an ATI.

Researchers led by Steve Deeks at the University of California, San Francisco, are combining therapeutic vaccines, a toll-like receptor (TLR) agonist and dual bNAbs (VRC07-523LS and 10-1074) in a small trial that aims to assess whether the use of multiple interventions can enhance control of viral load during an ATI. Researchers at Aarhus University have reported that the TLR-9 agonist being used, lefitolimod, promotes innate and adaptive immunity in people with HIV and may have latency-reversing activity in a subset of recipients.[31,32]

In Spain, the company Aelix Therapeutics is sponsoring a study of a prime-boost therapeutic vaccine regimen delivered with or without vesatolimod, a TLR-7 agonist developed by Gilead Sciences. Researchers have observed evidence that vesatolimod can reverse viral latency in some, but not all, preclinical studies.[33,34] Results from the first trials of vesatolimod in people with HIV were reported at IAS 2019[35] and CROI 2020,[36] demonstrating safety and evidence of immune-modulating activity.

The PENTA Foundation is supporting research into a variation on the kick and kill theme in children and youth who acquired HIV perinatally. The trial, named HVRRICANE, combines two therapeutic HIV vaccines with the HPV vaccine Cervarix, which includes a TLR-4 agonist as an adjuvant. Sites are located in South Africa, Thailand, and Italy.

The past year has seen the publication and presentation of results from several early attempts to assess the kick and kill strategy, including:

- The Research in Viral Eradication of HIV Reservoirs (RIVER) trial, which randomized 60 male participants with primary HIV infection to receive either ART or ART combined with two therapeutic HIV vaccines and a short course of the candidate latency-reversing agent vorinostat.[37]
- The BCN02 study, an open-label, single-arm trial of the candidate latency-reversing agent romidepsin plus a therapeutic vaccine (MVA.HIVconsv) in 15 people with HIV who initiated ART less than six months after infection.[38]
- ROADMAP, an investigation of romidepsin alone or combined with the bNAb 3BNC117 in 20 people with chronic HIV infection on long-term ART.[39]

No significant effects on the size of the HIV reservoir were observed in any of the studies. ROADMAP included an ATI but found no evidence of delayed viral load rebound or enhanced control of virus replication associated with the interventions. BCN02 also involved an ATI, and a preliminary finding that five out of 13 participants had maintained

relatively low viral loads over several months after ART interruption generated some excitement in 2017.[40] However, results from a subsequent randomized, placebo-controlled trial in a similar population showed equivalent rates of suppression after an ATI in the placebo arm, emphasizing the difficulty of interpreting results from uncontrolled trials.[41] The published results of BCN02 note that just three of the 15 total participants (23 percent) were able to maintain viral loads <2,000 copies/mL for 32 weeks.[38]

While these negative results are disappointing, they aren't necessarily the death knell for kick and kill. In addition to the other agents already undergoing clinical testing, preclinical results have raised hopes that a new class of latency-reversing agents known as SMAC mimetics may have superior activity compared with previous candidates.[42]

Antibodies

Two new trials of dual bNAb combinations have been registered over the past year but are yet to get underway. Both involve a combination of bNAbs that have already shown activity against HIV in humans,[43] 10-1074 and 3BNC117, with slight modifications to allow for less frequent dosing (designated by the addition of "LS" to the bNAb name). At Rockefeller University, the dual bNAbs will be tested in people with HIV who have yet to initiate ART.

The second study is led by Imperial College London and will administer 10-1074-LS and 3BNC117-LS to people with HIV who initiated ART early after infection. An ATI will be undertaken to evaluate whether the bNAbs can maintain viral load suppression.

New data from bNAb trials include the first description of elipovimab (formerly GS-9722) in people with HIV. Elipovimab is being developed by Gilead Sciences for use in HIV cure studies and is based on the bNAb PGT121, with modifications intended to enhance effector activities that can lead to the killing of HIV-infected cells.[44] Peter Ruane presented results at CROI 2020 indicating that intravenous infusion of elipovimab was safe and had favorable pharmacokinetics (suitable for dosing every other week) in study participants with HIV on suppressive ART.[45]

The activity of elipovimab's parent bNAb PGT121 was described by Kathryn Stephenson in a presentation at CROI 2019.[46] Significant viral load reductions were seen in people with HIV whose virus was sensitive to the bNAb. Two participants with low viral loads at baseline experienced over five months of virus suppression after a single infusion. PGT121 continues to undergo evaluation in combination with the bNAbs PGDM1400 and VRC07-523LS.

The first-in-human results for VRC07-523LS were published in August 2019, demonstrating safety in HIV-negative participants after either intravenous or subcutaneous administration.[47] Grace Chen presented data from a study in participants with HIV at IAS 2019, reporting that a single intravenous infusion led to a greater than one log decline in viral load in eight out of nine cases.[48] VRC07-523LS features in several new combination studies (see previous section).

Gene Therapies

Jim Riley at the University of Pennsylvania is leading a gene therapy trial that combines chimeric antigen receptor (CAR) T cells with CD4 cells modified to resist HIV infection using Sangamo Therapeutics SB-728mR zinc finger technology (which abrogates CCR5 coreceptor expression). CAR T cells have proved to be breakthrough treatments for certain cancers, but exploration in the context of HIV has been limited. Riley's CAR T cells are modified to enhance recognition of HIV and have shown promise in preclinical studies.[49,50] Blake Rust presented preliminary results obtained in SHIV-infected macaques at CROI 2020, showing evidence of delayed viral load rebound and suppression of viral replication after ART interruption.[51] Results from the human trial should become available next year.

Immune Checkpoint Inhibitors

Several immune checkpoint inhibitors are now approved for the treatment of cancers. The therapies consist of antibodies to molecules that are involved in suppressing T cell responses (particularly CTLA-4 and PD-1). Blocking these molecules can revive T cell activity against cancers or other targets. There is long-standing interest in immune checkpoint inhibitors in HIV because of evidence that they might have the potential to both reverse HIV latency and enhance virus-specific T cell function.[52,53]

Studies in people with HIV receiving immune checkpoint inhibitors for cancers have produced mixed and inconclusive evidence when it comes to effects on the viral reservoir[54] (preliminary evidence suggests the therapies can be as effective against cancer in people with HIV as they are in uninfected people[55]). The major drawback of the approach is the risk of serious side effects related to the enhancement of T cell responses against self-antigens, leading to autoimmunity.

A single-dose study of the anti-PD-1 antibody cemiplimab conducted by the AIDS Clinical Trials Group in people with HIV on ART was stopped when two participants showed possible evidence of autoimmune side effects, prompting caution about the conduct of future research outside of the cancer setting.[56]

Nevertheless, one new trial of the anti-PD-1 antibody budigalimab is being sponsored by the manufacturer AbbVie. The safety and pharmacokinetics of various doses will be investigated in people with HIV undergoing ART interruption. The design appears to be based on results reported by Afam Okoye in SIV-infected macaques, which showed that administration of an anti-PD-1 antibody at the time of ART cessation was associated with greater viral load suppression.[57]

Table 2. Immune-Based Therapy Pipeline 2020

Agent	Class/Type	Trial Registry Identifier(s)	Manufacturer/ Sponsor(s)	Status
isoprinosine		NCT03883334	Universidad San Francisco de Quito	Phase IV
metformin		NCT03774108	Hospital Civil de Guadalajara	Phase IV
canakinumab	IL-1β inhibitor	NCT02272946	University of California, San Francisco	Phase II
CD24Fc	Human CD24 extracellular domain and human IgG1 Fc fusion protein	NCT03960541	OncoImmune	Phase II
pyridostigmine	Acetylcholinesterase inhibitor	NCT03312244 (Suspended due to COVID-19: effective 3/19/2020 recruitment halted until further notice)	Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán	Phase II
visbiome	Probiotic	NCT02441231	University Health Network, Toronto/ CIHR Canadian HIV Trials Network	Phase II
allogeneic adoptive immune therapy	Granulocyte colony-stimulating factor-mobilized donor peripheral blood mononuclear cells	NCT02648516	Beijing 302 Hospital	Phase I/II
tocilizumab	IL-6 blockade	NCT02049437 (closed to enrollment)	Case Western Reserve University	Phase I/II
pembrolizumab	Anti-PD1 antibody, immune checkpoint inhibitor	NCT03367754	National Institutes of Health Clinical Center	Phase I
Yuyang capsule	Traditional Chinese medicine	ChiCTR1900023860	Sichuan Academy of Traditional Chinese Medicine	Phase 0
Bifidobacteria and Lactobacilli triple viable capsules	Probiotics	NCT04297488 (not yet open for enrollment)	Peking Union Medical College Hospital	Not specified
arabinoxylan rice bran supplementation (BRM4)	A product derived from rice bran treated with extracts from three mushrooms	NCT02922907 (closed to enrollment)	University of Southern California	Not specified
natural killer cell infusion	Adoptive immunotherapy with NK cells	ChiCTR1900021008 (not yet open for enrollment)	Beijing Youan Hospital, Capital Medical University	Not specified

Immune-based therapies (IBTs) in clinical trials represent a grab bag of approaches, almost all being evaluated by academic investigators rather than commercial sponsors. The exception is OncoImmune's evaluation of the effects of CD24Fc on low-density lipoprotein (LDL) and inflammation in people with HIV.

Only two new trials have been registered since the 2019 Pipeline Report. Both are taking place in China and are enrolling people on ART with suboptimal immune reconstitution; one is testing the effects of a traditional Chinese medicine while the other looks at probiotic capsules containing *bifidobacteria and lactobacilli.*

Benigno Rodriguez presented results from an ongoing study of tocilizumab in people with HIV at CROI 2020.[58] Tocilizumab is an FDA-approved antibody that blocks the pro-inflammatory cytokine interleukin-6 (IL-6), levels of which have been shown to predict an increased risk of morbidity and mortality in HIV. Thirty-four participants were randomized to receive either three tocilizumab or three placebo infusions spaced four weeks apart. After a 12-week washout period, the three-dose cycle was repeated but with placebo recipients switched to tocilizumab and vice versa.

Tocilizumab was generally well tolerated with two withdrawals due to adverse events (grade 3 rash and neutropenia that resolved after tocilizumab cessation). Treatment was associated with significant reductions in several inflammatory and coagulation biomarkers including C-reactive protein, soluble CD14 and D-dimer. However, levels of IL-6 were dramatically increased. Lipid and metabolic parameters were also altered in a manner associated with increased cardiovascular disease risk. It's unclear from these findings whether tocilizumab might be able to play a beneficial role as an adjunct to ART.

Simone de Barros Tenore and colleagues have published the outcome of a trial previously featured in the IBT pipeline table, which evaluated the probiotic *Lactobacillus casei* Shirota in people with poor CD4+ T cell recovery on ART.[59] The placebo-controlled trial recruited 48 participants but found no significant differences in measures of CD4+ T-cell counts, CD4:CD8 ratio, immune activation or inflammatory biomarkers associated with probiotic treatment.

Conclusion

Prospects for adjunctive immune-based therapies are clearly fading as the pipeline and commercial interest in the area dwindle. But as long as there remains a population of people with HIV who might conceivably benefit from therapies capable of promoting CD4+ T cell recovery or reducing inflammation, activists should continue to try to identify promising interventions and call for clinical testing. Results from the REPRIEVE trial may help shed light on whether reducing inflammation can reduce morbidity and mortality in people with HIV on ART.

The HIV cure research field is comparatively fecund, with a range of approaches being pursued. Although there are no extant candidates that appear likely to have broadly applicable curative potential, dialogues have begun between researchers, community, funders, and other stakeholders regarding what an ideal "target product profile" might look like for an HIV cure intervention in different settings.[1,60]

Global funding support for cure research continues to tick upward, increasing by 12 percent from 2017 to 2018 (US$288.8 million to US$323.9 million) according to the July 2019 report from the International AIDS Society Towards an HIV Cure Initiative, AVAC, and the Resource Tracking for HIV Prevention Research and Development Working Group.[61]

The current U.S. presidential administration has now settled into a predicable Janus-faced approach to HIV research funding, talking up its commitment while attempting to cut the budget of the U.S. National Institutes of Health—by far the largest global contributor to the pursuit of an HIV cure—every year. Thankfully, Congress has so far prevented proposed cuts being enacted. In FY 2020, HIV cure research ultimately received a slight 3.6% increase, bringing the annual total to $197.6 million and averting the administration's attempt to slash $31.3 million.[62] The president's FY 2021 budget request contains a decrease in HIV cure research support of $16.8 million, 8.5% less than the FY 2020 enacted level, which will again need to be headed off at the congressional pass.[63]

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EIN 13-3624785