Supplementary Appendix

Supplement to: Dickter JK, Aribi A, Cardoso AA, et al. HIV-1 remission after allogeneic hematopoietic-cell transplantation. N Engl J Med 2024;390:669-71. DOI: 10.1056/NEJMc2312556

This appendix has been provided by the authors to give readers additional information about the work.

Supplementary Appendix

Contents

Summary

A 67-year-old man with high-risk acute myeloid leukemia (AML) remains HIV-1-free 58 months after hematopoietic cell transplantation (HCT) from a homozygous 32-base CCR5 deletion (CCR5Δ32) donor, and 33 months after discontinuing antiretroviral therapy (ART). Because of his age we utilized a reduced-intensity conditioning (RIC) regimen without targeted T-cell depletion. Unlike the other HCT recipients of CCR5Δ32 donor cells, this case demonstrates that older adults with hematologic malignancy and HIV may achieve both cure of leukemia and durable HIV-1 control after HCT from CCR5Δ32 donors using a lower toxicity RIC regimen.

Introduction

Remission of HIV-1 following HCT for hematologic malignancies (HM) utilizing donors with CCR5Δ32 has been reported (Table S1).[1-5] The 32-base deletion in this gene results in a non-functional CCR5 receptor on $CD4^+$ cells and resistance to infection with CCR5-tropic HIV-1 strains.[6] Although the basis of success from this strategy is unknown, the effect of the HCT procedure on cells carrying the majority of the HIV-1-reservoir is assumed important for the success of the approach.[2,7] This is the first report of success in an older patient using reduced intensity of chemotherapy.

Case History

This Caucasian male was diagnosed with HIV-1 in 1988, with a nadir $CD4^+$ count <100 cells/μL and no prior opportunistic infections (Table S2). He started monotherapy ART in the early 1990s and transitioned to various ART regimens. Prior to his diagnosis of AML, he was taking lamivudine/abacavir/darunavir/cobicistat but changed to emtricitabine/tenofovir alafenamide/dolutegravir before initiating chemotherapy to minimize drug-drug interactions. His HIV-1 infection was well-controlled between 1997-2018 with $CD4^+$ counts between 243-1007 cells/μL and undetectable HIV-1 RNA. His hepatitis B virus (HBV) core antibody (HBcAb) and surface antibody (HBsAb) positive with a negative surface antigen (HBsAg).

At age 63, he was diagnosed with AML, failed primary induction therapy, but achieved complete remission after salvage chemotherapy. Due to elevated risk for relapse, a HCT was recommended for potential AML cure, and a CCR5Δ32 donor was identified selected based on human leukocyte antigen (HLA) match, age, sex, and ABO compatibility. Two of the three fully matched donors had permissive mismatch at DPB1 locus, which is preferred in myeloid malignancies to reduce the risk of AML relapse.[8] These two donors with permissive mismatch had similar age, blood types (both were O+), and CMV status (Table S3A). The one that was selected was secondary to donor time constraints. The potential for HIV remission was discussed with the patient, and after institutional review board approval, he consented to serial reservoir testing and eventual ATI conditional on hematologic recovery.

Methods

PATIENT AND DONOR EVALUATION

HLA and KIR Genotyping of Donor and Recipient

High-resolution HLA typing was reported by Next Generation Sequencing (Scisco Genetics). Genotyping of the donor and recipient and verification of the donor for CCR5 deletion was performed by PCR using a previously published primer pair.[9] KIR genotyping was analyzed by multiplex SSP[10] and confirmed by commercially available reagents (LinkeSeq Thermofisher). KIR Centromeric/Telomeric haplotype was assigned.[11]

Chimerism

Clinical donor recipient chimerism was monitored using the PowerPlex 21 system (Promega) with total DNA isolated from peripheral blood or individual cell populations (CD3, CD4, CD8, CD19). Cells were separated by magnetic beads using the RoboSep-S instrument (STEMCELL Technologies).

CCR5 Genotyping of Donor and Recipient

Primers TTCATTACACCTGCAGCTCTC and CCTGTTAGAGCTACTGCAATTAT were used to amplify the region containing the 32 base-pair deletion of the CCR5 gene. The PCR is carried out in a 25 µL volume with 15 pM of each primer. The PCR program includes an initial cycle of 95°C for 5 minutes and last cycle for 72°C for 7 minutes, 45 cycles at 95°C for 30 seconds, 60°C and 30

seconds and 72°C for 30 seconds. Amplification of the 304 bp and/or 272 bp products, corresponding to full and deleted form respectively, are analyzed by capillary electrophoresis using the QIAxcel system (QIAGEN).

DRUG LEVELS

Antiviral drug levels were obtained at 7 and 12 months into ATI.

Patient plasma samples were processed by protein precipitation and the drug levels determined by LC/MS/MS by: Darunavir, National Jewish Pharmacokinetics Lab; bictegravir, by University of Florida Infectious Disease Pharmacokinetics Laboratory; tenofovir, emtricitabine and dolutegravir, by City of Hope Analytical Pharmacology Core Facility (APCF).[12,13]

Tenofovir, emtricitabine and dolutegravir levels were measured by mass spectrometry in plasma samples using qualified LC/MS/MS protocols developed at City of Hope. Briefly, 750 µL methanol was added to 150 µL of plasma and then the solution was spiked with 10 µL of the internal standard (IS) solution (tenofovir-D6, 500 ng/mL). After vortex mixing and centrifugation at 15,000 × g for 15 min at 4 ˚C, 100 µL of supernatant was transferred to a 1.5 mL microcentrifuge tube, mixed with 200 µL of deionized water, and 5 µL of the final extract was injected into the LC-MS/MS. Instrumentation consisted of a Shimadzu Prominence HPLC system (Columbia, MD, USA) interfaced to an AB SCIEX QTRAP® 5500 system (Foster City, CA, USA). HPLC separation was achieved using a Waters Atlantis T3 3 µm 150 x 2.1 mm analytical column (Milford, MA, USA). Mobile phases consisted of 0.1% formic acid in deionized

water (mobile phase A) and 0.1% formic acid in acetonitrile (mobile phase B). The column temperature was maintained at 50°C, and the gradient flow rate was 0.4 mL/min. The following gradient program was used: 5% to 50% B (0 -2 min), 70% to 95% B (2 – 4 min), 95% B (4 -6 min). Detection of the analyte and internal standard was achieved by ESI positive ionization tandem mass spectrometry. The precursor/product transitions (m/z) monitored were 288.1/176.1, 248.0/130.2, 420.1/277.0 and 294.1/182.4 for tenofovir, emtricitabine, dolutegravir and tenofovir-D6, respectively. The lower limit of quantification of tenofovir, emtricitabine and dolutegravir were 0.2, 0.1 and 0.1 ng/mL, respectively.

HIV ANALYSIS

Viral Envelope Genotyping

Pre-HCT, the recipient's HIV DNA (V3) deep sequencing was performed using Nextera XT DNA Library Preparation Kit (Illumina). Genotropism was determined using WebPSSM.[14] Using Nextera XT DNA Library Preparation Kit (Illumina, FC-131-1096), indexing was performed on 96 samples per run (Nextera XT Index Kit, set A FC-131-2001) according to the manufacturer's protocols. Primers used for the first round were as follows: 5′-FENVouter (forward) TTAGGCATCTCCTATGGCAGGAA and 3′-RENVouter (reverse) TCTTAAAGGTACCTGAGGTCTGACTGG. First-round PCRs were performed using the Advantage 2 PCR Kit (Takara, catalog 639206) following the manufacturer's recommendations and 10× SA buffer (Takara, catalog 639206). Cycling conditions were as follows: 95°C for 1 minute, 35 cycles of 95°C for 15 seconds, 57°C for 30 seconds, 68°C for 3 minutes, with a final extension at 68°C for 10 minutes. The second-round PCRs were done using 5′-FENVinner (forward): GAGCAGAAGACAGTGGCAATGA and

3′RENVinner (reverse): CCACTTGCCACCCATBTTATAGCA. The cycling conditions were as follows: 95°C for 1 minute, 30 cycles of 95°C for 15 seconds, 64°C for 30 seconds, and 68°C for 3 minutes, with a final extension at 68°C for 10 minutes. PCR cleanups were performed on the second-round reaction products using a QIAquick PCR Purification Kit (QIAGEN, catalog 28106). DNA was quantified using a Qubit dsDNA HS Assay Kit (Invitrogen, Thermo Fisher Scientific, catalog Q32854). Quality and integrity were measured using Genomic DNA ScreenTape (Agilent Technologies, catalog 5067-5365) in combination with the 2200 TapeStation System (Agilent Technologies, Genomic DNA Reagents, catalog 5067-5366).

HIV Reservoir Analysis

Pre-HCT and post-HCT cellular RNA and DNA were extracted from total peripheral blood mononuclear cell (PBMC) and rectal tissue using the AllPrep DNA/RNA minikit (Qiagen, CA), following the manufacturer's protocol, with addition of a DNase step to avoid DNA contamination (RNase-free DNase Set; Qiagen). Extracted RNA (500 ng) was reverse transcribed into 20 µl of cDNA (iScript Advanced cDNA synthesis kit; Bio-Rad) using the manufacturer's protocol. The cDNA product (8 µl; approximately 300 ng) was added to the ddPCR mixture. Unspliced HIV Gag RNA (usGag) and multiply spliced HIV Tat/Rev RNA (msTat/Rev) PCRs were performed as a duplex with HEX (usGag) and FAM (msTat/Rev) probes. Total HIV-1 DNA (polymerase [Pol]) and the 2-long terminal repeat (2-LTR) junction were quantified by droplet digital PCR (ddPCR) from extracted DNA.

Intact Proviral DNA assay (IPDA)

IPDA testing was performed pre-and post-HCT at Accelevir Dx.[15] An in-depth description of the rationale underlying the assay design and procedure have been reported.[16] Briefly, the IPDA consists of two multiplex ddPCR reactions performed in parallel, with the first designed to distinguish and separately quantify intact and defective proviruses (HIV-1 Proviral Discrimination component reaction), and the second designed to quantify input cell equivalents and account for DNA shearing (Copy Reference/Shearing component reaction). Here, the assay was performed on genomic DNA extracted from PB $CD4^+$ T cells. Sample processing, assay performance, and analysis were performed under Accelevir standard operating procedures with operators blinded to donor identity and timepoint. Final assay results are reported as frequencies per million input $CD4^+$ T cells. In cases in which no proviruses of a particular class were detected, a proviral frequency per million of less than that of one provirus per input cell number is displayed.

When signals are not detected for a particular proviral class (i.e., intact, 5' defective, or 3' defective), values are reported using the calculation based on the frequency per million for a single provirus detected in that sample accounting for cell input: 1/(CD4 input) * $10^{6.}$ As the IPDA is run as a research/exploratory measurement for clinical studies, this is not based on a formally defined level of quantification/level of detection, but it is consistent with the general single molecule sensitivity of ddPCR as well as internal analytical performance.

In Vitro HIV Challenge Assay.

HIV challenge assays were performed using PBMC depleted of $CD8^+$ T cells using the CD8 Positive Isolation Kit (Invitrogen™ Dynabeads™). Cells were activated for 48 h in T cell activation media (ActiCyte-TC-Media Kit- CytoMedical), and infected with HIV strains provided by the NIH AIDS Reagent Program [HIV BaL, NL4-3 or 89.6 strains (MOI 0.01), in duplicates]. After 24 hrs. incubation, cells were washed and recultured in T cell activation media, with media changes twice a week. Culture supernatants were collected on days 4, 7, 11 and 14, and analyzed for presence of HIV capsid protein p24 by ELISA (PerkinElmer).

Memory T Cell Subsets by Flow Cytometry

For assessment of distribution of T cell memory subsets in circulating $CD4^+$ and $CD8^+$ T cells, a multiparametric flow panel was used with fluorochrome-conjugated antibodies for CD3, CD4, CD8, CD45RA, CD45RO, CD62L, CD127, CD27, CD28, CD57, CD95 and CD197 (Supplementary Table 4). PBMC were treated with fixable viability dye (Invitrogen, L23105) as per manufacturers' instructions, followed by incubation in brilliant staining buffer (BD, 563794) supplemented with 0.2% human gamma globulin (Grifols, NDC 13533-800-13). Cells were then incubated with antibodies, washed, and stored in 4% paraformaldehyde in PBS prior to acquisition on a BD LSRFortessa SORP Cell Analyzer. Acquisition was setup using DIVA software (BD) and data analyzed in the FlowJo software (Tree Star Inc./BD).

Subsets were defined as: naïve ($CD45RA^+$ $CD95^-$ $CD57^-$), stem cell memory (T_{scm}; $CD45RA^+$, $CD95^+$, $CD57^-$ $CD127^+$ $CD197^+$), central memory (T_{cm}; $CD45RO^+$, $CD27^+$, $CD197^+$), transitional memory (T_{tm}; $CD45RO^+$, $CD27^+$, $CD197^-$), effector memory (T_{em}; $CD45RO^+$, $CD27^-$, $CD197^-$), and terminal effector cells (T_{te}; $CD45RA^+$ $CD95^+$ $CD57^-$).

IMMUNOLOGICAL STUDIES

HIV-specific proteins were measured by HIV-1 Western Blot (ARUP Laboratories). Frequencies of $CD4^+$ and $CD8^+$ T-cells, and T-cell memory subsets were determined using a multiparametric flow panel.

Viral Recall T Cell Response by Activation-Induced Marker Assay

For evaluation of viral T cell recall responses, PBMC ($5x10^6$ cells/mL) were pulsed with CMV pp65 PepMix (PepTivator CMV pp65, Miltenyi Biotec) or HIV megapool (kindly provided by Dr. Alessandro Sette, La Jolla Institute for Immunology), in the presence of rhu IL-12. As activation control, PBMC were treated with Human T Activator CD3/CD28 Dynabeads (Gibco/Thermo 11161D), as well as non-pulsed PBMC, under the same culture conditions. After 20 h incubation, cells were harvested and incubated in PBS supplemented with 0.5% HSA and 0.02% human gamma globulin, and stained for 30 min with the fluorophore-conjugated antibodies shown in Supplementary Table 5. Cells were then washed, resuspended in buffer containing 7AAD (Miltenyi, 130-111-568) and acquired on a Miltenyi MACSQuant 10 flow cytometer. Data were analyzed using the FlowJo software.

Results

PRE-HCT EVALUATION

The City of Hope (COH) patient and donor were HLA-matched at the 11 of 12 level (DPB1 was mismatched) (Table S3A) but had different KIR genotypes (Table S3B).

Donor cells were CCR5 Δ32/Δ32, and recipient cells were wild-type homozygous CCR5. HIV-1 DNA (V3) from the recipient PBMCs had sequencing that predicted predominantly R5 virus (haplotypes with a frequency of 3% to 24%), but two low frequency variants with predicted X4 usage were noted (2%, 8%, representativity, 10% false positive rate). Donor was HBV negative by HBsAg, HBcAb, and HBV DNA PCR (Table S8).

HCT AND ATI INITIATION

The patient underwent HCT in February 2019 with a RIC fludarabine/melphalan pre-transplant conditioning regimen and systemic immunosuppression post-transplant using sirolimus and tacrolimus for graft-versus-host disease (GVHD) prophylaxis (Figure 1A). Bone marrow biopsies on days +30 and +100 were negative for leukemia and showed donor cell chimerism of 99.95% and 100%, respectively. He was monitored post-HCT on ART with HIV-1 RNA and DNA levels in blood and gut biopsies. Based on these

results, which were mostly negative (Figure 2A and 2B), ATI was initiated 25 months post-HCT following published recommendations.[17] HBV vaccination was initiated 10 months after HCT and post-vaccination HBsAb was consistent with immunity.

HIV RESERVOIR, IMMUNOLOGICAL STUDIES, HIV CHALLENGE

Analysis of the HIV-1 reservoir showed detectable HIV-1 DNA in the COH patient's PBMC pre-HCT, but not post-HCT. Low level un-spliced HIV-1 RNA was detectable at week 8 post-HCT and multiply spliced HIV-1 RNA was detectable at weeks 41 and 78 (Figure 1B, Table S4). No HIV-1 DNA or RNA copies have been detected in PBMC since ATI initiation (week 108). Analysis of cells from rectal biopsies showed the presence of HIV-1 DNA at week 25, but not at later timepoints (Figure 1C).

Reservoir analysis using IPDA pre-HCT showed 607 HIV-1 proviruses, consistent with the median total proviral frequency measured in PWH on long-term ART initiated during chronic infection.[18] A more than 2-log reduction in total proviruses was observed post-HCT and during ATI, with no intact or total proviruses detected at week 179 (12 months into ATI) among > $2x10^6$ $CD4^+$ T cells analyzed (imputed to be < 0.48 total proviruses in the sample) (Table S6).

Other *in vitro* immunological and HIV-1 challenge studies were performed 12 months into ATI (167 weeks post-HCT). A multiparametric flow panel was used to measure T cell memory subsets (Table S9), and $CD4^+$ T cells represented 32.2% T cells, with naïve T cells (19.9%), T_{cm} (17.8%) and T_{em} (28.4%) representing the most abundant subsets (Figure S1). $CD8^+$ T cells were

predominantly terminally differentiated and T_{em}, with low levels of naïve and T_{cm} subsets. Analysis of response to viral antigens with the AIM assay showed a robust response to CMV stimulation of $CD4^+$ and $CD8^+$ T cells (Figure 1E), which is significant as the donor was not reactive to CMV at the time of graft's harvest. Importantly, no T cell activation in response to HIV megapool peptides was detected (Figure 1E), suggesting lack of donor T cell priming to HIV antigens post-HCT. Finally, to confirm R5 HIV-1 resistance, CD8-depleted engrafted PBMC were challenged in vitro with the CCR5-tropic BaL HIV strain, with levels of HIV p24 capsid protein measured at different culture timepoints. At 30 months post-HCT, the engrafted PBMC did not support infection with BaL HIV, whereas infection was seen in cells from two healthy controls and when the patient's T cells were challenged with X4-tropic and dual-tropic HIV strains (Figure 1D).

The COH patient's plasma was tested for anti-HIV-1 antibodies at multiple time points into ATI. Antibodies were detected for all HIV-1 proteins tested, and decreased levels of HIV p18-, p31-, gp41-, p65- and pg120- bands were observed on Western blot (Table S7).

CITY OF HOPE PATIENT CHIMERISM, CELL COUNTS, AND ART LEVELS

Thirty months post-HCT, and five months into ATI, engraftment analysis on peripheral blood showed full donor chimerism for $CD4^+$ T helper cells, $CD3^+$ total T cells, $CD14^+$ monocytes, $CD15^+$ granulocytes,and $CD33^+$ myeloid cells. Despite the late persistence of HIV-1 antibody, at 43 months post-HCT and 19 months into-ATI, B cell chimerism was determined to be 99.9% donor cells.

Since ATI, $CD4^+$ T cell counts have ranged from 356 to 1271 cells/μL. The COH patient had slow $CD4^+$ reconstitution and reached pre-transplant levels 19 months post-HCT (6 months before ATI). HIV-1 RNA levels remained undetectable at < 20 copies/mL (Table S5).

During the period of ATI, the COH patient reported he was not taking pre-exposure anti-HIV prophylaxis (PrEP). At seven months into ATI he was found to have subtherapeutic levels of tenofovir, dolutegravir, and darunavir. Tenofovir level was only 4.3% of mean trough concentration level expected for TAF, and 1% for TDF.[19,20] Measured dolutegravir and darunavir levels were also low at 2.7%[21] and 1.7%[22] of expected mean trough concentration, respectively. There were no detectable emtricitabine, tenofovir, dolutegravir, darunavir, and bictegravir levels at 12 months into ATI (Table S9).

Discussion

It is clear from the literature that allogeneic HCT with CCR5Δ32 donors can result in an HIV cure,[1-5] but it is not clear why the procedure is only variably successful. It has been proposed that the chemo- or radio-therapy conditioning regimens in preparation for

the HCT are needed for the eradication of the HIV reservoir[2,7]. The COH patient illustrates that success is possible using a RIC regimen.

It is possible that innate immunity could have played a role in outcome since innate immunity appears to be important for HIV outcome.[23-26] In PWH, the interaction of HLA-C ligands (grouped as C1, C2) and inhibitory KIR2DL receptors (KIR2DL1/L2/L3) may help immune control of HIV-1 infection,[26] and the presence of 3DS1 in HLA-Bw4 persons is associated with disease protection.[27] The COH patient was Bw4 negative, C1 homozygous, and homozygous for 2DL3, factors that increase inhibitory KIR signals, but the donor was positive for 2DS2, NK cell activator via C1. We can only speculate that KIR/HLA interaction may be important in long term control of HIV,[27] but any role in protection against HIV reactivation after HCT remains unclear.

The HIV reservoir is a likely factor in outcome. The Essen patient, who received similar treatment to the Berlin patient but developed rebound viremia during engraftment harbored an HIV CXCR4 quasi-species.[28] In the COH patient, the HIV reservoir appears to have been small, based on pre-HCT provirus analyses, likely due to reservoir decay after decades of good HIV-1 control. As with the Berlin patient[1], there were CXCR4-predicted minority viruses present prior to HCT that did not rebound post-HCT suggesting that these were non-replication competent DNA sequences or were integrated viral elements that could not replicate due to coreceptor dependence on CCR5 for replication.[29]

The COH patient remains in HIV-1 remission 33 months into ATI with plasma and intestinal biopsy samples negative for intact HIV-1 RNA, HIV-1 DNA, with a few sporadic low-level detectable levels, as reported in the others of the 'cured' HCT recipients[1-5,30]

The possibility of PrEP use was considered to explain detectable drug levels at early time points knowing that passive diffusion of drug in seminal plasma from a partner on ART is possible.[31-34] However, these low levels would not contribute to long-term HIV-1 RNA suppression. Repeat testing 12 months into ATI revealed undetectable levels for emtricitabine, tenofovir, dolutegravir, darunavir, and bictegravir.

One test of whether HIV-1 is now absent in our patient is whether the immune system is making either antibody or T cells specific for HIV-1. Although HIV-1 Western Blot antibody patterns remain positive, our patient is losing protein bands, similar to the course seen in the Berlin[1], London[2,3], Düsseldorf[4] and IMPAACT P1107[5] patients. Immunological studies indicated that one year into ATI, our patient had T-cells that were responsive to mitogenic stimuli to CMV, but not to HIV, findings similar to those seen in the other successfully transplanted patients.[1-5]

Late after HCT our patient's PBMC cells were challenged in vitro with HIV-1 X4- and dual-tropic virus, and the cell cultures developed detectable levels of p24 antigen by day 7. However, when challenged with R5-tropic virus, the p24 level remained

undetectable. This confirms complete donor T cell chimerism, and indicates the need to continue protective measures to prevent infection with CXCR4 strains of HIV.

In conclusion, our patient is unique because of his advanced age, long-duration of HIV-1 infection, and the use of an RIC regimen designed for transplant of older people with hematologic malignancy. This case suggests that replacement of cells composing the HIV-1 reservoir during RIC HCT is all that is required for long-term remission from HIV. As PWH live longer, and with the availability of donors with permissive genetics and the introduction of novel GVHD prophylaxis methods allowing higher degrees of HLA-mismatch, there will be additional opportunities for such personalized approaches to managing PWH with concomitant HM. Our patient is doing well with chronic oral GVHD treated with topical therapy and remains in remission from HIV and AML. This case demonstrates that for such older persons, remissions and potential cure can be obtained for both the HM and HIV.

Table S1 - Summary of background and treatment of the Berlin,[1,35] London,[2,3] Düsseldorf,[4] IMPAACT P1107[5] and the City of Hope patients.

	The City of Hope Patient	IMPAACT P1107	The "London" Patient	The "Düsseldorf" Patient	The "Berlin" Patient
Demographics	Caucasian male, 63 years old at time of HCT	Woman, mixed race, "middle aged"	Latino male, 40 years old at time of HCT	Caucasian male, 43 years old at time of HCT	Caucasian male, 40 years old at time of HCT
Underlying malignancy	Myelodysplastic syndrome diagnosed July 2018, transformed to acute myeloid leukemia October 2018	Acute Myeloid Leukemia diagnosed March 2017	Hodgkin's Lymphoma, diagnosed December 2012	Acute Myeloid Leukemia, diagnosed January 2011	Acute Myeloid Leukemia, diagnosed 2006
HIV diagnosis, # years living with HIV prior to HCT	1988, 31 years	2013, 6 years	2003, 9 years	October 2010, 3 years	1990s, 12 years
Therapies prior to HCT	Induction chemotherapy: failed 7 + 3 (cytarabine for seven days, idarubicin hydrochloride for 3 days), then reinduced with FLAG-Ida (fludarabine, cytarabine, and idarubicin hydrochloride for five days), and failed to achieve remission. Received salvage decitabine for 10 days with venetoclax and achieved complete remission.	Induction chemotherapy [7+3, cytarabine, idarubicin, consolidation X 1 high dose cytarabine	HL refractory to first-line ABVD and multiple salvage regimens (ESHAP, an anti-CD30 monoclonal antibody (brentuximab) and mini-LEAM. CR achieved with IGEV chemotherapy in March 2016.	Induction therapy with ICE X 2, then 3 consolidation courses (AML-SG07/04), in CR. Relapsed Sept 2012: A-HAM + 2nd cycle high dose cytarabine	Induction chemotherapy X 2, consolidation chemotherapy X 1
HCT Donor and Graft	HLA-matched at the 11 of 12 level (DPB1 was mismatched) CCR5Δ32 Graft: peripheral blood stem cells Engraftment: Day +15	Haplo-cord HCT, combined CCR5Δ32 cord blood cells (5/8 HLA-matched) with haploidentical adult donor without CCR5 mutation Graft: peripheral blood	9/10 HLA Matched + CCR5Δ32 Graft: peripheral blood stem cells	10/10 HLA Matched + CCR5Δ32. Graft: peripheral blood stem cells	10/10 HLA Matched + CCR5Δ32 Graft: Bone marrow cells
Transplant #1	Reduced-intensity fludarabine 25 mg/m^2 plus melphalan 140 mg/m^2	2017: Fludarabine/melphalan/ 400-cGy	May 2016. Conditioning: lomustine, ARA-C, cyclophosphamide,	February 2013. Conditioning: Fludarabine/treosulfan	February 2007. Conditioning: fludarabine, cytarabine, amsacrine

Days to engraftment (if known) Length of hospitalization of HCT (if known)		TBI/antithymocyte globulin	etoposide (LACE). T-cell depletion with Alemtuzumab (anti-CD52)		(FLAMSA), cyclophosphamide, rabbit antithymocyte globulin (ATG), 400-cGy TBI
Transplant #2	n/a	n/a	n/a		March 2008. Conditioning: cytarabine, gemtuzumab ozogamicin (anti-CD33), 200-cGy TBI
Post-HCT relapse	n/a	n/a	n/a	2nd relapse June 2013, achieved molecular remission after 8 courses of 5-azacytidine and 4 donor lymphocyte infusions.	
GVHD prophylaxis/Immuno-suppression	Tacrolimus/sirolimus post-HCT. Tacrolimus discontinued 6 ½ months post-HCT, sirolimus discontinued 16 months post-HCT. Oral topical dexamethasone started 18 months post HCT for oral GVHD. Sirolimus briefly restarted for chronic GVHD weeks 161-100 post-HCT.	Mycophenolate mofetil, stopped day +28 post-HCT, tacrolimus, discontinued until day +180 post-HCT.	Cyclosporine A, short course of methotrexate, < 1 year of treatment.	Full details not reported.	Cyclosporine, mycophenolate mofetil after procedure.
GVHD	Chronic oral GVHD noted 17 months post-HCT	None	Acute GI GVHD Grade 1, day +77 post-HCT, resolved without intervention	Moderate acute, mild chronic GVHD after donor lymphocyte infusions, tacrolimus stopped Oct 2017	Grade 1 liver, skin following 1st HCT, treated with cyclosporine A, methyprednisolone, MMF.

				(4 years 8 months post-HCT)	immunosuppression ended 38 months post-HCT.
Post-HCT Infection complications	None	Rituximab pre-conditioning as prophylaxis against EBV; developed EBV reactivation +28 months post-HCT, treated with 2nd dose rituximab (2nd dose), and +2 months post-HCT. CMV reactivation treated with valganciclovir	EBV reactivation, treated with rituximab; CMV treated with ganciclovir	Not reported	None
ATI started	51 months post-HCT	37 months post-HCT	16 months post-HCT	Nov 2018 (5 years, 9 months post-HCT	Day 0 of HCT
ART-Free HIV remission	31 months	>18 months	>5 years	>5 years	13 years (deceased from relapsed AML 2020)
This table represents the medical histories of the Berlin,[1,35] London,[2,3] Düsseldorf,[4] IMPAACT P1107[5] and the City of Hope patients.					

Table S2 - Medical history of the City of Hope patient. This table summarizes the City of Hope patient's demographics, HIV history, and hematologic history.

Demographics	Caucasian male, age 63 at time of HCT
Underlying malignancy	Myelodysplastic syndrome (MDS) diagnosed July 2018, transformed to acute myeloid leukemia (AML) October 2018 associated with chromosome trisomy 8 cytogenetic abnormalities, next generation sequencing showed no mutations.
HIV History	Diagnosed in 1988, nadir $CD4^+$ count <100 cells/μL, no prior opportunistic infections.
HIV Course of Therapy	Started monotherapy antiretroviral therapy (ART) early 1990s, transitioned to various regimens. ART prior to diagnosis of AML: lamivudine/abacavir/darunavir/cobicistat. Before initiating chemotherapy ART changed to emtricitabine/tenofovir alafenamide/dolutegravir to minimize drug-drug interactions. HIV-1 was well-controlled between 1997-2018 with $CD4^+$ counts between 243-1007 cells/μL and undetectable HIV-1 RNA.
Hepatitis B Virus (HBV) History	Hepatitis B core antibody (HBcAb) and HBV surface antibody (HBsAb) positive, HBV surface antigen (HBsAg) negative.

Table S3A - HCT Information and HLA/KIR Typing and KIR ligands for donor and recipient. The permissive mismatch at DPB1 locus is preferred in myeloid malignancies to reduce the risk of AML relapse.

	Donor	**Recipient (COH patient)**	**KIR ligands for Donor and Recipient**
Age (years)	35	63	
Blood Group (Rhesus)	O (+)	B (+)	
CMV Status	Negative	Positive	
HLA-A	01:01, 03:01	01:01, 03:01	A3 (Bw4 negative)
HLA-B	07:02, 08:01	07:02, 08:01	(Bw4 negative)
HLA-C	07:01, 07:02	07:01, 07:02	C1C1 (C2 negative)
HLA-DRB1	03:01, 15:01	03:01, 15:01	
HLA-DQB1	02:01, 06:02	02:01, 06:02	
HLA-DPB1	04:01	04:01, 04:02	

Table S3B - KIR-HLA combinations. Summary of KIR results for both recipient and donor. KIR is listed by chromosome location, centromeric, telomeric or both, or framework, based on previously published descriptions.[11]

KIR	2DS2	2DL2	2DL3	2DP1	2DL1	3DL1	2DS4F	2DS4S	3DS1	2DS1	2DL5	2DS3	2DS5	3DL3	3DP1	2DL4	3DL2	KIR haplotypes
Donor	+	+	+	+	+	+		+	+	+	+	+		+	+	+	+	Cen A/B, Tel A/B
Patient			+	+	+				+	+	+		+	+	+	+	+	Cen A/A, Tel B/B
Known KIR ligands (HLA)	**C1** A11	**C1** B46 B73	**C1** B46 B73		C2	Bw4 (A/B)	**C1** C2 A11 *F*		B51 *F*	C2			C2			G	**A3** A11	

Patient/donor ligands are marked in red. + for gene presence, white wells for gene absence.

2DS4F – Full (expressed)

2DS4S -Secreted (not expressed)

HLA-F – not tested.

Table S4 - HIV-1 reservoir analysis on the City of Hope patient pre- and post-HCT and after initiation of ATI on peripheral blood mononuclear cells (PBMC) and gut biopsies.

Week of pre- and post- HSCT	**Number of $CD4^+$ cells analyzed**	**RNA: msTatRev copies/10^6 CD4+ T cells**	**RNA: skGag copies/10^6 CD4+ T cells**	**DNA: skGag copies/10^6 CD4+ T cells**
Pre-HSCT (-12 weeks) PBMC	3.89×10^5	-	-	80.25
Week +8 PBMC	3.84×10^5	0	35	0
Week +13 PBMC	4.22×10^5	0	0	0
Week +25 gut biopsy	2.84×10^5			4.22
Week +27 PBMC	3.99×10^5	0	0	0
Week +41 PBMC	3.78×10^5	11.4	0	0
Week +55 gut biopsy	3.54×10^5			0
Week +57 PBMC	1.14×10^6	0	0	0
Week +78 PBMC	4.18×10^5	21.9	0	0
Week +107 PBMC	5.22×10^5	0	0	0
ATI – Week +108				
Week +134 PBMC	4.22×10^5	0	0	0
Week +161 PBMC	2.61×10^5	0	0	0
Week +161 gut biopsy	4.35×10^5			0
Week +212 PBMC	3.33×10^5	0	0	0

Table S5 - City of Hope patient laboratory testing over time: flow cytometry ($CD4^+$ cells, $CD8^+$ cells, $CD3^+$ cells, $CD19^+$ cells, NK cells) white blood counts, platelet counts, calculation of absolute neutrophil counts (ANC), and absolute lymphocyte counts (ALC), HIV-1 RNA, ART therapy, and immunosuppression [tacrolimus (tacro), sirolimus (siro)].

Week of trans-plant	$CD4^+$ cells/ µL (%)	$CD8^+$ cells/µL (%)	Helper/ Suppressor Ratio	$CD3^+$ Count Cells/ cells/µL (%)	$CD19^+$ Count cells /µL (%)	NK Cells cells/ µL (%)	Total WBC K/µL	Platelet Count K/µL	ANC K/µL	ALC K/µL	HIV-1 RNA copies /mL (UD= Un-detectable)	ART	Immuno-suppression
-14	422 (41.38%)	471 (46.21%)	0.9	896			1.4	53	0.3	1.0	UD < 20 copies	FTC/TAF/ DTG	Day 1 7+3 induction chemo
Day 0 HCT	14 (58.72%)	10 (43.99%)	1.3				2.0	42			UD < 20 copies	FTC/TAF/ DTG	Tacro, Siro
7	372 (22.31%)	481 (28.85%)	0.8	1,107 (66.33 %)			3.9	138	1.9	1.3	UD < 20 copies	FTC/TAF/ DTG	Tacro, Siro
15	312 (28%)	358 (32%)	0.8 8	770 (69%)	22 (2%)	290 (26%)						FTC/TAF/ DTG	Tacro, Siro

26	324 (28%)	393 (34%)	0.82	809 (70%)	23 (2%)	289 (25%)	3.4	130	1.7	1.2	UD < 20 copies	FTC/TAF/ DTG	Tacro, Siro
27	281 (30.29%)	314 (33.78%)	0.9	663 (71.61%)	20 (2.16%)	241 (26.1%)	4.5	138	3.1	0.9	UD < 20 copies	FTC/TAF/ DTG	Tacro discontinued, Siro continued
37	343 (28%)	490 (40%)	0.7	918 (75%)	37 (3%)	233 (19%)	3.6	147	1.7	1.2	UD < 20 copies	FTC/TAF/ DTG	Siro
53	353 (21%)	840 (50%)	0.42	1,243 (74%)	67 (4%)	319 (19%)	3.5	160	1.1	1.7	UD < 20 copies	FTC/TAF/ DTG	Siro
66	385 (13%)	1,986 (67%)	0.19	2,460 (83%)	178 (6%)	326 (11%)	5.7	144	2.0	3.0	UD < 20 copies	FTC/TAF/ DTG	Siro
71													Siro discontinued
74	382 (16.1%)	1,501 (63.19%)	0.3	1,929 (81.2%)			5.3	165	2.0	2.6	UD < 20 copies	FTC/TAF/ DTG	None
78													Dexamethasone oral solution swish and spit

83	645 (17%)	2,239 (59%)	0.29	2,960 (78%)	531 (14%)	304 (8%)	6.9	165	2.3	3.8	UD < 20 copies	FTC/TAF/ DTG	Dexamethasone oral solution swish and spit
100	800 (19%)	2,317 (55%)	0.35	3,159 (75%)	800 (19%)	253 (6%)	7.8	212	2.5	4.2	UD < 20 copies	FTC/TAF/ DTG	Dexamethasone oral solution swish and spit
107 **ATI start date**	555 (11.51%)	>1600 (71.08%)	0.2	4,059 (84.15%)			7.3	211	1.3	4.9	UD < 20 copies	FTC/TAF/ DTG dis-continued	Dexamethasone oral solution swish and spit
109	455 (12.37%)	>1600 (63.19%)	0.2	2,857 (77.7%)			9.3	215	2.7	5.3	UD < 20 copies	ATI	Dexamethasone oral solution swish and spit
111	511 (15.31%)	>1600 (59.37%)	0.3	2,550 (76.37%)							UD < 20 copies	ATI	Dexamethasone oral solution swish and spit
112	691 (14.87%)	>1600 (54.87%)	0.3	3,309 (71.23%)							UD < 20 copies	ATI	Dexamethasone oral solution swish and spit
114	475 (11.68%)	>1600 (64.66%)	0.2	3,160 (77.74%)			8.7	196	3.8	4	UD < 20 copies	ATI	Dexamethasone oral solution swish and spit
116	535 (14.07%)	>1600 (62.02%)	0.2	2,944 (77.43%)							UD < 20 copies	ATI	Dexamethasone oral solution swish and spit

118	508 (11.81%)	>1600 (67.43%)	0.2	3,464 (80.56 %)							UD < 20 copies	ATI	Dexamethasone oral solution swish and spit
120	667 (14.73%)	>1600 (66.98%)	0.2	3,692 (81.52 %)							UD < 20 copies	ATI	Dexamethasone oral solution swish and spit
122	711 (15.29%)	>1600 (62.35%)	0.3	3,635 (78.2%)			8.4	208	1.9	5.2	UD < 20 copies	ATI	Dexamethasone oral solution swish and spit
124	651 (15.35%)	>1600 (66.17%)	0.2	3,405 (80.27 %)							UD < 20 copies	ATI	Dexamethasone oral solution swish and spit
126	833 (15.3%)	>1600 (62.94%)	0.2	4,262 (78.25 %)								ATI	Dexamethasone oral solution swish and spit
128	1271 (19.71%)	>1600 (51.7%)	0.4	4,673 (72.45 %)							UD < 20 copies	ATI	Dexamethasone oral solution swish and spit
130	390 (10.9%)	>1600 (61.18%)	0.2	2,612 (73.14 %)			10.1	244	5.7	3.8	UD < 20 copies	ATI	Dexamethasone oral solution swish and spit
132	430 (11.16)	>1600 (56.17%)	0.2	2,627 (68.11 %)							UD < 20 copies	ATI	Dexamethasone oral solution swish and spit

134	356 (10.54%)	>1600 (61%)	0.2	2,436 (72.14 %)							UD < 20 copies	ATI	Dexamethasone oral solution swish and spit
136	597 (11.07%)	>1600 (64.52%)	0.2	4,092 (75.83 %)							UD < 20 copies	ATI	Dexamethasone oral solution swish and spit
138	663 (10.05%)	> 1600 (69.85%)	0.1	>4,700 (80.39 %)	787 (12.72%)	377 (6.1%)	12.1	196	4.8	6.5	UD < 20 copies	ATI	Dexamethasone oral solution swish and spit
140	1091 (14.74%)	> 1600 (67.31%)	0.2	>4,700 (82.26 %)							UD < 20 copies	ATI	Dexamethasone oral solution swish and spit
142	939 (14.09%)	>1600 (71.53%	0.2	>4,700 (85.9%)							UD < 20 copies	ATI	Dexamethasone oral solution swish and spit
144	738 (14.41%)	>1600 (65.10%)	0.2	4,109 (80.23 %)			9.8	241	3.8	4.9	UD < 20 copies	ATI	Dexamethasone oral solution swish and spit
146	716 (15.745)	>1600 (66.27%)	0.2	3,746 (82.39 %)							UD < 20 copies	ATI	Dexamethasone oral solution swish and spit
148	835 (17.91%)	>1,600 (62.82%)	0.3	3,656 (81.31 %)							UD < 20 copies	ATI	Dexamethasone oral solution swish and spit

150	574 (12.57%)	>1,600 (65.16%)	0.2	3,599 (78.84 %)							UD < 20 copies	ATI	Dexamethasone oral solution swish and spit
152	689 (14.05%)	>1,600 (66.32%)	0.2	3,980 (81.22 %)			9.0	244	4.3	3.8	UD (< 20 copies)	ATI	Dexamethasone oral solution swish and spit
154	994 (15.36%)	>1,600 (64.21%)	0.2	>4,700 (80.32 %)							UD (< 20 copies)	ATI	Dexamethasone oral solution swish and spit
156	577 (15.015)	>1,600 (63.10%)	0.2	3,048 (79.31 %)							UD (< 20 copies)	ATI	Dexamethasone oral solution swish and spit
158	601 (15.65%)	>1,600 (61.51%)	0.3	2,978 (77.51 %)							UD < 20 copies	ATI	Dexamethasone oral solution swish and spit
160	1,201 (15.26%)	>1,600 (63.87%)	0.2	>4,700 (79.51 %)							UD < 20 copies	ATI	Dexamethasone oral solution swish and spit
161	756 (16.44%)	>1,600 (63.34%)	0.3	3,711 (80.26 %)	473 (10.17%)	378 (8.12 %)	9.2	228	3.1	5.3	UD < 20 copies	ATI	Sirolimus restarted, dexamethasone oral solution swish and spit
166	762 (18.62%)	>1,600 (56.01%)	0.3	3,070 (75.03 %)							UD < 20 copies	ATI	Sirolimus, dexamethasone oral solution swish and spit

179	827 (20.74%)	>1,600 (57.64%)	0.4	3,148 (78.91 %)			9.3	364	4.4	4.1	UD < 20 copies	ATI	Sirolimus, dexamethasone oral solution swish and spit
187	431 (20.76%)	1,090 (52.45%)	0.4	1,523 (74.44 %)			8.0	250	4,4	2.8	UD < 20 copies	ATI	Sirolimus, dexamethasone oral solution swish and spit
199	645 (18.39%)	>1,600	0.4	2,409 (68.69 %)			7.8	248	3.7	3.4	UD < 20 copies	ATI	Sirolimus discontinued, dexamethasone oral solution swish and spit
212	911	>1,600		3975			9.5	306	22.	5.9	UD < 20 copies	ATI	Dexamethasone oral solution swish and spit
219	810	>1,600		3573			10.1	280	2.9	4.3	UD < 20 copies	ATI	Dexamethasone oral solution swish and spit
232	1036	>1,600		4145			12.1	323	2.9	7.0	UD < 20 copies	ATI	Dexamethasone oral solution swish and spit
239	1,077 (18.39%)	>1,600	0.4	4700			10.8	342	2.5	6.7	UD < 20 copies	ATI	Dexamethasone oral solution swish and spit

Table S6 -HIV reservoir analysis by IPDA

Timepoint	Number of $CD4^+$ T-cells Analyzed	Intact Proviruses (per $1x10^6$ $CD4^+$ T cells)	Total Proviruses Detected
Pre-HCT	2.98×10^4	<33.55	607.43
Wk. 9	1.23×10^4	<81.25	<81.25
Wk. 90	1.66×10^5	<6.03	<6.03
Wk. 179 (in ATI)	2.08×10^6	<0.48	<0.48

Pre-HCT sample collected 12 weeks prior HCT.

Table S7 - Western Blot data.

Date	Bands 2+ (strongly positive)	Bands 1+ (weak positive)	Bands +/-	Bands 0 (negative)
+31 months post HCT, +6 months into ATI	p24, p31, p40, gp41, p51/55, p65, gp120, gp160	p18	none	none
+37 months post-HCT, +12 months into ATI	p24, p31, p40, gp41, p51/55, p65, gp120, gp160	none	p18	none
+41 months post-HCT, 16 months into ATI	p24, p40, p51/55, gp120, gp160	p31, gp41, p65	p18	none
+50 months post-HCT, 25 months into ATI	p24, p31, p40, p51/55, p65, gp160	gp41, gp120	p18	none

Table S8 - Hepatitis B Antibody and DNA levels in donor and City of Hope patient at different timepoints.

Donor	City of Hope patient pre-HCT	City of Hope Patient 3 years post-HCT
HBsAg negative HBcAb negative HBV DNA negative	HBsAg negative HBsAb positive HBcAb positive HBV DNA negative	HBsAg negative HBsAb positive HBcAb positive HBV DNA negative

Table S9 - Drug levels at 7 and 12 months into ATI.

Drug	7 months into ATI	12 months into ATI	Pharmacokinetic parameters
Emtricitabine	0.00 ng/mL	0.00 ng/mL	
Tenofovir	0.40 ng/mL	0.00 ng/mL	Tenofovir levels were measured, which is the active metabolite of TAF and TDF.[20] TAF: Steady state pharmacokinetic parameters of plasma TFV Cmax: 15.7 ng/mL, Cmin 9.2 ng/mL[20] TDF: Steady state pharmacokinetic parameters of plasma TFV Cmax: 252.1 ng/mL, Cmin 38.7 ng/mL[20]
Dolutegravir (dosed at 50 mg daily)	0.03 ng/mL	0.00 ng/mL	Steady-state pharmacokinetic parameters: Cmax 3.67 µg/mL and Cmin 1.11 µg/mL.[21]
Darunavir	0.06 mcg/mL	0.00 mcg/mL	Therapeutic peak concentrations range 5-8 mcg/mL at 2.5-4 hours post-dose. Trough concentrations range 1.2-7.4 mcg/mL with a median of 3.6 mcg/mL[22]
Bictegravir	Not done	0.00 mcg/mL	

Table S10 - Antibodies used in T Cell Memory Phenotype Panel.

Antibody/Fluorochrome	Vendor	Cat#
CD8 BUV395	BD (Horizon)	563795
CD197 BV711	Biolegend	353228
CD28 BV650	Biolegend	302946
CD57 BV605	Biolegend	393304
CD4 BV510	Biolegend	357420
CD127 BV421	Biolegend	351310
CD45RO PerCP-Cy5.5	Biolegend	304221
CD45RA FitC	Biolegend	304106
CD95 PE-Cy7	Biolegend	305622
CD27 PE-Dazzle594	Biolegend	356422
CD3 AF700	BD (Pharmingen)	557943
CD62L APC	Biolegend	304810

Table S11 - Antibodies used in AIM Phenotype Panel.

Antibody/Fluorochrome	Vendor	Cat#
CD3- BV510	Biolegend	317331
CD4- APC-Cy7	Biolegend	357416
CD8- FitC	Biolegend	301050
CD25- APC	Miltenyi	130-113-284
CD137- BV421	Biolegend	309820
PD-L1- PE	Biolegend	393607
OX40- PE-Vio770	Miltenyi	130-104-210

Figure S1 - Relative distribution of T cell memory subsets in $CD4^+$ T cells (upper pie chart) and $CD8^+$ T cells (lower pie chart) at 12M ATI (37M post-HCT). PBMC were analyzed using a multiparametric flow panel, with the memory subsets defined.

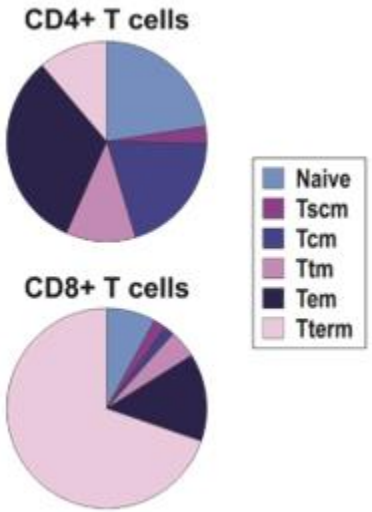
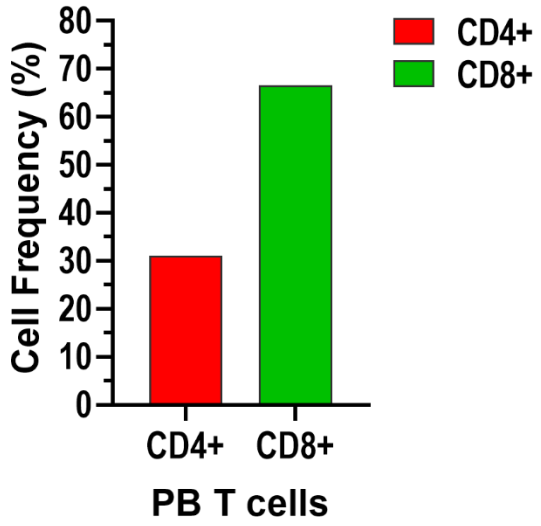


Figure S2 - Relative distribution of CD4+ and CD8+ T cells in PB at 12M ATI (37M post-HCT). PBMC were analyzed using a multiparametric flow panel, with the antibodies indicated in Table S3.



Acknowledgments

Thank you to Tim Synold from the Analytical Pharmacology Core Facility, at the City of Hope, Andrea Lynch at City of Hope's Center for Informatics Division of Library Services, Caroline Ignacio, and Gemma Caballero from UCSD, and the Matched Unrelated Donor staff at City of Hope National Cancer Center.

Supplement References

1. Hütter G, Nowak D, Mossner M, et al. Long-term control of HIV by CCR5 Delta32/Delta32 stem-cell transplantation. N Engl J Med 2009;360:692-8.
2. Gupta RK, Abdul-Jawad S, McCoy LE, et al. HIV-1 remission following CCR5Δ32/Δ32 haematopoietic stem-cell transplantation. Nature 2019;568:244-8.
3. Gupta RK, Peppa D, Hill AL, et al. Evidence for HIV-1 cure after CCR5Δ32/Δ32 allogeneic haemopoietic stem-cell transplantation 30 months post analytical treatment interruption: a case report. Lancet HIV 2020;7:e340-e7.
4. Jensen B-EO, Knops E, Cords L, et al. In-depth virological and immunological characterization of HIV-1 cure after CCR5Δ32/Δ32 allogeneic hematopoietic stem cell transplantation. Nature Medicine 2023.
5. Hsu J, Van Besien K, Glesby MJ, et al. HIV-1 remission and possible cure in a woman after haplo-cord blood transplant. Cell 2023;186:1115-26.e8.
6. Lederman MM, Penn-Nicholson A, Cho M, Mosier D. Biology of CCR5 and Its Role in HIV Infection and Treatment. JAMA 2006;296:815-26.
7. Li J. Advances toward a cure for HIV: getting beyond n=2. Top Antivir Med 2020;27:91-5.
8. Malki MMA, Gendzekhadze K, Stiller T, et al. Protective effect of HLA-DPB1 mismatch remains valid in reduced-intensity conditioning unrelated donor hematopoietic cell transplantation. Bone Marrow Transplant 2020;55:409-18.
9. Petz LD, Redei I, Bryson Y, et al. Hematopoietic cell transplantation with cord blood for cure of HIV infections. Biol Blood Marrow Transplant 2013;19:393-7.
10. Sun JY, Gaidulis L, Miller MM, et al. Development of a multiplex PCR-SSP method for Killer-cell immunoglobulin-like receptor genotyping. Tissue Antigens 2004;64:462-8.

11. Cooley S, Weisdorf DJ, Guethlein LA, et al. Donor selection for natural killer cell receptor genes leads to superior survival after unrelated transplantation for acute myelogenous leukemia. Blood 2010;116:2411-9.
12. Patel SH, Ismaiel OA, Mylott WR, Jr., Yuan M, Hauser KF, McRae M. Simultaneous determination of intracellular concentrations of tenofovir, emtricitabine, and dolutegravir in human brain microvascular endothelial cells using liquid chromatography-tandem mass spectrometry (LC-MS/MS). Anal Chim Acta 2019;1056:79-87.
13. Bennetto-Hood C, Tabolt G, Savina P, Acosta EP. A sensitive HPLC-MS/MS method for the determination of dolutegravir in human plasma. J Chromatogr B Analyt Technol Biomed Life Sci 2014;945-946:225-32.
14. Jensen MA, Li FS, van 't Wout AB, et al. Improved coreceptor usage prediction and genotypic monitoring of R5-to-X4 transition by motif analysis of human immunodeficiency virus type 1 env V3 loop sequences. J Virol 2003;77:13376-88.
15. Accelevir Dx. 2022. 2022, at https://www.accelevirdx.com/.)
16. Bruner KM, Wang Z, Simonetti FR, et al. A quantitative approach for measuring the reservoir of latent HIV-1 proviruses. Nature 2019;566:120-5.
17. Julg B, Dee L, Ananworanich J, et al. Recommendations for analytical antiretroviral treatment interruptions in HIV research trials-report of a consensus meeting. Lancet HIV 2019;6:e259-e68.
18. Simonetti FR, White JA, Tumiotto C, et al. Intact proviral DNA assay analysis of large cohorts of people with HIV provides a benchmark for the frequency and composition of persistent proviral DNA. Proc Natl Acad Sci U S A 2020;117:18692-700.
19. Calcagno A, Gonzalez de Requena D, Simiele M, et al. Tenofovir plasma concentrations according to companion drugs: a cross-sectional study of HIV-positive patients with normal renal function. Antimicrob Agents Chemother 2013;57:1840-3.
20. Guidelines for the Use of Antiretroviral Agents in Pediatric HIV Infection. 2023. (Accessed March 16, 2023, 2023, at https://clinicalinfo.hiv.gov/en/guidelines/pediatric-arv/tenofovir-af#_ENREF_2.)
21. Dolutegravir (Tivicay) Package Insert. FDA, 2020. (Accessed March 16, 2023, 2023, at https://rsc.niaid.nih.gov/clinical-research-sites/dolutegravir-tivicay-package-insert.)

22. Advanced Diagnostic Laboratories. 2022. (Accessed January 25, 2022, 2022, at https://www.nationaljewish.org/for-professionals/diagnostic-testing/adx/tests/darunavir,-level.)
23. Kaslow RA, Duquesnoy R, VanRaden M, et al. A1, Cw7, B8, DR3 HLA antigen combination associated with rapid decline of T-helper lymphocytes in HIV-1 infection. A report from the Multicenter AIDS Cohort Study. Lancet 1990;335:927-30.
24. Goulder PJ, Walker BD. HIV and HLA class I: an evolving relationship. Immunity 2012;37:426-40.
25. Thomas R, Apps R, Qi Y, et al. HLA-C cell surface expression and control of HIV/AIDS correlate with a variant upstream of HLA-C. Nat Genet 2009;41:1290-4.
26. Vollmers S, Lobermeyer A, Niehrs A, et al. Host KIR/HLA-C Genotypes Determine HIV-Mediated Changes of the NK Cell Repertoire and Are Associated With Vpu Sequence Variations Impacting Downmodulation of HLA-C. Front Immunol 2022;13:922252.
27. Bashirova AA, Thomas R, Carrington M. HLA/KIR Restraint of HIV: Surviving the Fittest. Annual Review of Immunology 2011;29:295-317.
28. Kordelas L, Verheyen J, Beelen DW, et al. Shift of HIV tropism in stem-cell transplantation with CCR5 Delta32 mutation. N Engl J Med 2014;371:880-2.
29. Symons J, Vandekerckhove L, Hütter G, et al. Dependence on the CCR5 coreceptor for viral replication explains the lack of rebound of CXCR4-predicted HIV variants in the Berlin patient. Clin Infect Dis 2014;59:596-600.
30. Yukl SA, Boritz E, Busch M, et al. Challenges in detecting HIV persistence during potentially curative interventions: a study of the Berlin patient. PLoS Pathog 2013;9:e1003347.
31. Kashuba AD, Dyer JR, Kramer LM, Raasch RH, Eron JJ, Cohen MS. Antiretroviral-drug concentrations in semen: implications for sexual transmission of human immunodeficiency virus type 1. Antimicrob Agents Chemother 1999;43:1817-26.
32. Imaz A, Martinez-Picado J, Niubó J, et al. HIV-1-RNA Decay and Dolutegravir Concentrations in Semen of Patients Starting a First Antiretroviral Regimen. J Infect Dis 2016;214:1512-9.

33. Imaz A, Niubó J, Cottrell ML, et al. Seminal Tenofovir Concentrations, Viral Suppression, and Semen Quality With Tenofovir Alafenamide, Compared With Tenofovir Disoproxil Fumarate (Spanish HIV/AIDS Research Network, PreEC/RIS 40). Clin Infect Dis 2019;69:1403-9.
34. Lê MP, Chaix ML, Raffi F, et al. Once-daily darunavir/ritonavir 400/100 mg in triple therapy: efficacy and penetration in seminal compartment in ANRS-165 DARULIGHT study. Br J Clin Pharmacol 2019;85:277-80.
35. Hütter G, Bodor J, Ledger S, et al. CCR5 Targeted Cell Therapy for HIV and Prevention of Viral Escape. Viruses 2015;7:4186-203.