Berlin, London, Dusseldorf and New York Patients

Session 1: Lets Talk about HIV Cure

Kumitaa Theva Das
Universiti Sains Malaysia

AIDS 2022

Affiliated Independent Event

Timothy Ray Brown

BERLIN PATIENT, FIRST PERSON CURED OF HIV

Lived with HIV-1 for about ten years.

On ART for four years (efavirenz, emtricitabine, tenofovir) with CD4+ T cell of 415/mm^3 and undetectable HIV-1 RNA.

AIDS 2022

Affiliated Independent Event

Long-term HIV Control

Towards an HIV Cure
IAS

CCR5 delta 32 stem cell transplantation

Diagnosed with AML

Was put on induction and consolidation chemotherapy.

HSCT

HSCT with CD34+ peripheral blood-stem cell from an HLA-identical (10/10) donor with homozygous CCR5Δ32 mutation.

Second HSCT

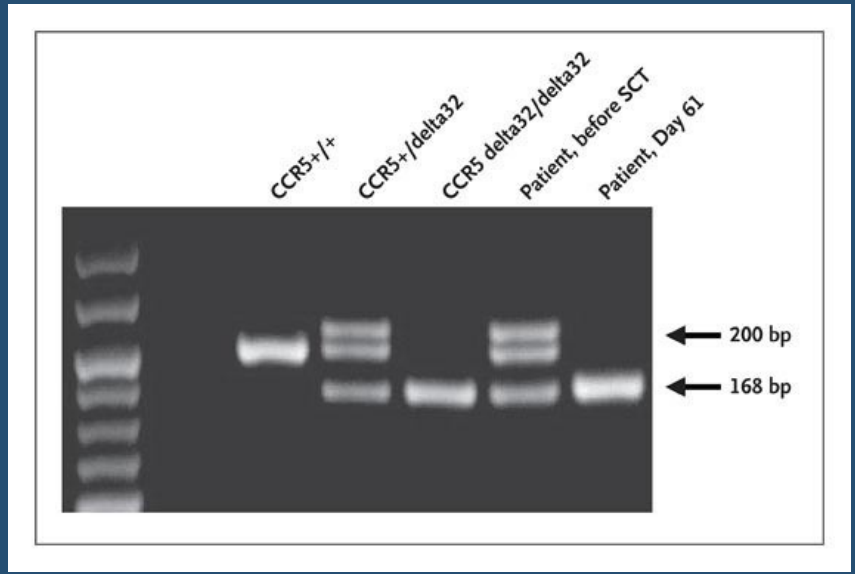
AML relapsed. Received HSCT again from the same donor, and whole-body irradiation, which led to complete eradication of AML.

No rebound

Post-transplantation, HIV-1 RNA and proviral DNA were not detectable. No virus rebound in the absence of ART.

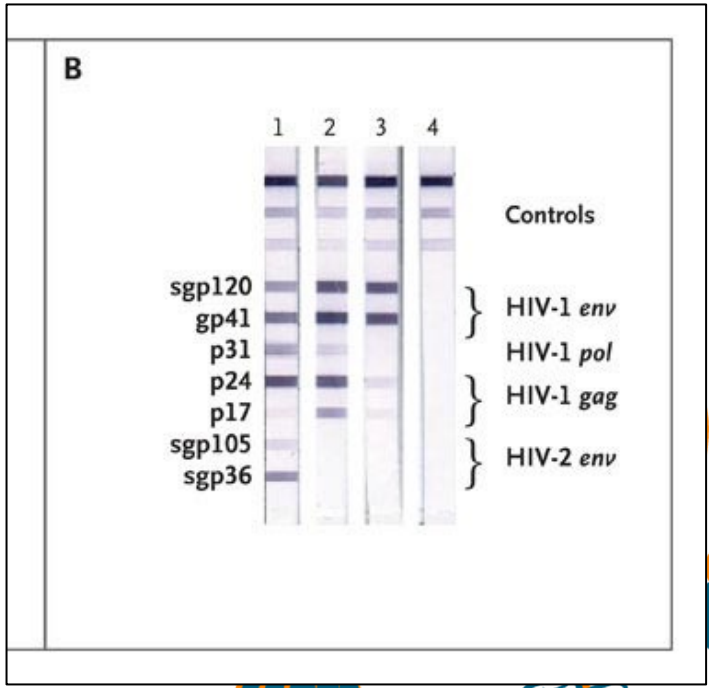
Genotyping of CCR5 alleles

After transplantation, with engraftment, the genotype changed to CCR5 delta32/delta32.



Cellular and humoral immune responses

Specific T-cell responses increased after transplantation, lost T-cell reactivity against HIV.

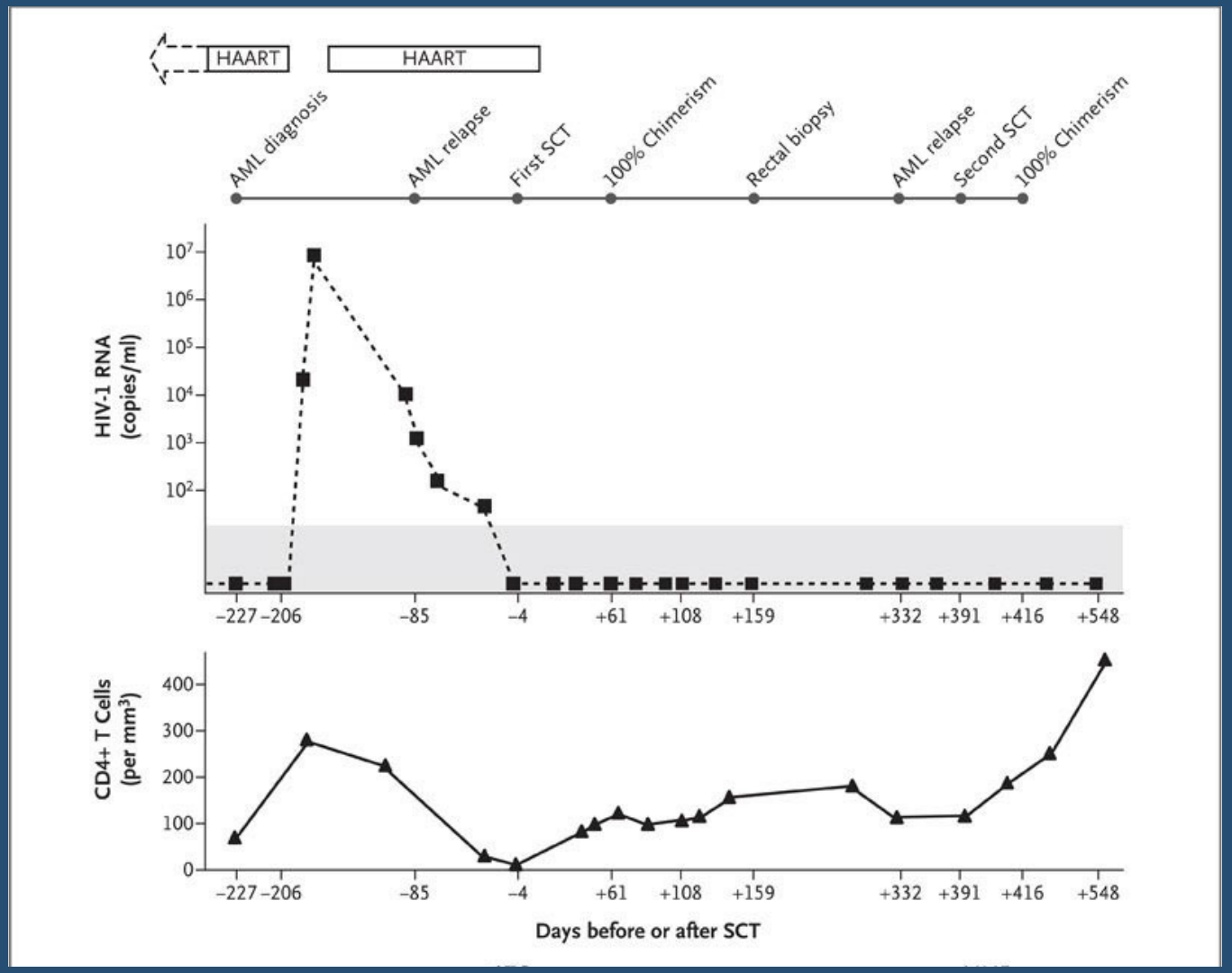


AIDS 2022

Affiliated Independent Event

Quantification of viremia

HIV-1 RNA was not detected in peripheral blood or bone marrow from when ART was discontinued, 1 day before SCT, until the follow-up of 548 days after SCT.



Hutter et al (2009)

AIDS 2022

Affiliated Independent Event

Adam Castillejo

LONDON PATIENT, SECOND PERSON CURED OF HIV

Lived with HIV-1 since 2003, with CD4+ T cell of 290/mm^3 and viral load of $1.8x10^5$ copies/ml.

ART regimen (tenofovir disoproxil fumarate, emtricitabine, efavirenz) was initiated in 2012.

AIDS 2022

Affiliated Independent Event

Long-term HIV Control

Towards an HIV Cure
IAS

CCR5 delta 32 stem cell transplantation

Diagnosed with NSHL

Was put on chemotherapy and salvage chemotherapy.

HSCT

Donor carried CCR5Δ32 mutation with one allelic mismatch at HLA-B. He received the graft and was on a conditioning regimen.

GVHD and ART

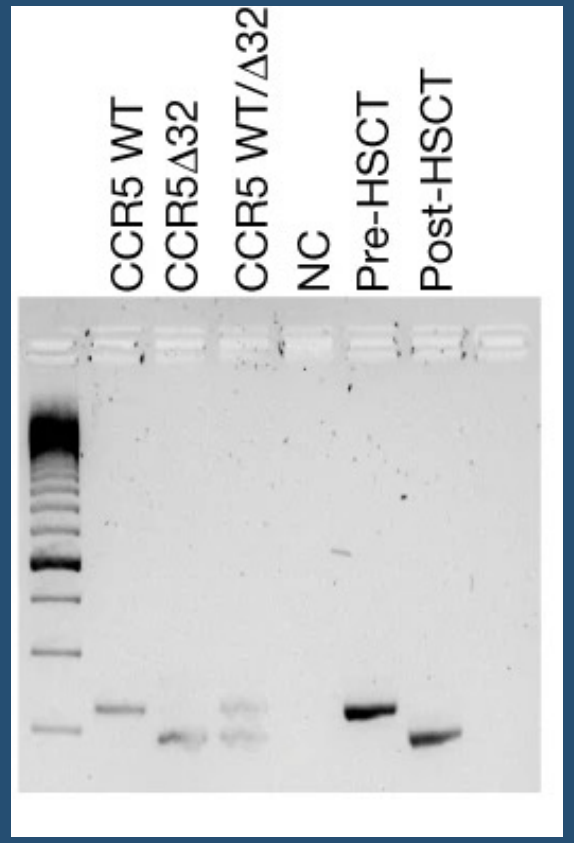
Cyclosporine-A and methotrexate were administered to prevent GVHD. ART regimen was continued throughout the procedure.

No rebound

Full donor chimerism was achieved. ART interruption was started at day 510. Viral load, HIV-1 DNA, and HIV-1 RNA were undetectable.

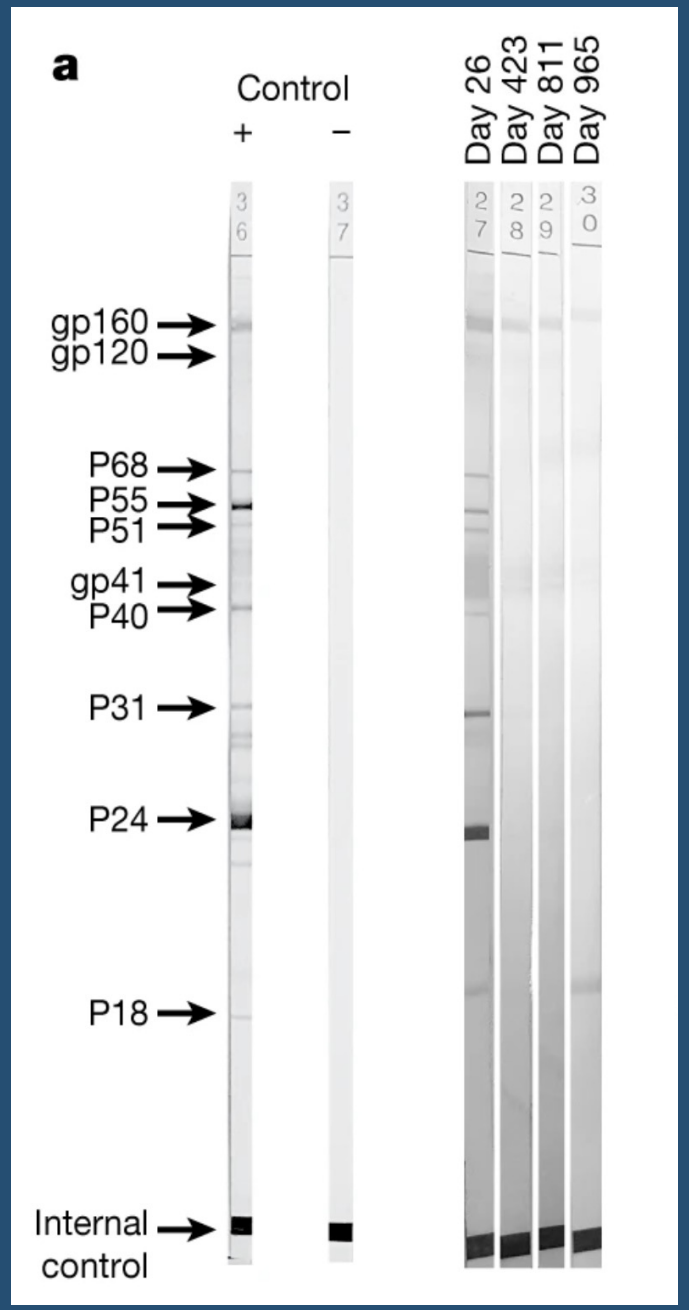
Genotyping of CCR5 alleles

After transplantation, with engraftment, the genotype changed to CCR5Δ32.



Humoral response

Western blot analysis demonstrated loss of antibodies post-transplant.

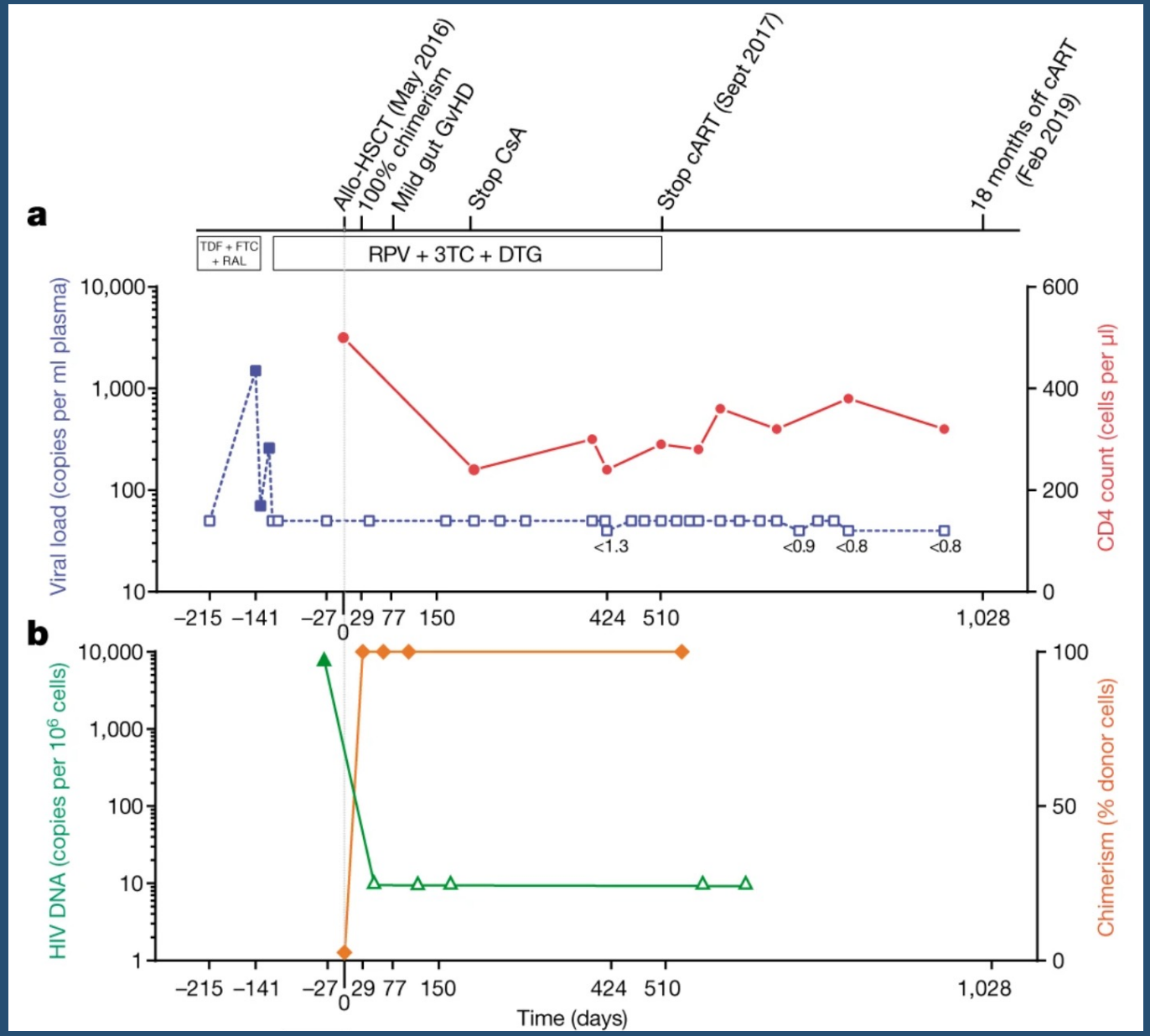


AIDS 2022

Affiliated Independent Event

Quantification of viremia

HIV-1 RNA was not detected, and there was a reduction in the reservoir. Full-donor chimerism was achieved.

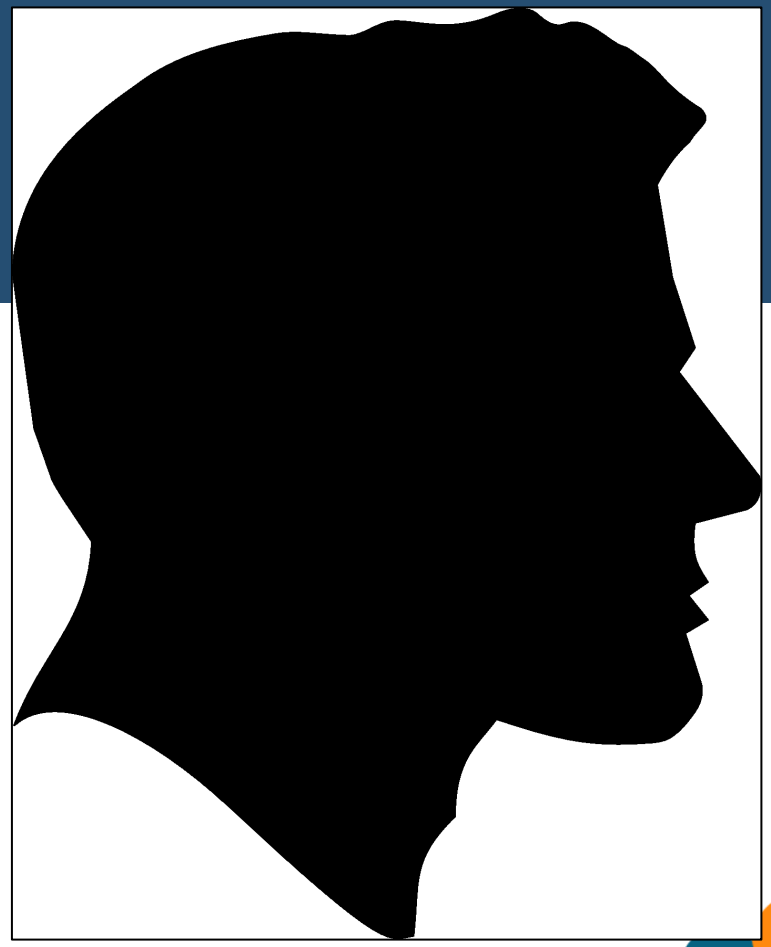


Gupta et al (2019)

AIDS 2022

Affiliated Independent Event

Dusseldorf Patient



DUSSELDORF PATIENT, IN REMISSION

Had an HIV-1 viral load of $2.9x10^4$ copies/ml.

ART regimen (tenofovir disoproxil fumarate, emtricitabine, darunavir) was initiated in 2011 and resulted in a decreased viral load.

AIDS 2022

Affiliated Independent Event

Long-term HIV Control

Towards an HIV Cure
IAS

CCR5 delta 32 stem cell transplantation

Diagnosed with AML

Was put on chemotherapy resulting in remission.

HSCT

Received HSCT from a fully matched (10 out of 10) female CCR5Δ32 donor.

GVHD and ART

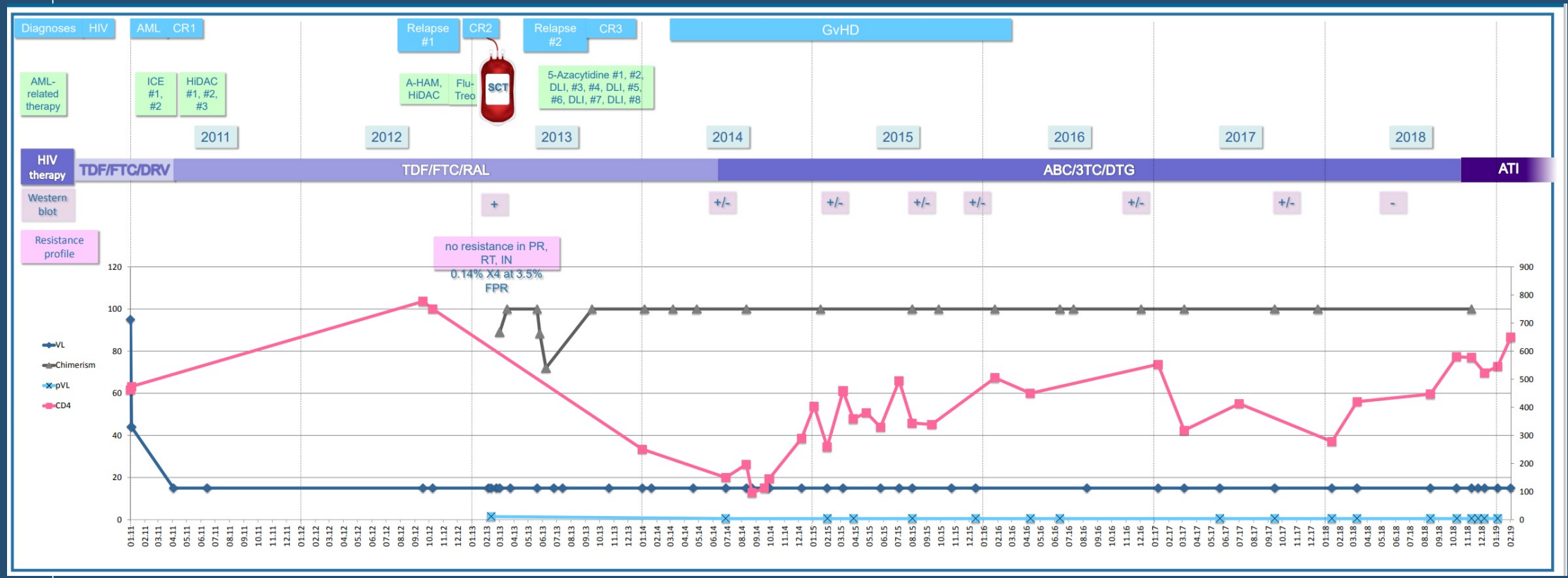
Developed GVHD within two years. ART regimen was changed and he remained on ART with undetectable viral load.

No rebound

CCR5-negative HIV-CTL. ART interruption was initiated in 2018, and no rebound occurred.

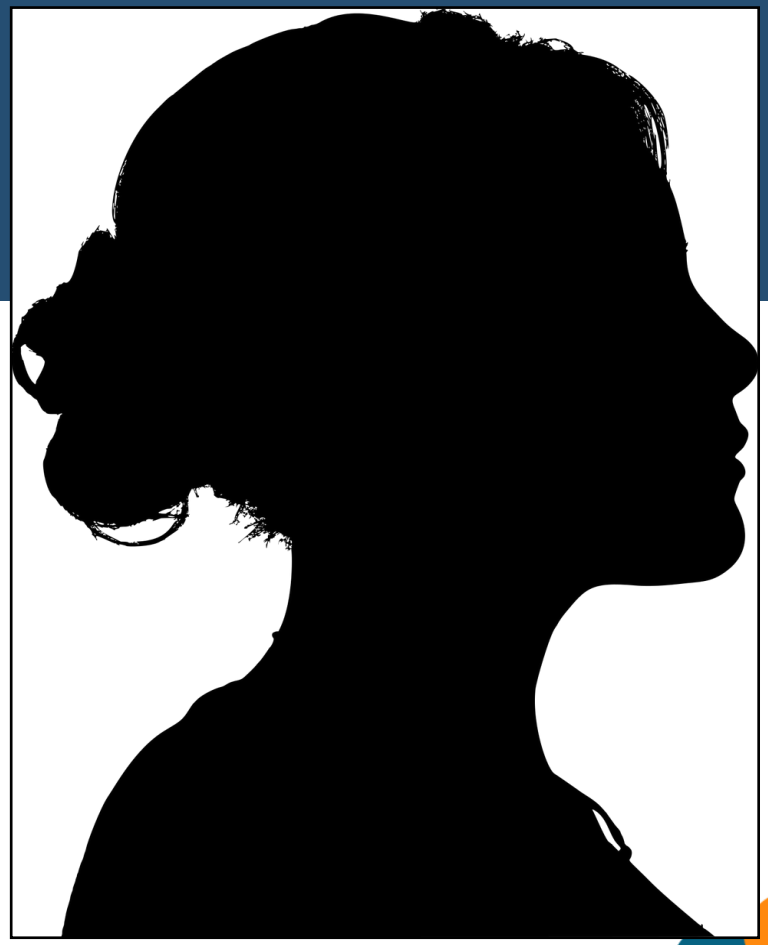
Quantification of viremia

HIV-1 RNA was not detected in PBMC, rectum, ileum and bone marrow from when ART was discontinued until the end of follow-up.



Jensen et al (2019)

New York Patient



NEW YORK PATIENT, THIRD PERSON CURED OF HIV

The mixed race woman lived with HIV-1 since 2013, with CD4+ T cell of 1003/mm^3 and viral load of $1x10^6$ copies/ml.

ART regimen (tenofovir, emtricitabine and raltegravir) was initiated in 2013 and resulted in an undetectable viral load.

AIDS 2022

Affiliated Independent Event

Long-term HIV Control

Towards an HIV Cure
IAS

CCR5 delta 32 haploidentical cord transplantation

Diagnosed with AML

Was put on induction chemotherapy and whole body irradiation.

Haplo cord transplant

Combined CCR5Δ32 cord blood cells with partially matched (5 out of 8) donor stem cells from her relative without the mutation.

No GVHD and ART

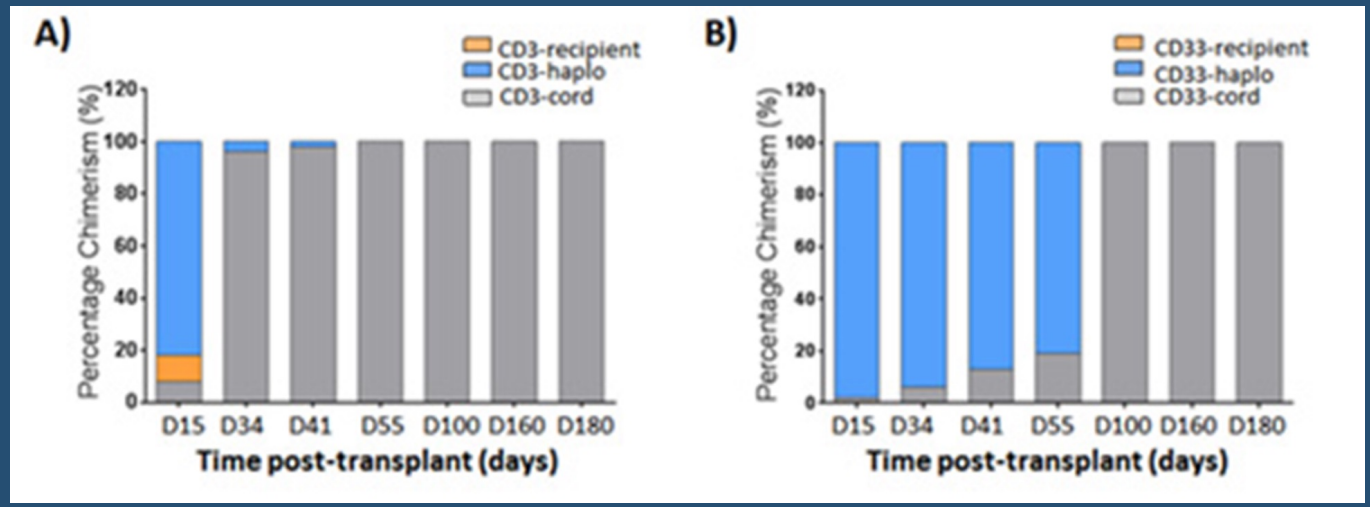
Did not develop GVHD. ART regimen was changed and she remained on ART with undetectable viral load.

No rebound

Undetectable HIV-1. CCR5-negative HIV-CTL. No virus rebound in the absence of ART, even with X4-tropic virus.

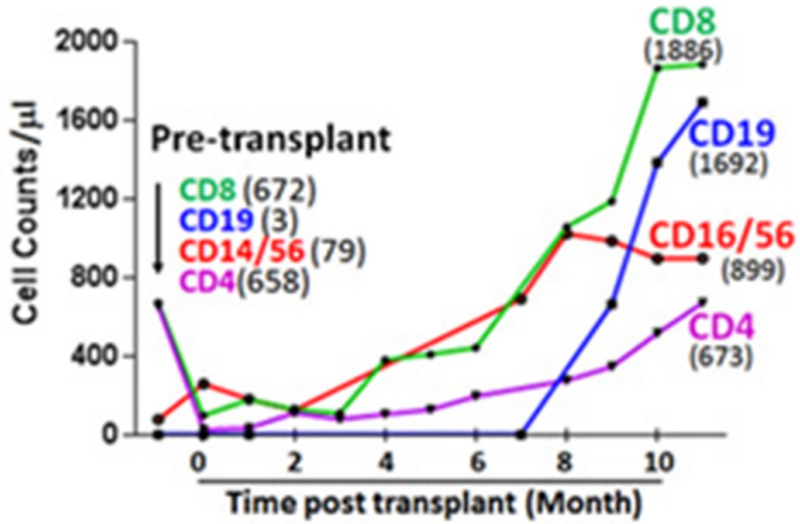
Chimerism dynamics

Post allogeneic stem cell transplant, by day 100, both CD3 and CD33 became 100% cord blood donor.



Immune reconstitution

Post allogeneic stem cell transplant, there was a huge increase in T cell subset, B cell, and NK cell recovery post-transplant by month 10.



Hsu et al (2018)

AIDS 2022

Affiliated Independent Event

Key differences

01

Conditioning

London patient received reduced-intensity chemotherapy, while Berlin and New York patient received total body irradiation.

02

GVHD

London patient had GVHD and Berlin patient had severe GVHD, while New York patient did not have GVHD.

03

HSCT vs Haplo cord

London patient received single HSCT, Berlin patient received double HSCT, while New York patient received haplo cord transplant.

Conclusion

01

ART treatment

When did they start ART? Does ART switching affect success? When should ART be interrupted?

02

Safety

Are these methods safe for all PLWH? What if they did not have a condition like AML? Would they be protected against X4-tropic virus?

03

HIV Cure

What were the key factors to this cure? How does this compare to other cure strategies?

Acknowledgements

Towards an HIV Cure
IAS

USM
UNIVERSITI SAINS MALAYSIA

UNIVERSITY OF MALAYA

UMS
UNIVERSITI MALAYSIA SABAH

IAS

ISID
INTERNATIONAL SOCIETY FOR INFECTIOUS DISEASES

ESCMID
EUROPEAN SOCIETY OF CLINICAL MICROBIOLOGY AND INFECTIOUS DISEASES

UNIVERSITY OF OXFORD
DOMINUS ILLVMINATIO MEA

THE UNIVERSITY OF CALIFORNIA
LET THERE BE LIGHT
DAVIS

AIDS 2022

Affiliated Independent Event