*Corresponding author: Dr Olivia ZAEGEL-FAUCHER - Olivia.ZAEGEL@ap-hm.fr

Absence of viral rebound without antiretrovirals after CCR5Δ32/Δ32 allogeneic hematopoietic stem cell transplantation: A new case of a potential cure of HIV?

Zaegel-Faucher Olivia, MD,[1] Boschi Céline, PharmD, PhD,[1,2,3] Benkouiten Samir, MPH, PhD,[1] Laroche Hélène, MD,[1] Dos Santos Maëva Cacilda, MD,[1] Motte Anne, MD,[1,2] Izadifar-Legrand Faezeh, MD,[4] Olive Daniel, MD, PhD,[5] Colson Philippe, MD, PhD,[1,2,3] Bregigeon-Ronot Sylvie, MD,[1]

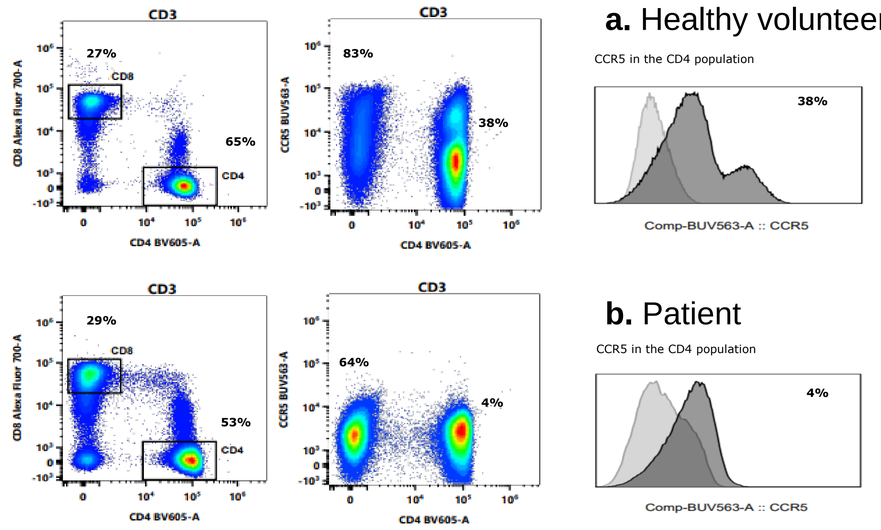
[1]Assistance Publique-Hôpitaux de Marseille (AP-HM), Marseille, France. [2]IHU Méditerranée Infection, Marseille, France. [3]Institut de Recherche pour le Développement (IRD), Microbes Evolution Phylogeny and Infections (MEPHI), Aix-Marseille Université, Marseille, France. [4]Institut Paoli-Calmettes, Marseille, France. [5]Equipe Immunité et Cancer, Centre de Recherche en Cancérologie de Marseille (CRCM), INSERM U1068, CNRS UMR7258, Institut Paoli-Calmettes, Aix-Marseille Université, UM 105, 13009 Marseille, France.

BACKGROUND

Six cases of HIV-1 remission have been reported to date, five of them after CCR5Δ32/Δ32 allogeneic hematopoietic stem cell transplantation (aHSCT).

We report a woman in her 50s diagnosed with HIV-1 in 1999, who initiated early antiretroviral therapy (ART) and exhibited undetectable HIV loads in 2010. She developed acute myeloid leukemia (AML) in February 2020 and had a splenectomy 2 months later due to subcapsular hematoma rupture. She received CCR5Δ32/Δ32 aHSCT from an HLA-mismatched (HLA-A) donor in July 2020 after a Baltimore-based conditioning (fludarabine 150 mg/m2, cyclophosphamide 29 mg/kg and total body irradiation 200 cGy) and GvHD prophylaxis (cyclosporin A, mycophenolate mofetil, and cyclophosphamide (100 mg/kg) on days three and four post-aHSCT). Full donor chimerism was obtained after three donor lymphocyte infusions (DLI). She developed acute cutaneous GVHD in October 2020, quickly resolved. Pre-aHSCT, she was on Tenofovir DF/FTC and Raltegravir, CD4 count were 250 cells/mm3, HIV-1 DNA was 32 copies/10^6 PBMCs, and HIV-1 RNA was undetectable (<20 copies/mL).

Post-aHSCT, analysis of CCR5 expression showed low expression on CD4 cells, whereas CCR5 was highly expressed on CD8 cells (**Figure 1**). No HIV-1 DNA or RNA were detected in circulating CD4+ cells or plasma. Treatment interruption (TI) occurred in October 2023, 39 months post-aHSCT, while she was on Abacavir/3TC and Raltegravir therapy.



CCR5 expression analysis showing low expression on CD4 cells, whereas CCR5 is highly expressed on CD8 cells.

Figure 1. CCR5 typing

MATERIALS AND METHODS

Post-TI samples were collected every week for 2 months, then once a month. HIV-1 RNA/DNA were measured using NeuMoDx (Qiagen)/Xpert (Cepheid) and generic (Biocentric) assays, respectively, and by ultrasensitive (US) assays for some samples. HIV-1 RNA/DNA sequencing was performed by Sanger or Next-Generation Sequencing (NGS) (Illumina) technologies with quasispecies analysis. HIV-1-specific antibodies were detected by Western blot analysis (MP Diagnostics) on sequential samples. Standard HIV-1 co-culture and cell permissiveness to R5 HIV-1 strains were assayed using in-house protocols.

RESULTS

Samples were collected at 18 post-TI time points.

No antiretroviral drugs were detected in plasma samples at 7 time points post-TI.

Twelve months post-TI, CD4 count and percent were 1289 cells/mm^3 and 28.2%, respectively, and CD4:CD8 ratio was 0.67.

No HIV-1 DNA or RNA were detected in circulating CD4+ cells or plasma, even using US assays (**Figure 2**).

HIV-1 antibodies slightly declined over time post-aHSCT (**Figure 3**).

HIV-1 co-culture was negative and host cells were non-permissive for R5-tropic HIV-1 strains while preaHSCT HIV genotypic tropism tests using NGS showed the presence of an R5-tropic virus population without minority X4-tropic variants.

HIV remission has been sustained to date, with no significant clinical events, except pneumococcal meningitis in November 2023, in a context of splenectomy and patient's refusal of prophylaxis.

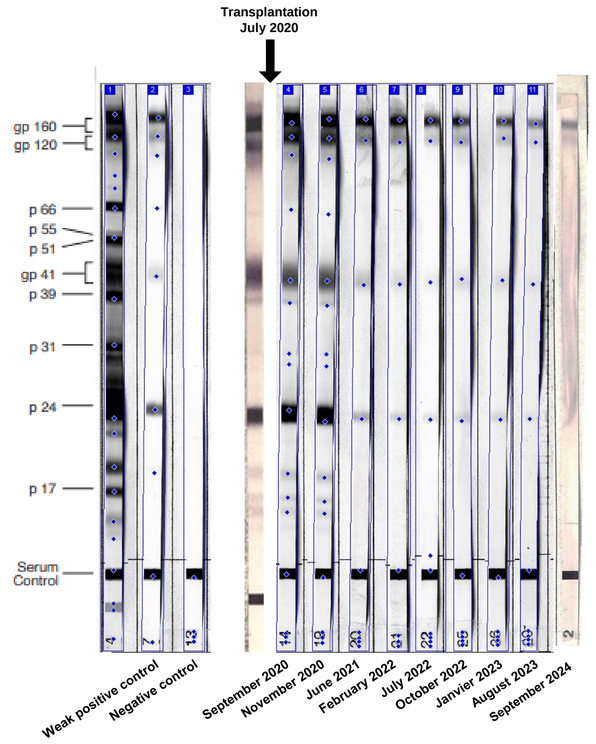


Figure 3. Sequential Western Blots

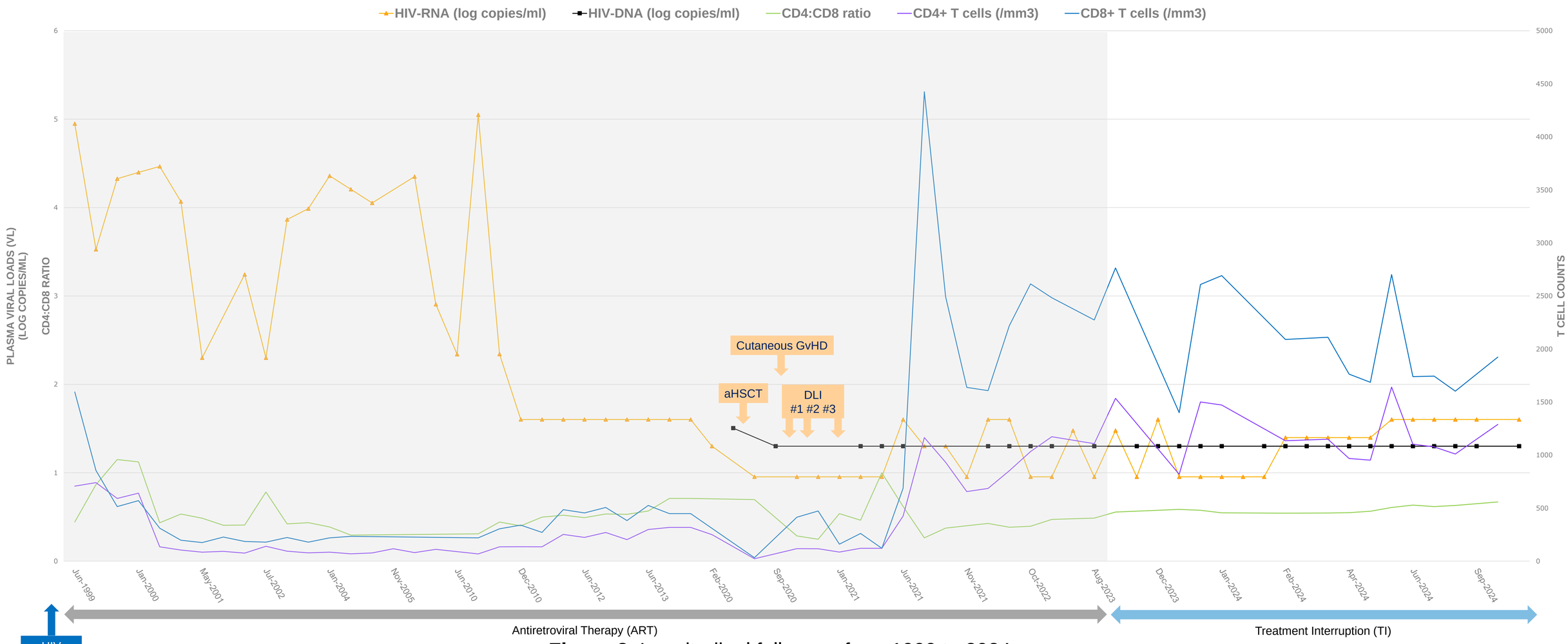


Figure 2. Longitudinal follow-up from 1999 to 2024

CONCLUSIONS

We report a new case of remission and possible HIV-1 cure in a woman with no evidence of HIV-1 RNA rebound and no detectable HIV-1 DNA at twelve months post-TI and 51 months post-CCR5Δ32/Δ32 aHSCT for AML.

Presented at HIV DRUG THERAPY
10-13 November 2024