IAS 2023
23 – 26 July

TITLE

Absence of viral rebound for 18 months without antiretrovirals after allogeneic hematopoietic stem cell transplantation with wild-type CCR5 donor cells to treat a biphenotypic sarcoma

PRESENTER

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BACKGROUND: Durable HIV-1 remission after antiretroviral treatment (ART) discontinuation has been reported for 5 individuals receiving allogeneic hematopoietic stem cell transplant (aHSCT) from CCR5?32 homozygous donors. We report here a Caucasian male (Icistem-34), diagnosed with HIV-1 in 1990 and on continuous suppressive-ART since 2005. In 2018, he received chemotherapy followed by aHSCT from an unrelated HLA-matched (9/10) wild-type CCR5 donor to treat a biphenotypic sarcoma. ART was discontinued in November 2021. His viral load has remained undetectable for 18 months so far.
METHODS: Samples, pre-aHSCT, pre and/or post treatment interruption (TI), were analyzed for HIV RNA, HIV DNA, antiretrovirals, HIV-1 antibodies, NK and T cells phenotype, and HIV/CMV T-cell responses. Intact proviral DNA analyses (IPDA), tests of viral production by purified CD4+ T cells and their susceptibility to HIV were performed post-aHSCT.
RESULTS: Ultrasensitive HIV RNA (4 copies/ml) and HIV DNA (457 and 1096 copies/million CD4 cells in blood and bone marrow) were detected before aHSCT. The virus was predicted R5. Full chimerism was achieved within a month post-aHSCT. Acute hepatic graft vs host diseases (GVHD) occurred soon after aHSCT, and was treated with corticosteroid/calcineurin inhibitor. Chronic hepatic GVHD occurred 8m after aHSCT and was treated with ruxolitinib, which was transiently discontinued but had to be resumed due to GVHD relapse. Standard plasma viremia remained undetectable after aHSCT, ultrasensitive RNA dropped to undetectable values. Proviral DNA also decreased significantly, despite low levels (4 to 40 copies/million cells) being detected sporadically post-aHSCT, including defective but not intact HIV DNA by IPDA. No virus was amplified from in vitro stimulated CD4+ T cells post-TI. Cells remained susceptible to HIV-1 in vitro. ART levels were undetectable post-TI except coinciding with two episodes of event-driven "PreP" (4 pills) at M2 and M12 post-TI. HIV-1 antibodies slightly declined since aHSCT. No HIV-specific T cell responses were detected post-TI.
CONCLUSIONS: We report an individual with HIV-1 who at 18m post-TI, 57m post-aHSCT with cells from a wild-type CCR5 donor, has no evidence of HIV-1 RNA rebound or replicating virus. These results suggest that HIV remission could be achieved in some cases in the context of aHSCT with wild-type CCR5.

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