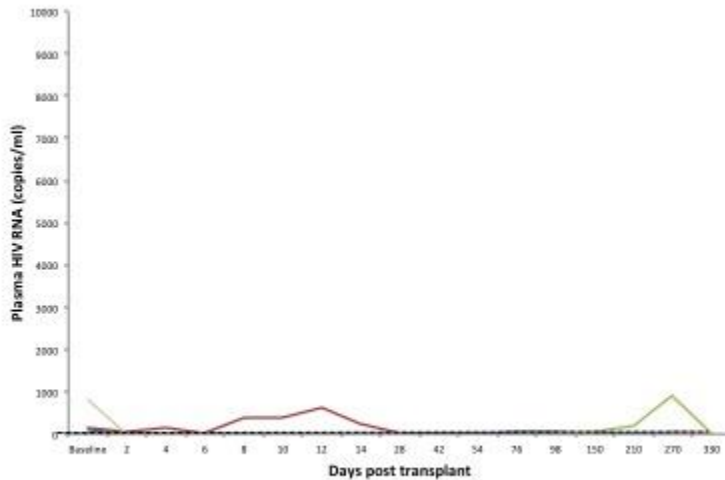


ART therapy during BMT is not a double edge sword

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Of fifteen HIV-infected persons who underwent hematopoietic cell transplantation (HCT) on combination antiretroviral therapy, ten had sustained virologic suppression, while five had low-level HIV RNA, which was quickly suppressed upon therapy modification. Each color represents a different patient. The dotted line represents the limit of detection.

Image provided by Dr. Christine Johnston.

Antiretroviral therapy (ART) has deeply transformed the outcome and management of HIV infection. Thanks to its ability to control viral replication and CD4+ T cell depletion, ART introduction has changed the HIV epidemic from a fatal disease to a chronic infection. As such, other health conditions can emerge as a result of longer survival and aging, as an effect of either HIV infection or prolonged therapy. Blood malignancies, such as non-Hodgkin lymphomas, leukemias and myelomas disproportionately affect HIV-infected subjects. While at the beginning of the HIV epidemic bone marrow transplantation (BMT) was not appropriate for HIV-infected subjects for the possible recrudescence of viral replication, the advent of ART changed the scenario. In fact, outcomes of autologous and, to a certain extent, of allogenic bone marrow transplantations have a similar success rate in HIV infected and uninfected subjects. Furthermore, the only documented HIV cure occurred in a subject that received bone marrow from an HIV-resistant donor, carrying the mutation that causes a lack of expression of CCR5, co-receptor for HIV infection. Although the situation was pretty unique, the transplantation was successful, the patient has still undetectable viral load and is cancer-free (See the featured story of the [Berlin patient](#)).

The conundrum now to be faced is whether the ART regimen should be maintained during the transplantation. In fact, while maintaining the anti-retroviral regimen could be beneficial by inhibiting

viral expansion and infection of the transplanted cells, it could also create interactions with chemotherapy or immunosuppressive drugs. Drs. Christine Johnston (Vaccine and Infectious Disease Division) and Ann Woolfrey (Clinical Research Division) from the Fred Hutch, together with a group of scientists affiliated with Fred Hutch and University of Washington, addressed this question by looking at the outcomes of 15 bone marrow transplantats carried on HIV-positive subjects receiving ART. The study was recently published in the journal *Biology of Blood and Marrow Transplantation*.

The observation of the outcomes was informative on different aspects of the BMT procedure. First of all, ART was well tolerated in all patients: in eight cases, ART was uninterrupted for the duration of the procedure, while few doses were missed by the remaining patients due to side effects of the drugs. ART regimens maintained the viral RNA plasma load below the detection limit in all but five patients, some of whom required a modification in the treatment, which promptly decreased the viral load to undetectable levels for an average time of 259 days. Importantly, the treatment did not modify the transplantation course, and no adverse interactions between ART and either chemotherapy or immunosuppressive drugs were observed. Four patients were cancer-free at the end of the study, while malignant disease relapse was observed in eleven other patients.

Even though the study describes the effects of maintaining ART during bone marrow transplantation only in 15 participants, the results strongly support its use, so much that the authors have now outlined recommendation for ART use in HIV-infected individuals undergoing transplantation. This study shed light on a central question and will be of fundamental importance for the clinical management of HIV-infected subjects affected by blood malignancies. Dr. Johnston said: "This work demonstrates that combination ART, which is selected to minimize drug-drug interactions and maximize tolerability can be safely given to persons with HIV infection during hematopoietic cell transplant (HCT). ART maintains HIV suppression without introduction of resistance during the peri-transplant period. These data have implications not only for HIV-infected persons undergoing HCT for hematologic malignancies, but may also be relevant for strategies which are being investigated to "cure" HIV."

[Johnston C, Harrington R, Jain R, Schiffer J, Kiem H-P, Woolfrey A.](#) 2016. Safety and efficacy of combination antiretroviral therapy in HIV-infected adults undergoing autologous or allogeneic hematopoietic cell transplant for hematologic malignancies. *Biol Blood Marrow Transplant*. 22(1):149-56. doi: 10.1016/j.bbmt.2015.08.006.

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