Optimized antiretroviral therapy during allogeneic hematopoietic stem cell transplantation in HIV-infected individuals

A. Cash1, A. Capollemi1, D. Xu1, H. Michugh1, O. Laeyendecker1-2, S. Saksanen1, L. Tony1, C. Bullen1, C. Pohlmeyer1, P. Pham1-3, J. Lal1, J. Gallant4, R.F. Siliciano1,2, C. Flexner4, K. Pratz4, M. Levis4, R. Jones4, Y. Kasamon4, R. Ambinder4, C.M. Durand1,4

1Johns Hopkins University, Department of Medicine, Baltimore, United States, 2Howard Hughes Medical Institute, Baltimore, United States, 3Sidney Kimmel Cancer Center, Baltimore, United States, 4Sidney Kimmel Cancer Center (P30CA006973) and the Howard Hughes Medical Institute.

INTRODUCTION

Due to improvements afforded by ART, HIV+ patients receive standard of care treatment for hematologic malignancies, and this includes allogeneic hematopoietic stem cell transplantation (alloHSCT). Components of alloHSCT include cytotoxic therapy and allogeneic or graft versus host/tumor (GVH) effects. The GVH effect refers to the process where donor immune cells recognize recipient hematopoietic-derived cells as other and kill and replace them.

RESULTS

Primary endpoints included adverse events (AE) from ENF and respectively after alloHSCT, no HIV was detected in peripheral blood. Cells per million (IUPM) by viral outgrowth assay were also measured. It is difficult to maintain ART during alloHSCT. ART interruptions are associated mucositis and vomiting compromising oral ART delivery. Here mechanism is shown in Figure 1, with reduction or elimination of HIV latency and infected memory T cells from 4 to 8 weeks after alloHSCT.

HYPOTHESIS

Optimized ART can be well tolerated by HIV+ adult patients receiving chemotherapy and alloHSCT for hematologic malignancies. Furthermore, the combination of the allogeneic effect and continuous ART can reduce or completely eradicate HIV reservoirs.

METHODS

We evaluated the safety and feasibility of continuing ART during alloHSCT in HIV+ individuals with hematologic malignancy. Optimized ART included: 1) Avoidance of PIs to minimize drug interactions 2) ART changes for organ dysfunction 3) Subcutaneous enfuvirtide (ENF) during posttransplant cyclophosphamide and if oral ART was not tolerated. Primary endpoints included adverse events (AE) from ENF and maintenance of ART through day 60. Donor chimerism and HIV infected cells per million (IUPM) by viral outgrowth assay were also measured.

DISCUSSION

During alloHSCT, with optimized ART, it is feasible to maintain ART but regimen changes are common due to drug interactions and organ dysfunction. ENF is a well tolerated alternative to oral ART. Newer, non oral and long acting antiretroviral agents may offer the same benefit. Notably, Patient 3 experienced viral rebound and meningococcal meningitis after self-discontinuing ART despite 100% donor chimerism (see abstract #MOPDA0105 for a detailed case report). At early time points, in patients with mixed chimerism, HIV persists in the VOA, but further reports are needed over time to determine the size of the reduction of the HIV reservoir and the long term cure strategy implications.

CONCLUSIONS

There is a growing need for alloHSCT in the HIV+ population. This strategy has cure implications for HIV+ individuals with hematologic malignancy. Further studies are needed over time to determine whether alloHSCT could be a successful cure strategy in combination with other potential strategies including latency reversing agents, or therapeutic vaccination.

Works Cited

1. Antiretroviral Therapy Cohort Collaboration (2010) CID
2. Nishioka M et al. (2011) JCI
3. Huttel O et al. (2009) NEJM

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