Can You Put a Price on a Cure for HIV/AIDS?

Iris Liu, MSc[a]

KEYWORDS: *HIV treatment, ethics, cost, CCR5, bone marrow transplant*

By the end of 2002, 22 million people were estimated to have died from secondary infections as a result from being infected by Human Immunodeficiency Virus (HIV).[1] In 2007, 33 million people were living with HIV/AIDS and 2 million people succumbed to the disease.[2] There are currently no vaccines available, and those that are under development are fraught with complications. For example, in 2007, a large scale clinical trial had to be discontinued because of safety concerns.[3]

This article will review and comment on a recent case study published in *The New England Journal of Medicine* (NEJM), by Hutter and colleagues, describing a patient who received a bone marrow transplant (BMT) that successfully conferred resistance to HIV.[4] While this type of a therapeutic intervention holds much promise, a number of bio-ethical and economic concerns are raised. How much are we willing to spend to treat HIV victims in the midst of a global epidemic?

The infection mechanism of HIV is well understood and majority of the current treatments and research invest in blocking this pathway at multiple steps in the infection process. Normally, the virus requires two receptors in order to enter cells: chemokine receptor 5 (CCR5) and CXC chemokine receptor 4 (CXCR4). Importantly, it has been reported that individuals with mutations in the CCR5 gene are resistant to HIV. Hutter and colleagues describe a patient who was seropositive for HIV. When he subsequently developed acute myeloid leukemia, he was treated for it with a bone marrow transplant from a donor who carried a homozygous mutation for the CCR5 gene. By replacing the patient's bone marrow with one that did not express CCR5, this group hoped to confer "resistance" towards the virus in this patient. Remarkably, over the next 20 months, both blood and rectal biopsy specimens had non-detectable levels of HIV.[4] This finding provided strong evidence for a new modality in HIV treatment: bone marrow transplant (BMT). Typical treatments have been pharmacologic blockade of the HIV virulence pattern, but now BMT might be an effective alternative.

[a] Island Medical Program 2012, University of British Columbia
Correspondence: Iris Liu, irisliu@interchange.ubc.ca

The concept of conferring HIV infection resistance to individuals through bone marrow raises a number of ethically contentious issues. First,where would this supply of CCR5-mutation cells be harvested from? This mutation is found in only 1 – 3% of the European population. Extensive screening programs would have to be established; what incentives would there be for volunteers to step forward?[5] Even if individuals were to consent to the donation, the ethics around selecting worthy and appropriate recipients, amongst the masses of victims infected with this disease, would likely be even more complicated. HIV is a disease that afflicts both the wealthy and the impoverished. What controls would there be to ensure equal access a costly, but potentially life-saving, intervention?

> "Is bone marrow transplant an ethically responsible treatment for HIV?

Even if the ethical considerations in selecting donors and recipients were to be resolved, the financial burden for this type of therapy would far exceed the current status quo. In British Columbia, antiretroviral drugs (ARVs) are provided to patients at no cost.[6] The costs are absorbed by the publicly-funded health care system at approximately $2,700 per year, per patient, depending on the drug regimen.[7] Assuming that a patient is diagnosed with AIDS at 25 years of age, and will require ARVs for the next 50 years (an assumption for normal lifespan), this brings the total cost of treatment to $135,000. This does not factor in other medical expenses such as physician visits, laboratory tests, and additional medications for treatment of secondary infections. Meanwhile, the average cost for a BMT in the United States can range from $150,000 to $200,000.[8] Considering, however, that the price for treatments can vary with time (e.g. in the 1980's, the cost of ARVs was $10,000 per year[8]), the price difference is not large enough to determine whether this is a good treatment plan for HIV.

One also needs to consider the safety of such a treatment option. BMT, conducted on a large-scale, is associated with significant health risks and complications. Current statistics

reveal the mortality rate for BMT to be 17% mortality overall, but worse in compromised patients. For example, there is a 30% mortality rate for BMT with cancer. Further, BMT is associated with numerous, and severe complications, including interstitial pneumonitis, acute graft versus host disease, and graft rejection.[10] In fact, Hutter and colleagues themselves question the feasibility of BMT as a treatment option because of the inherent risks.

Yet, is BMT an ethically responsible treatment for HIV? Suppose a patient is informed about these dangers, but still requests it as a treatment. Who should be responsible for paying? More importantly, would it be ethical to provide such treatment given the risks and costs involved? Those who favour patient autonomy may argue that this would be an ethical decision. Those who favour the principle of nonmaleficence may argue that this is not a viable option because of the harms associated with the BMT procedure. While we are in the early stages of research in BMT as a possible treatment option for HIV infection, the questions raised in this article will become increasingly important as more sophisticated and risky treatment options become available.

In conclusion, the multitude of ethical issues raised by this NEJM case report warrant further discussion on a scientific and ethical front.

REFERENCES

1. WHO. Global summary of the AIDS epidemic, December 2007. 2007 [cited 2009; Available from: http://www.who.int/hiv/data/en/]
2. NIAID. HIV vaccines: where we are and where we're headed. 2008 [cited 2009; Available from: http://www3.niaid.nih.gov/topics/vaccines/research/hivVaccines.htm]
3. Hutter G, Nowak D, Mossner M, Ganepola S, Mussig A, Allers K, et al. Long-term control of HIV by CCR5 Delta32/Delta32 stem-cell transplantation. N Engl J Med. 2009 Feb 12; 360(7):692-8.
4. van Marle G, Gill MJ, Kolodka D, McManus L, Grant T, Church DL. Compartmentalization of the gut viral reservoir in HIV-1 infected patients. Retrovirology. 2007;4(87):87.
5. Berger EA, Murphy PM, Farber JM. Chemokine receptors as HIV-1 coreceptors: roles in viral entry, tropism, and disease. Annu Rev Immunol. 1999;17:657-700.
6. HIV/AIDS BCCfEi. B.C. HIV/AIDS Drug Treatment Program. [cited; Available from: http://www.cfenet.ubc.ca/content.php?id=11]
7. Worldbank. Cost of providing anti-retroviral therapy. [cited 2009; Available from: http://www.worldbank.org/aidsecon/arv/floyd/whoarv-webp3.htm]
8. Transplant NBM. Resource Guide for Bone Marrow/Stem Cell Transplant. [cited 2009; Available from: http://www.nbmtlink.org/resources_support/rg/rg_costs.htm]
9. Schoofs M. A Doctor, a Mutation and a Potential Cure for AIDS. [cited 2009; Available from: http://online.wsj.com/article/SB122602394113507555.html]
10. Bacigalupo A, Oneto R, Bruno B, Soracco M, Lamparelli T, Gualandi F, et al. Early predictors of transplant-related mortality (TRM) after allogeneic bone marrow transplants (BMT): blood urea nitrogen (BUN) and bilirubin. Bone Marrow Transplant. 1999 Sep;24(6):653-9.