Strategies for a Cure Reviewed in Vienna

July 19, 2010 By Tim Horn

True to tradition, several world-renowned key opinion leaders opened this year's International AIDS Conference, being held July 18 to 23 in Vienna, with a detailed review of the state of the HIV epidemic. Among the speakers was Sharon Lewin, FRACP, PhD, director of the infectious diseases unit at The Alfred Hospital in Melbourne, Australia, who made a provocative call to move full-steam ahead with strategies to cure HIV.

Though researchers, health care providers and people living with HIV—working in tandem—have made considerable progress in the prevention, care and treatment of the virus, Lewin noted that life expectancy following HIV infection, even under the best of circumstances, remains below that of those who are HIV negative. She also noted that antiretroviral (ARV) therapy continues to bear significant side effects and that higher rates of comorbidities, such as cardiovascular disease and cancers, continue to be documented among people living with HIV. Additionally, on a global scale, for every two people started on ARV treatment, five new HIV infections occur.

Finding a cure for HIV is feasible, Lewin noted. She illustrated the case of a Berlin patient living with HIV and acute myeloid leukemia who underwent high-dose chemotherapy and total body irradiation, followed by a stem cell transplant involving donor cells with the CCR5-delta32 deletion—cells incapable of expressing CCR5, one of the main HIV receptors on lymphocytes and macrophages. The patient, Lewin reports, has remained negative for HIV since his transplant in 2008 and has not resumed antiretroviral therapy.

There are two distinct types of cures that may be possible in people living with HIV. First there is the sterilizing cure, where the goal is to completely eliminate all HIV from the body. The second possibility is a functional cure, where HIV remains completely suppressed—but is still present—without the need for ongoing ARV treatment.

Achieving either of these goals will not be easy, Lewin said, pointing out three key scientific challenges. First and most challenging is the persistence of latent HIV infection—inactive cells harboring the virus that cannot be targeted by available ARVs. Second, there is residual replication by these cells, even when the most potent ARV regimens are used. Finally, some anatomical sites—notably the central nervous system, the gut and genital tract—are not easily reached by many of today's ARVs.

Strategies to circumvent these obstacles are currently being explored. One possibility highlighted by Lewin, drawing upon data published by a Spanish team of researchers, involves intensifying ARV treatment. This approach showed potential promise using Merck's Isentress (raltegravir), according to the paper published earlier this year in Nature Medicine.

Another approach is to reduce the pools of latently infected cells through earlier treatment and by using medications such as interleukin-7 and histone deacetylase inhibitors.

Another possibility is using genetic therapies, such as modifying stem cells or delivering genes using a vector, to knock out CCR5, one of two major co-receptors used by HIV to infect CD4 cells.

Lewin noted that although these particular strategies are still in the proof-of-concept stage of development, they are grounds for optimism. She also pointed out that cure-based treatment approaches will be a major theme throughout the weeklong conference.
