Immunotherapy in HIV infection; current and future challenges

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Administration of HAART has resulted in significant improvements in the survival of HIV-infected patients. However, despite now reaching a point where we can achieve durable, maximal suppression of plasma viral load in most of our HAART-treated patients, non-AIDS-related morbidity and mortality among these patients remain a concern. Conditions typical of aging, such as cardiovascular disease and cancer, are seen at a higher rate in HIV-infected patients compared to the general population, potentially because the ability of HAART to restore immunocompetence appears incomplete–even in patients who have long-term undetectable HIV-1 RNA.

New insights into the pathogenesis of HIV-1 infection highlight several new and promising areas of investigation for immune-based therapies, including strategies that target T-cell homeostasis and immune activation, as well those targeted at restoring immune responses directed against HIV.

The rationale behind the investigation of a of cytokines such as IL-2 and IL-7 as adjunctive therapies to antiretroviral treatment is to improve the restoration of the immune system and improve HIV-directed immune responses. Among cytokines, IL-2, was extensively studied in several phase II and two large phase III studies. Results from these studies showed that IL-2 increases signficantly CD4 counts in the long term. However, this biological effect did not translate into clinical benefit. These results raise several questions about the functionality of IL-2 expanded CD4 T cells that will be discussed.

The potential interest of IL-7 is based on its crucial role on T cell homeostasis both in thymic output and peripheral T proliferation and survival. This new promising cytokine is currently under evaluation is several I/II clinical trials in chronically HIV-infected patients with low level of immune restoration despite controlled viral load. Results from these studies will be presented and discussed.

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