

Study: Antiretroviral therapy for HIV-1 in first four months is crucial

January 16 2013

Patients who are started on antiretroviral therapy for HIV-1 infection within four months of estimated infection date—and who have higher counts of CD4+ T-cells at the initiation of therapy—demonstrate a stronger recovery of CD4+ T-cell counts than patients in whom therapy is started later, a new study shows.

The report, to be published Thursday in *The [New England Journal of Medicine](#)*, is co-authored by physicians of UT Medicine San Antonio and the University of California, San Diego and drew data from 468 patients followed in the San Diego Primary Infection Cohort. UT Medicine is the clinical practice of the School of Medicine at The University of Texas Health Science Center San Antonio. Co-authors are from the University of California, San Diego School of Medicine, the San Antonio Military Medical Center and Monash University in Australia.

Transient increase, then decline

In the four months after HIV-1 ([human immunodeficiency virus](#) type 1) infection, the immune system mounts an immune response toward a temporary restoration of CD4+ T-cell counts; CD4+ T-cells are specialized immune cells that are required to fight infections and are depleted during HIV infection. After this transient increase, the CD4+ count progressively declines. The study, funded by the National Institute of Allergy and Infectious Diseases and other sources, offers insight into

the optimal timing of therapy.

"This study suggests greater urgency to start antiretroviral therapy earlier, when the most weapons in the immunity armamentarium are at the body's disposal," co-lead author Sunil K. Ahuja, M.D., said. Dr. Ahuja is professor of medicine, microbiology/immunology and biochemistry in the School of Medicine at the UT Health Science Center and director of the Veterans Administration Center for AIDS and [HIV](#) Infection, a national center within the South Texas Veterans Health Care System.

Narrow window

Observation of the transient restoration of CD4+ T-cell counts and their subsequent decline "raised the possibility that after acute infection there may be a narrow 'restorative [time window](#)' wherein the immune system could be strategically poised for recovery and that the likelihood and rate of recovery may be augmented by earlier initiation of potent antiretroviral therapy," co-lead author Susan J. Little, M.D., said. Dr. Little is professor of medicine at the University of California, San Diego School of Medicine.

Results

Recovery of CD4+ T-cell counts to approximately normal levels of 900 or more cells per cubic milliliter was observed in 64 percent of participants who were put on antiretroviral therapy (ART) within four months of estimated date of infection, compared to 34 percent of participants in whom ART was initiated later.

"Even a fairly short deferral of ART after closure of this time window may come at the expense of compromised CD4+ T-cell recovery,

irrespective of the CD4+ count at the time of treatment initiation," Dr. Ahuja said. "Further studies are needed to determine whether starting ART within the restorative time window promotes strategies that help fully reconstitute the immune system."

Timing of ART

In an accompanying editorial, Bruce Walker, M.D., and Martin Hirsch, M.D., of Harvard Medical School wrote: "The question of when to initiate ART remains a difficult one, particularly in resource-limited settings, but the studies in this issue of the *Journal* provide strong supportive evidence suggesting a benefit for early therapy." The authors noted that the study relies on a surrogate measure of disease progression, CD4+ T-cell count, rather than on clinical outcomes.

"Future studies of treatment even earlier in the course of infection may show additional benefits, and a population of such patients will be an important study group for eventual studies aimed at 'cure' of [infection](#)," Drs. Walker and Hirsch wrote.

Provided by University of Texas Health Science Center at San Antonio

Citation: Study: Antiretroviral therapy for HIV-1 in first four months is crucial (2013, January 16) retrieved 24 June 2024 from <https://medicalxpress.com/news/2013-01-antiretroviral-therapy-hiv-months-crucial.html>

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