Starting HIV Treatment Sooner Leads to Better Immune Recovery

Each day of delay during primary HIV infection lowered the odds of reaching a CD4 count above 900.

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People who start antiretroviral therapy (ART) soon after acquiring HIV are more likely to experience full immune recovery, according to study findings published in the journal AIDS. In fact, each day of delay during the first six months after infection reduced the chances of reaching a normal CD4 T-cell count and CD4/CD8 ratio.

“[T]he sooner ART is started after primary HIV infection diagnosis, the greater the chance of immune recovery,” the study authors wrote. “This is a key message to support rapid or immediate ART start amongst all new HIV-1 diagnoses, but especially in primary HIV infection.”

Research has shown that starting treatment as soon as possible after an HIV diagnosis leads to better outcomes. Early treatment initiation after HIV infection can be even more advantageous. Studies have shown that starting antiretrovirals during acute HIV infection (the first month) can limit the size of the viral reservoir and increase the likelihood of long-term remission. Starting treatment during primary HIV infection (the first six months), before the virus has done extensive damage, is also beneficial.

John Patrick Thornhill, MD, PhD, of Imperial College London, and colleagues evaluated a large cohort of people who started antiretroviral therapy during primary HIV infection, asking how time between HIV acquisition and ART initiation influences clinical outcomes.

The HEATHER study was an observational cohort of people with documented primary HIV infection who started treatment within three months after diagnosis. They were enrolled at four clinical sites in the United Kingdom. Of the 204 participants, 144 enrolled between 2009 and 2015—before the advent of pre-exposure prophylaxis (PrEP) and universal ART regardless of CD4 count—and 90 enrolled between 2015 and 2020.

Most participants (84%) were men who have sex with men, only 4% were women and about three quarters were white. The median age at the time of primary HIV infection was 33 years. Even at this early stage, most already had some evidence of immune dysfunction, as indicated by a CD4/CD8 ratio below 1.0. About a third were deemed to have early primary or acute infection, as

indicated by the presence of HIV RNA or antigens before the development of HIV antibodies.

Almost everyone achieved a viral load below 200 after starting treatment, with a median time to viral suppression of 115 days. Men and people who used integrase inhibitors as part of their initial ART regimen had a shorter time to viral suppression.

The researchers saw an association between earlier ART initiation during primary HIV infection and increased immune recovery. Over a median follow-up period of 33 months, 47% of participants reached a CD4 T-cell count above 900, and 64% achieved a CD4/CD8 ratio greater than 1.0. (A normal CD4 count in HIV-negative people is between 500 and 1,500 cells.)

Having a lower CD4 count, a lower CD8 count or a lower CD4/CD8 ratio at the time of ART initiation was associated with a longer time to CD4 cell recovery. For every day that treatment was delayed, there was a lower likelihood of achieving a CD4 count above 900 and a CD4/CD8 ratio greater than 1.0. The researchers suggested that more people might have reached a high CD4 count if follow-up had been longer.

More effective treatment may have also played a role in immune recovery. There was a trend towards a shorter time to CD4/CD8 recovery for participants who used integrase inhibitors. People diagnosed between 2009 and 2015 were less likely to achieve a CD4/CD8 ratio below 1.0 than those diagnosed between 2015 and 2020, although this was no longer statistically significant after adjusting for other factors.

Historically, treatment initiation after HIV diagnosis was sometimes delayed while waiting for results from resistance testing to guide drug selection. The researchers suggested that this is not necessary given the availability of second-generation integrase inhibitors with a high barrier to resistance. Same-day ART initiation when primary HIV infection is diagnosed “can be safely recommended” if non-nucleoside reverse transcriptase inhibitors (NNRTIs) are avoided, they wrote.

Although there was once uncertainty about how soon to start antiretrovirals, it is now firmly established that the earlier treatment starts, the better. But many people with HIV still have limited access to testing and remain unaware of their status, which delays treatment and raises the risk for immune damage and disease progression.

“Whilst immediate or rapid ART is controversial in some settings, there is compelling evidence that rapid ART initiation, even on the same day as confirmed HIV-1 diagnosis, is associated with reduced loss to follow-up in low-middle income settings and more rapid viral suppression,” the study authors concluded. “Our findings further the rationale for same-day or earlier ART, even during primary HIV infection, to support more rapid immune recovery.”

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