A few reasons for starting therapy at CD4+ counts above 350 cells

New treatment guidelines reflect a trend toward earlier initiation of HAART, generally when the CD4+ count falls below 350 cells. Several guidelines even encourage the consideration of initiation of HAART when the CD4+ count is greater than 350. In this report, we combine suggestions from different guidelines and their reasons for starting therapy, in selected cases, in people who have more than 350 CD4+ cells.

Life-threatening infections

Results from at least one clinical trial (ACTG 5164) suggest that there is a beneficial effect of starting HAART within two weeks of beginning therapy for a life-threatening infection rather than delaying initiation of HAART for four weeks. In this trial, the most common life-threatening infection was a lung infection called PCP (Pneumocystis jirovecii pneumonia). HAART reduced the risk of two important events:

- dying from PCP (an often fatal infection in people with weakened immune systems)
- developing yet another life-threatening infection

Rapid decreases in CD4+ cell counts

In some HIV positive people, the CD4+ count may decrease rapidly—by more than 100 cells per year. If their cell counts were low to begin with, this change could place people at high risk for AIDS-related complications. In these cases of rapid decline in the CD4+ count, doctors may wish to consider earlier use of HAART.

Hepatitis B and C co-infection

Infection with hepatitis C virus can accelerate liver-related injury in people co-infected with HIV. At least one study from Western Europe suggests that HIV positive people who have hepatitis co-infection(s) have a significantly reduced rate of death when HAART is initiated at a CD4+ count of 500 or more cells.

In cases of HIV positive people co-infected with hepatitis B virus (HBV), treatment guidelines recommend that regimens for the treatment of HIV contain the drugs tenofovir (Viread) and either 3TC (lamivudine) or FTC (emtricitabine, Emtriva), as these can suppress both HIV and HBV.

HIV-related kidney problems

The technical name for this is HIV-associated nephropathy and it occurs mainly in people of African descent. If left untreated, the kidneys can become severely damaged and eventually stop working. After HIV-associated nephropathy has been diagnosed and HAART has been started, the kidneys generally do not fully recover. So researchers suggest that doctors consider starting HAART in patients who have early evidence of HIV-related kidney problems.

Pregnancy

In high-income countries, when pregnant women know that they are HIV positive and they seek prenatal care and receive HAART, their viral load can often be successfully suppressed (below 50 copies). This, combined with therapy for the baby during and after birth and the avoidance of breastfeeding, greatly reduces the risk of infecting the infant, usually to less than 1%. As a result, major treatment guidelines recommend HAART for all pregnant women, regardless of their CD4+ count.

Age
A general trend is that as people get older their immune systems get weaker. So European HIV experts suggest that doctors caring for people who are older than 55 and whose CD4+ counts are greater than 350 cells consider prescribing early treatment.

**Cardiovascular disease (CVD) risk**

HIV infection is associated with inflammation (details on this appear later in this issue of *TreatmentUpdate*—Section G), and this increases the risk for several conditions, including CVD. One American guideline (developed by the IAS-USA group) suggests that early initiation of therapy can be considered in HIV positive people at heightened risk for CVD.

**A public health measure**

Early treatment may help reduce the risk of transmitting HIV from one person to another. This may be helpful for people who are in relationships where one partner is positive or for people who engage in high-risk behaviour. Bear in mind that firm evidence about the infection-reducing effects of HAART is not yet available. However, a clinical trial to test this idea in heterosexual couples is about to start in low-income countries where HIV infection is common. The results from this study will be available in a few years.

**Should everyone start HAART even earlier?**

The International Network for Strategic Initiatives (INSIGHT) is planning a large clinical trial to assess the impact of early therapy in HIV positive people who have more than 500 CD4+ cells. This study will randomly assign participants to either immediately begin HAART or to delay starting HAART until their CD4+ count has fallen to less than 350 cells. First, a pilot study will recruit about 1,200 people to find out the rate of serious events in both groups. Once this is done, thousands of people will be enrolled for the larger study.

The HIV Prevention Network plans to study whether or not HAART can reduce the risk of infection in 1,500 heterosexual couples where one partner is HIV negative. This trial will take place in low-income countries where HIV infection is common. The partners who are HIV positive will be randomly assigned to either immediately begin HAART or to delay therapy until their CD4+ count has fallen below 250. Although this study is primarily designed to assess HIV transmission rates, it will also be able to shed light on the effect of early treatment on health and survival. Similar trials to assess early vs. late therapy are planned for Haiti and other countries.

**REFERENCES:**

Decisions about particular medical treatments should always be made in consultation with a qualified medical practitioner knowledgeable about HIV- and hepatitis C-related illness and the treatments in question.

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