

TIMING OF HAART INITIATION

Four key variables should be considered when deciding if HAART should be initiated for an individual infected with HIV: 1) HIV-related symptoms; 2) CD4+ T cell count; 3) HIV viral load; and 4) the patient's potential for adherence.

Patients with significant symptoms attributable to HIV infection should generally be offered HAART as soon as possible. Initiation of therapy for those individuals with no symptoms or only mild HIV-related symptoms should largely depend upon CD4+ T cell count measurements (or total lymphocyte count if CD4+ T cell count testing is not available).

Some controversy remains as to the optimal CD4+ T cell count threshold for initiation of HAART in the asymptomatic patient. When HAART first became available with the development of PIs in the late 1990s, most experts and guidelines advocated aggressive use of HAART, even for patients with relatively high CD4+ T cell counts and low HIV viral load levels. However, it was soon discovered that while HAART can suppress HIV replication to undetectable levels, HAART cannot fully eradicate the virus. Furthermore, long-term adverse effects associated with ARV agents were increasingly recognised as individuals continued therapy for several years. These factors have prompted most experts to favour a less aggressive approach to HAART than was advocated in the past.

Several observational cohort studies of HIV-infected patients have suggested that patients who initiate HAART before their CD4+ T cell count falls to <200 cells/mm³ have a higher likelihood of durable virologic suppression, a lower likelihood of progression of HIV disease, and more robust immune reconstitution as compared to patients who initiate HAART after their CD4+ T cell counts have dropped to <200 cells/mm³. While these studies suggest a benefit associated with initiation of therapy at CD4+ T cell counts >200 cells/mm³, studies have not consistently suggested a significant benefit of initiation of HAART at higher CD4+ T cell counts (>350 cells/mm³). Earlier studies in the pre-HAART era documented a relatively high rate of progression to AIDS among patients with viral loads of $<55,000$ copies/mm³, regardless of their CD4+ T cell count. More recent studies have also suggested that a high baseline viral load ($>100,000$ copies/mm³) at the time HAART is initiated may be associated with less favourable clinical outcomes, though this phenomenon has not been seen consistently in studies of more potent regimens that include EFV or LPV/r.

These guidelines therefore recommend initiation of treatment (HAART) for patients with significant or AIDS-defining symptoms, regardless of CD4+ T cell count or HIV viral load. Initiation of HAART is also recommended for asymptomatic patients with a CD4+ T cell count of <200 cells/mm³. For asymptomatic patients with a CD4+ T cell count between 200 and 350 cells/mm³, HAART should generally be offered, recognising that a better response to HAART is likely if treatment is initiated before the CD4+ T cell count falls to <200 cells/mm³. Finally, for patients who are asymptomatic and have a high CD4+ T cell count (>350 cells/mm³) or a high total lymphocyte count ($>1,200$ cells/mm³), HAART may generally be deferred. Because the response to HAART correlates strongly with adherence, the patient's potential for adherence should be assessed carefully, and attempts should be made to address and correct potential obstacles to adherence prior to initiation of therapy.¹

A patient's baseline HIV viral load level is not as important as symptoms or CD4+ T cell count in deciding when to initiate therapy. However, if available, this information can be used to estimate the anticipated rate of disease progression: in the absence of therapy, higher viral loads typically correlate with faster rates of disease progression and CD4+ T cell count decline. Furthermore, some studies suggest that initiation of HAART at lower baseline viral loads is associated with a better clinical response to treatment than in patients who initiate HAART at higher baseline viral loads. Some experts and clinical guidelines therefore recommend initiation of HAART for patients with high viral loads (e.g. $>50,000$ to $100,000$ copies/mL), even if the CD4+ T cell count is >350 cells/mm³. Other experts might recommend simply following the CD4+ T cell count more carefully in patients with high baseline viral loads to ensure that treatment is initiated before the CD4+ T cell count falls to <200 cells/mm³.

Table 3 summarises these guidelines for initiation of HAART. In regions where CD4+ T cell count testing is not available, the total lymphocyte count (TLC) can be used as a marker of immunosuppression in symptomatic patients. Because the TLC does not accurately reflect HIV-related immunosuppression in asymptomatic patients, recommendations for initiation of HAART for asymptomatic patients cannot be made on the basis of the TLC.

Table 3: General Recommendations for Initiation of HAART for HIV-Infected Adults and Adolescents. Please refer to text for additional guidance and considerations.

¹Adherence is discussed in more detail later in this chapter, as well as in *Chapter 1: Comprehensive Management of Persons with HIV Infection*.

IF CD4+ T CELL COUNT TESTING IS AVAILABLE			
Symptoms of HIV	CD4+ T Cell Count (cells/mm³)	Viral Load (copies/mL)	Recommendation
Symptomatic	Any	Any	Treat
Asymptomatic	<200	Any	Treat
Asymptomatic	200-350	Any	Treatment should generally be offered
Asymptomatic	>350	>100,000	Treatment decision controversial; monitor CD4+ T cell count closely
Asymptomatic	>350	<100,000	Treatment not recommended
IF CD4+ T CELL COUNT TESTING IS UNAVAILABLE			
Symptoms of HIV Infection		Total Lymphocyte Count (cells/mm³)	Recommendation
AIDS or Severe Symptoms		Any	Treat
WHO Stage II or III (minor symptoms)		<1200	Treat
WHO Stage II or III		>1200	Consider treatment
Asymptomatic		Any	Treatment not recommended