Universal Antiretroviral Therapy Initiation

Guideline of the HIV/AIDS Division at San Francisco General Hospital

Statement of Guideline: All patients, regardless of CD4 count, will be evaluated for initiation of antiretroviral therapy (ART).

Background: Recent data support earlier ART initiation in HIV-infected individuals. Randomized controlled trials clearly demonstrate the benefit of ART in patients with CD4 cell count ≤350 cells/mm^3.[1] While randomized controlled evidence for patients with higher CD4 counts is not yet available, well-designed retrospective and cohort studies support benefit in these patients. For example, the NA-ACCORD collaboration demonstrated an increase in mortality among patients who deferred therapy until CD4 ≤350 cells/mm^3 compared to those who initiated between 351 and 500 cells/mm^3 (risk ratio: 1.69, 95% CI: 1.26 to 2.26). There was also an increase in mortality among patients who deferred therapy until CD4 ≤500 cells/mm^3 compared to those who initiated >500 cells/mm^3 (risk ratio: 1.94, 95% CI: 1.37 to 2.79).[2] Additionally, a subanalysis of the SMART study including 249 patients who were treatment naïve at entry showed a trend toward lower risk of serious AIDS- and non-AIDS-related events in patients who initiated therapy at CD4 count ≥350 cells/mm^3 compared with those who deferred therapy until CD4 count dropped to <250 cells/mm^3 (p = 0.06).[3]

Multiple other lines of evidence support early ART initiation. ART has long been indicated irrespective of CD4 count in all pregnant women[4], all patients with HIV-associated nephropathy[5], and in patients co-infected with hepatitis B virus who require hepatitis B therapy.[6] There is evidence that ART may slow progression of liver fibrosis in patients co-infected with hepatitis B or hepatitis C virus.[7] Neurological complications and cognitive impairment that may accompany uncontrolled HIV replication and CD4 depletion may be reversed or at least prevented by earlier ART initiation.[8, 9] There is growing awareness that untreated HIV infection may be associated with development of many non-AIDS-defining diseases, including cardiovascular disease, kidney disease, liver disease and malignancy[10], which again argues for earlier initiation of ART. Moreover, initiation of ART at higher CD4 count has been associated with less drug resistance during subsequent virologic failure.[11] Finally, initiation of ART at an older age is associated with a less robust CD4 gain despite increased rates of virologic suppression.[12]

Taken together, these observations – combined with the availability of antiretroviral regimens that are more effective, more convenient, and better tolerated than previously used antiretroviral combinations – argue in favor of early ART initiation for all motivated patients, regardless of CD4 count or HIV viral load. The strength of this recommendation is greater in patients with CD4 counts < 500 cells/mm^3. However, in general all patients should be offered ART unless there is a reason to defer therapy.

In addition to the individual benefit of early ART initiation, there is increasing evidence that virologically suppressive ART reduces HIV transmission. This information should be conveyed in the context of comprehensive prevention-with-positives assessment and appropriate education and referrals.

This guideline is meant for use on Ward 86, the clinic of the UCSF HIV/AIDS Division at San Francisco General Hospital. Application in areas with different HIV expertise and/or resources may or may not be appropriate.

This HIV/AIDS Division Guideline is consistent with the December 1, 2009 update of the US Department of Health and Human Services Guidelines for the Use of Antiretroviral Agents in HIV-1 Infected Adults and Adolescents.[13]

Frequently Asked Questions:

Must ART be initiated on all patients?

No. After evaluation of a patient's appropriateness and readiness for ART, a patient and provider together may determine that deferral of ART is the best course of action. Risks of short- or long-term drug-related complications, medical contraindications to treatment, certain psychosocial situations, nonadherence to lifelong therapy in asymptomatic patients, and potential for development of drug resistance may be judged to offset benefits of earlier initiation of therapy. Additionally, patients who are appropriate candidates for ART may decide not to initiate therapy after reviewing the risks and benefits of initiation vs. deferral with their provider.

Should ART be started on "elite controllers" – ie, a patient whose HIV viral load is undetectable without ART?

Possibly. While elite controllers typically have slower disease progression and longer time to AIDS than non-controllers, CD4 decline and the development of AIDS may still occur.[14] HIV replication has been demonstrated in elite controllers, most often at levels higher than that of ART-treated patients.[15] The effect of elite control of HIV replication on non-AIDS defining conditions is unclear.

When should ART be started in the setting of an acute opportunistic or serious bacterial infection?

Recent data indicate a survival benefit for patients with certain acute opportunistic or invasive bacterial infections.[16] This topic is discussed in detail in another HIV/AIDS Division Clinical Guideline. The exact timing of ART initiation in patients with tuberculosis is under active investigation.

Should ART be initiated during acute HIV infection?

Randomized, controlled studies are not available to answer this question; however, available evidence indicates immunologic benefit when ART is initiated during acute infection.

What resources are available for patients on this topic?

The patient education group has created a patient handout on starting ART. Patients initiating ART may also be seen for counseling by the pharmacy staff on Ward 86.

What resources are available to get patients' medication paid for?

The Social Work department at Ward 86 can assist patients in enrolling in drug benefit programs for which they are eligible, such as Medi-Cal, Healthy San Francisco, and ADAP. Patients with issues around pharmacy coverage should be referred to social work.

What resources are available for patients who may have adherence challenges?

Ward 86 has a Medication Adherence Program, operated by the Pharmacy department with close coordination with the Social Work department. Any patient may be referred to Ward 86 pharmacists for a thorough adherence assessment and individualized support.

Optimal HIV management is continually informed by ongoing research, and many questions remain unanswered. The HIV/AIDS Division is committed to conducting studies that will address important scientific questions. These guidelines will be updated to reflect relevant findings from future studies.

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