AETC AIDS Education & Training Center Program
National Coordinating Resource Center

Immediate ART Initiation: Guide for Clinicians

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Immediate antiretroviral therapy (ART) refers to starting HIV treatment as soon as possible after the diagnosis of HIV infection, preferably on the first clinic visit (and even on the same day the HIV diagnosis is made). This strategy also is known as "rapid ART," "same-day ART," and "treatment upon diagnosis."

Rationale

Immediate ART initiation may bring earlier benefits in personal health, and earlier reductions in the risk of onward transmission of HIV. For persons with acute infection, immediate ART may limit the HIV viral reservoir.

In pilot studies in the United States and in randomized controlled trials in resource-limited settings, rapid ART initiation has been shown to reduce time to linkage to care and viral load suppression. Immediate ART protocols have been piloted in various U.S. clinics,(1, 2, 3) and initiating ART on the first clinic visit after HIV diagnosis has become standard of care in a number of clinics and jurisdictions, including the city of San Francisco (under the municipal "Getting to Zero" initiative [4, 5]) and New York City (in the Department of Health Sexual Health Clinics).

Immediate ART is supported by the International AIDS Society-USA (IAS-USA) guidelines, which state that "ART should be initiated as soon as possible after diagnosis, including immediately after diagnosis, unless [the] patient is not ready to commit to starting therapy (evidence rating A1a)."(6) The Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents Living with HIV from the U.S. Department of Health and Human Services, on the other hand, state that despite its potential benefits, ART initiation on the day of diagnosis "remains investigational."(7)

This Clinicians' Guide is a distillation of best practices for immediate ART initiation, and is based on resources from San Francisco's Getting to Zero RAPID program and San Francisco General Hospital's RAPID (Rapid ART Program Initiative for HIV Diagnoses) program.(4, 8)

Immediate ART program overview

Successful rapid ART programs benefit from coordinated activity among HIV testing sites, immediate-ART clinical care site(s), and, ideally, involvement of HIV care navigators and public health tracking systems.

Within the HIV clinic itself, optimal implementation of a rapid ART program is supported by specific structures and procedures, including:

- Efficient and reliable notification about persons with a new diagnosis of HIV (eg, referral via a single point of contact such as a dedicated pager, front desk staff member, or advice nurse)
- Activation of a "rapid" multidisciplinary team (social worker, eligibility/insurance specialist, clinician, laboratory services) that can mobilize quickly to see the patient on a same-day basis (one person may fill multiple roles)
- Availability of follow-up care within 1 week of the initial visit

Patient screening for immediate ART

Immediate ART is appropriate for:

- Nearly all persons with confirmed new diagnoses of HIV
- Persons with suspected acute HIV, whose HIV diagnosis may not yet be confirmed (e.g., the HIV antigen or antibody test result may be negative at the time of evaluation)
- Persons with positive results of rapid HIV antibody tests, before confirmatory test results are available, if the pretest probability of HIV infection is high (after counseling, immediate ART can be offered with the understanding that if confirmatory tests are negative, the patient would stop ART)
- Chronically infected patients who are returning to care after being out of care also can be started rapidly if they have a known wild-type virus or if the resistance pattern of their virus can be predicted

Immediate ART is not appropriate for:

- Persons with certain untreated opportunistic infections (OIs) such as cryptococcal meningitis and central nervous system (CNS) tuberculosis for whom a short period of treatment for the OI is recommended before ART initiation, to reduce risk of dangerous IRIS (immune reconstitution inflammatory syndrome); note that this is very rare in the outpatient clinic setting
- Persons with a preliminary positive rapid HIV test who have a low pretest probability of HIV infection. For persons who fit this description (e.g., from a low-risk demographic group with no discernable individual risk factors for HIV) the preliminary result is more likely to be a false-positive and clinicians should probably wait for a positive confirmatory test result before starting ART.

Persons who decline immediate ART initiation:

Patients who are not willing or ready to start ART on the first clinic visit should be followed closely and offered ART at subsequent visits; in our experience, patients who are not ready at the first visit may be ready as soon as several days later.

Intake appointment

The immediate-ART intake appointment is a compressed version of the standard HIV intake procedure. Goals include: support, counseling, HIV education, insurance enrollment or optimization, baseline lab tests, and ART start. Ideally, a specialized multidisciplinary team comprising a social worker, a nurse, and a clinician meet with the patient and conduct the intake, either together or sequentially. All clinicians provide the patient with emotional support around the diagnosis of HIV (if needed), and education about HIV infection. Most intake appointments last about 2-3 hours.

The social worker assists with insurance enrollment or optimization (including access to prescription medications), and addresses any immediate needs for stabilization.

The clinician takes the patient's history and performs an assessment in condensed format, with goals of:

- Obtaining enough history to form a decision about whether to start ART and what ARV medications to use
- Beginning education about HIV, ART (including the possible benefits of early ART, and why adherence is important), and preventing transmission to others
- Obtaining consent from the patient to start ART immediately
- Engaging the patient to return to clinic for follow-up appointments

Baseline laboratory testing

- Confirmatory HIV testing (if needed)
- HIV viral load
- CD4 cell count
- HIV genotype, including integrase
- HLA-B*5701
- Metabolic panel (creatinine, electrolytes, glucose, liver function tests)
- Hepatitis A IgG
- Hepatitis B sAb, cAb, Ag
- HCV IgG
- STD testing: RPR or VDRL, chlamydia and gonorrhea NAAT tests (urine, pharynx, rectum as indicated by sites of exposure)
- TB screening test (e.g., Quantiferon)
- Pregnancy test (if appropriate)
- Consider: lipids, G6PD, toxoplasma IgG

Recommended regimens for immediate ART

ART is started at the first clinic visit, before the results of baseline testing (including HIV RNA, CD4 count, genotype, HLA-B*5701, and creatinine) are available. Thus, the ART regimens must be potent and effective in the setting of high viral load and/or transmitted NRTI resistance (Table 1). The regimens can be modified later, if indicated, based on the genotype results. Regimens also must be simple, easy to take, and have minimal risks of adverse events.

Table 1. Recommended Immediate ART Regimens

Rank	Regimen
Preferred (based on clinical trial data and clinical experience)	• Dolutegravir (Tivicay) + TAF/FTC (Descovy) • Darunavir (Prezista) + booster (ritonavir or cobicistat) + TAF/FTC (or TDF/FTC, TDF/3TC)
Reasonable alternative (based on clinical trial data in first-line ART, though no data or clinical experience in immediate ART)	• Bictegravir/TAF/FTC (Biktarvy)
Acceptable if recommended regimens are not available (less potent and with lower barrier to resistance than recommended regimens)	• Raltegravir (Isentress) + TAF/FTC (Descovy) or (TDF/FTC, TDF/3TC) • Elvitegravir/cobicistat/TAF/FTC (Genvoya)

Abbreviations: FTC = emtricitabine; 3TC = lamivudine; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate

Other regimens may be appropriate for individual patients.

For women who are pregnant, wish to become pregnant, or are at risk of becoming pregnant:

Dolutegravir is not currently recommended for use at the time of conception or during the early weeks of pregnancy. Elvitegravir and cobicistat (including darunavir/cobicistat) are not recommended for pregnant women, and bictegravir and TAF have not been studied in pregnancy.

Thus, rapid-ART regimens for a woman who is pregnant or may become pregnant must be selected individually, after careful discussion with her. Current HHS perinatal guidelines include raltegravir + TDF/FTC and darunavir + ritonavir + TDF/FTC among their recommended regimens for pregnant women.(9)

If patient is taking PrEP (pre-exposure prophylaxis) or PEP (post-exposure prophylaxis), or took it at the time of HIV infection or since HIV infection:

- Take a careful history to determine the last time the patient took PrEP or PEP medications
- If there is concern that resistance to the ARVs may have developed, start a reinforced ART regimen consisting of an integrase inhibitor (dolutegravir or bictegravir) + boosted darunavir + TAF/FTC (or TDF/FTC or TDF/3TC) while awaiting the results of the genotype assay

ARVs to AVOID for immediate ART:

- NNRTIs – high risk of transmitted resistance
- Abacavir (including coformulations that include abacavir)
    - Risk of hypersensitivity reaction if positive for HLA-B*5701

- 2-drug ARV regimens (e.g., dolutegravir + 3TC, dolutegravir/rilpivirine [Juluca])
    - Risk of transmitted resistance to NRTI or NNRTI components, risk of virologic failure at high viral load, not studied in immediate ART

Starter packs:

Starter packs containing a 3- to 5-day supply of the selected ART regimen can be helpful if they are available; they ensure that patients can actually start on ART on the day of the first clinic visit (by bypassing any delays in obtaining ARVs because of pharmacy-level issues or snags with insurance activation). They are less important if immediate access to ARVs can be assured (e.g., via an in-clinic pharmacy).

Follow-Up

Patients started on ART at the first clinic visit often need additional education and extra supports in the days and weeks that follow. Because they have recently been diagnosed with HIV and started on ART with little or no advance preparation, they will need additional HIV-related education, information regarding the importance of medication adherence, counseling about preventing HIV transmission, and encouragement about living healthy lives with HIV.

We recommend scheduling a phone check-in with a social worker, nurse, or clinician 2-3 days after the intake appointment, and a clinic follow-up appointment at 1-2 weeks. The timing of subsequent visits will depend on the needs of the patient, but in general the next appointment should take place within 1 month of the start of ART and at least monthly thereafter until the HIV viral load is suppressed and the patient is well engaged in care.

At the follow-up appointment, clinicians should review baseline lab results with the patient, evaluate ART adherence, screen for side effects, and provide further counseling and education. When the genotype result is available, the clinician can make decisions about whether a change in ART is indicated, though unnecessary changes generally should be avoided.

Consult with experts

Clinical questions frequently arise in the evaluation and management of persons with new HIV diagnoses. These include uncertainties about interpretation of discordant HIV test results, risk of transmitted or acquired drug resistance, and decisions about which ART regimens to start. Clinicians should seek expert consultation if they have questions or concerns. The Clinician Consultation Center, a component of HRSA's AIDS Education and Training Center (AETC) Program, provides free phone consultation on immediate ART through its HIV/AIDS Management call line (800-933-3413, Monday-Friday 9 am-8 pm ET) and Perinatal HIV hotline (888-448-8765, 24 hours a day).

References

1. Pilcher CD, Ospina-Norvell C, Dasgupta A, et al. The effect of same-day observed initiation of antiretroviral therapyon HIV viral load and treatment outcomes in a U.S. public health setting. J Acquir Immune Defic Syndr. 2017 Jan1;74(1):44-51.
2. Ford N, Migone C, Calmy A, et al. Benefits and risks of rapid initiation of antiretroviral therapy. AIDS. Jan 2; 32(1):17-23.

3. Colasanti J, Sumitani J, Mehta CC, et al. Implementation of a rapid entry program decreases time to viral suppression among vulnerable persons living with HIV in the southern United States. Open Forum Infect Dis. 2018 Jun 28;5(6):ofy104.
4. Getting to Zero San Francisco. San Francisco Program for RAPID ART Initiation and Linkage to Care SOP. Available at http://www.gettingtozerosf.org/rapid-committee. Accessed 12/10/18.
5. Coffey S, Bacchetti P, Sachdev D, et al. RAPID ART: High virologic suppression rates with immediate ART initiation in a vulnerable urban clinic population. AIDS. 2018 Dec 21.
6. Saag MS, Benson CA, Gandhi RT, et al. Antiretroviral Drugs for Treatment and Prevention of HIV Infection in Adults: 2018 Recommendations of the International Antiviral Society-USA Panel. JAMA. 2018 Jul 24;320(4):379-396.
7. HHS Panel on Antiretroviral Guidelines for Adults and Adolescents Panel Members and Consultants. Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents Living with HIV. October 25, 2018, update. Available at https://aidsinfo.nih.gov/guidelines/html/1/adult-and-adolescent-arv. Accessed 12/10/2018.
8. Getting to Zero San Francisco. RAPID ART Program Initiative: How immediate ART improves health outcomes. Available at http://www.gettingtozerosf.org/rapiddetailingbrochure/. Accessed 12/10/2018.
9. HHS Panel on Treatment of Pregnant Women with HIV Infection. Update to the Recommendations for the Use of Antiretroviral Drugs in Pregnant Women with HIV Infection and Interventions to Reduce Perinatal HIV Transmission in the United States. December 7, 2018. Available at https://aidsinfo.nih.gov/guidelines. Accessed 12/10/2018.