AETC AIDS Education & Training Center Program
National Coordinating Resource Center

Immediate ART Initiation & Restart: 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 Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents with HIV from the U.S. Department of Health and Human Services, which recommend “initiating ART at the time of diagnosis (when possible) or soon afterwards to increase the uptake of ART, decrease the time required to achieve linkage to care and virologic suppression, and improve the rate of virologic suppression among individuals who have recently received HIV diagnoses.” (6)

This Clinicians' Guide is a distillation of best practices for immediate ART initiation (and re-initiation for persons who have stopped ART) 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)

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 (e.g., 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 concern for 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 or who not on ART also can be started (or restarted) rapidly if they have a known wild-type virus or if the resistance pattern of their virus can be predicted (See **Immediate ART Restart for Persons Returning to Care**).

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 result who have a low pretest probability of HIV infection. For persons who fit this description (e.g., those with no discernable individual or demographic 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 (ART can be started immediately if the confirmatory test is positive).

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 hours.

The social worker (or a benefits specialist) 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 a 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 (including via viral suppression on ART [U=U])
- 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 RNA (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: syphilis test (RPR, VDRL, or treponemal), 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

For persons with a new diagnosis of HIV, ART will be 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 and NNRTI resistance, at least until the lab test results are available. Regimens can be modified, if indicated, based on the genotype results or other results. Regimens also must be simple, easy to take, and have minimal risk of adverse events.

- Bictegravir/TAF/FTC (Biktarvy), 1 po once daily
- Dolutegravir (Tivicay) 50 mg po daily + (TAF/FTC [Descovy], TDF/FTC [Truvada], or TDF/3TC), 1 po once daily
- Darunavir/cobicistat/TAF/FTC (Symtuza), 1 po once daily

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

Other regimens may be appropriate for individual patients.

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

Discuss possible risks and benefits of specific ARVs in pregnancy; select a rapid-ART regimen individually, based on shared decision making.

Current HHS perinatal guidelines include dolutegravir, + TDF/FTC or TDF/3TC, and darunavir + ritonavir + TDF/FTC or TDF/3TC among their preferred regimens for pregnant persons, and list TAF/FTC as an "alternative" to TDF/FTC. (8)

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 contain abacavir)
    - Risk of hypersensitivity reaction if positive for HLA-B*5701
- 2-drug ARV regimens (e.g., dolutegravir + 3TC [Dovato], dolutegravir/rilpivirine [Juluca], cabotegravir + rilpivirine [Cabenuva], others)
    - Risk of virologic failure if transmitted resistance to NRTI or NNRTI components is present, 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 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 after Immediate ART Start

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.

Immediate ART Restart for Persons Returning to Care

While a key goal of HIV care is for people with HIV (PWH) to achieve continuous viral suppression on ART, in actuality many PWH may stop ART or fall out of care for periods of time. It is important to reengage these patients in care at the earliest opportunity, and to support them in restarting ART.

For these patients, we recommend immediate ART restart (or initial start, if not previously on ART) at the first reengagement visit if the patient is willing. Immediate restart is particularly important if the CD4 count is <200 cells/mm^3.

Immediate ART restart is appropriate for:

- Nearly all persons who are reengaging in care
- Persons for whom the ART history is known, and HIV resistance is known or can be predicted (based on previous resistance testing, HIV viral load while on ART, and adherence history)
- An appropriate ART regimen can be devised without information from current resistance test results.

Immediate ART restart is not appropriate for:

- Persons with certain untreated opportunistic infections (OIs), e.g., central nervous system OIs, for whom a short period of treatment for the OI is recommended before ART initiation.
- An appropriate ART regimen cannot be devised without information from current resistance test results.

Intake Appointment

The first clinic appointment for re-engaging patients is similar to the initial rapid ART visit (see above). The clinician takes the patient's interval history and performs an assessment in a condensed format, with goals of:

- Obtaining enough history to form a decision about whether to restart ART immediately, what ARV medications to use, and whether prophylaxis or treatment for an OI is indicated
- Continuing education about HIV, the benefits of ART (including the importance of adherence and viral suppression) for personal health and for preventing transmission to others
- Obtaining buy-in from the patient to restart ART immediately
- Engaging the patient to return to clinic for follow-up appointments

Patients who are reengaging in care should receive enhanced clinical supports to optimize the likelihood of successful reengagement in care and adherence with ART. This includes same-day evaluation by a social worker or counselor; insurance enrollment or optimization; referral for mental health, substance use, or other services as needed; and close follow up with the primary care provider.

Laboratory Testing

- HIV RNA (viral load)
- CD4 cell count
- HIV resistance test: generally, a genotype (including integrase if past ART included an integrase inhibitor)
    - A resistance test may not be needed if new acquired resistance is unlikely (e.g., for patients who had viral suppression at the time they discontinued ART).
    - Resistance test results may not detect mutations if the patient has been off ART for about 4 weeks or more – consult with an expert
- Creatinine, liver transaminases
- Other tests as indicated or if not previously done (see **Baseline laboratory testing**, above)

ART Regimens for Immediate Restart

Regimens should be selected individually, based on the patient's specific HIV, ART, and resistance history; as well as their comorbidities, tolerance of previous ARVs, adherence challenges, and other factors. Consult with an HIV expert.

It is not possible to make recommendations for individual patients, but common ART restart scenarios include:

- The patient was taking a 1st or 2nd ART regimen and there is no suspected resistance: can start one of the regimens for initial immediate ART (e.g., bictegravir/TAF/FTC or dolutegravir + TAF/FTC), or (unless contraindications) can restart the patient's previous regimen.
- The patient has a known or suspected history of virologic failure with acquired ART resistance: select the ART regimen based on the suspected resistance mutations; consult with HIV experts.
    - If there is concern for NRTI and/or NNRTI resistance, consider a boosted protease inhibitor + 2 NRTIs +/- an integrase inhibitor (e.g., darunavir/cobicistat/TAF/FTC + dolutegravir).
    - If there is concern for NRTI and/or INSTI resistance, consider a boosted protease inhibitor + 2 NRTIs +/- a 2nd generation NNRTI (if no history of treatment with an NNRTI) (e.g., darunavir/cobicistat/TAF/FTC + doravirine).
    - If more extensive resistance may be present, consider a multi-class regimen with a boosted darunavir + an integrase inhibitor +/- an NNRTI +/- NRTIs +/- fostemsavir or other ARVs as indicated.

For persons who are pregnant or who may become pregnant on a rapidly restarted regimen:

- Certain ARVs are not recommended during pregnancy. Providers should discuss possible risks and benefits of ARVs with persons who are pregnant or may become pregnant and select ARVs through shared decision making. Consult with an HIV expert.

The following generally **should NOT be prescribed** for immediate ART restart:

- 2-ARV regimens, e.g., dolutegravir/3TC (Dovato), dolutegravir/rilpivirine (Juluca), cabotegravir + rilpivirine [Cabenuva], others (high risk of virologic failure if resistance is present; some studied only for ART switch in persons with suppressed HIV viral load)
- Abacavir, unless HLA B5701 is known to be negative

Persons who decline immediate ART restart

Re-engaging patients who decline immediate restart (or who are not restarted for other reasons) should be followed closely (e.g., in 1-2 weeks) and restarted at the earliest appropriate time.

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

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