

When to Start Antiretroviral Therapy

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Outline of this Unit

By the end of this unit, you will understand

- When and why HIV infected individuals should start antiretroviral therapy.
- If there are exceptional situations to general recommendations.

When To Start Antiretroviral Therapy

Balance *is* tipping in favour of earlier initiation, due to evidence that supports the importance of preserving immunity, decreasing inflammation and prevention of HIV transmission.

Before

- Drug toxicity
- Preservation of limited Rx options
- Cost

Now

- Harmful effects of uncontrolled viremia at all CD4 levels
- Increased treatment options: improved potency, tolerability, durability, simplicity
- Increased ability to suppress multidrug resistance virus and decrease emergence of resistance
- Prevents HIV transmission

When To Start Antiretroviral Therapy

ART is recommended:

- For treatment of HIV infection regardless of CD₄ count.
- To prevent the transmission of HIV (e.g. pregnancy, individuals at risk to transmitting to sexual partners).

There are significant clinical benefits and minimal demonstrated harm with early initiation.

When To Start Antiretroviral Therapy

- ART initiation should be seen as an elective priority.
- It is important that the individual is ready to commit to ART, understands benefits and risks of being on treatment and the importance of adherence to treatment.
- Patients not ready to start ART should remain in care, with regular monitoring and ongoing discussion about need for ART.

When To Start Antiretroviral Therapy

- Offer ART to all patients with acute or early infection, regardless of symptoms.
- Start as soon as possible to maximize benefit.
- Reduced pro-viral DNA, lower viral set point, and robust immune reconstitution are benefits of early initiation of ART.
- Planned interruption or discontinuation is not recommended.
- ART is not recommended in the elite controller (i.e. naturally controlled undetectable HIV plasma viral load) with a normal CD₄ count.

Timing of Starting ART

- In patients with opportunistic infections and AIDS defining illnesses, ART should be started as soon as possible, preferably within the first 2 weeks of diagnosis.
- However, the optimal timing for patients with cryptococcal meningitis and tuberculosis (TB) meningitis is unclear, and should involve management by experts.

Data to support early ART initiation

- Recent data supports the initiation of ART regardless of CD4 count.
- The international START INSIGHT trial demonstrated a 57% reduction in serious AIDS events, serious non-AIDS events, or death when ART was initiated immediately (CD4 > 500 cells/uL) versus delaying until CD4 count was < 350 cells/uL. The benefit was seen regardless of age, gender, race, or region of the world.

Data to support early ART initiation

- The TEMPRANO trial conducted in Africa also demonstrated that starting ART with CD₄ >500 cells/uL reduced the risk of serious illness including tuberculosis (TB), and death, by 44% when compared to delaying treatment initiation according to World Health Organization (WHO) guidelines at the time.
- These results align the benefits to individual patients with the public health benefit of ART in reducing the risk of viral transmission.

ART to prevent transmission

- An additional benefit of early ART initiation is the decreased risk of HIV transmission
- For example, the HPTN 052 study demonstrated a 93% reduction in HIV transmission within serodiscordant couples (i.e. one HIV-positive, one HIV-negative individual) when ART was started in the HIV-positive partner earlier (CD₄ 350 to 550 cells/uL) compared to delaying until CD₄ was <250 cells/uL.

Summary

- Early initiation of ART is recommended for all HIV-infected individuals to prevent disease progression (regardless of CD₄ count)
- ART is also recommended for HIV-infected individuals to prevent transmission of HIV.