

HIV Treatment Guidelines

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Available Guidelines

- US DHHS : Department of Health and Human Services
- IAS-USA : International AIDS Society
- BHIVA : British HIV Association
- EACS: European AIDS Clinical Society
- WHO: World Health Organization



What the Guidelines Address

- Laboratory testing
- When to start treatment
- What medications to start
- When to change therapy
- Treatment of special populations
- Treating co-infected patients
- Medication side effects and drug interactions



When to Start Therapy

What to Start

When to Change Therapy



Treatment Initiation Over Time

| | 1998 | 2001 | 2002 | 2004 | 2007 | 2009 | 2012 |
|-----------|-------------|-------------------------------------------|-------------------------------------------|-------------------------------------------|----------------------------|-----------------------------------------|-------------------------------------------------------|
| CD4 Count | Treat: <500 | Treat: <200 Offer: <350 Indiv. >350 | Treat: <200 Offer: <350 Indiv. >350 | Treat: <200 Offer: <350 Indiv. >350 | Treat: <350 Indiv. >350 | Treat: <350 Rec: <500 Indiv. >500 | Treat everyone <350 (AI) <500 (AII) >500 (BIII) |
| VL | >20,000 | | >55,000 | >100,000 | | | |



When to Start Treatment

- Therapy is recommended in all patients
 - <350 cells/mm³ (AI)
 - 350 – 500 cells/mm³ (AII)
 - >500 cells/mm³ (BIII)
- Regardless of CD4 count
 - Pregnancy (AI)
 - AID-defining illness (AI)
 - HIV associated nephropathy (AII)
 - HIV/HBV co-infection(AII)

Recommendation Rating

A – Strong
B – Moderate
C – Optional

Evidence Rating

I – Randomized controlled trials
II – Well designed observational trials with long-term outcomes
III – Expert opinion



When to Start Treatment

- ART should be offered to those at risk of transmitting to
 - a heterosexual partner (AI)
 - other transmission risk groups (AIII)
- Patients starting ART should be willing and able to commit to treatment and should understand the benefits/risks of therapy and importance of adherence (AIII)



Benefits of Early Treatment

- Maintain higher CD4 count to prevent damage to the immune system
- Decrease risk of HIV associated complications
 - Opportunistic infections
 - Underlying inflammation
- Decrease risk of transmission



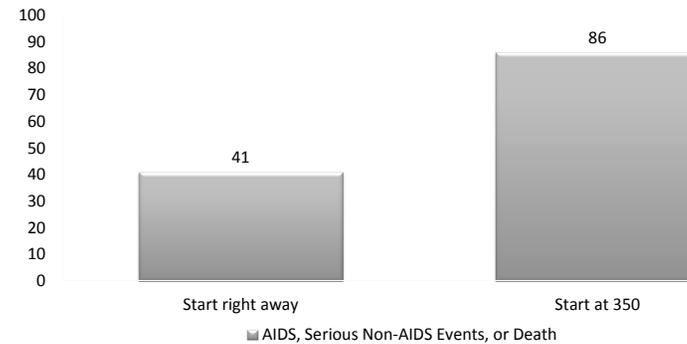
START Study

- International Study
 - 215 sites in 35 countries
- 4,685 patients with CD4 counts above 500 enrolled
 - Half started medications right away
 - Half waited till CD4 dropped below 350

<http://www.niaid.nih.gov/news/newsreleases/2015/Pages/START.aspx>



START Study Results

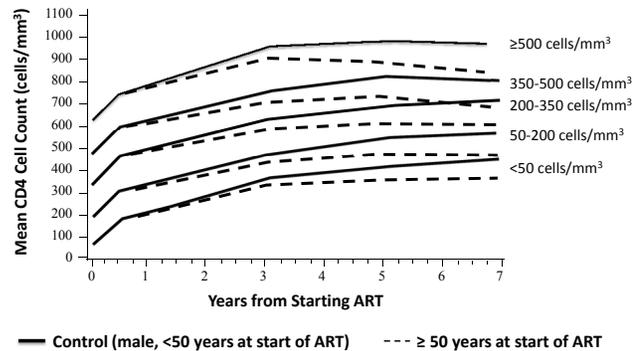


<http://www.niaid.nih.gov/news/newsreleases/2015/Pages/START.aspx>



Increase in CD4 Count

Median CD4 Response in Patients ≥ 50 Years at the Start of ART



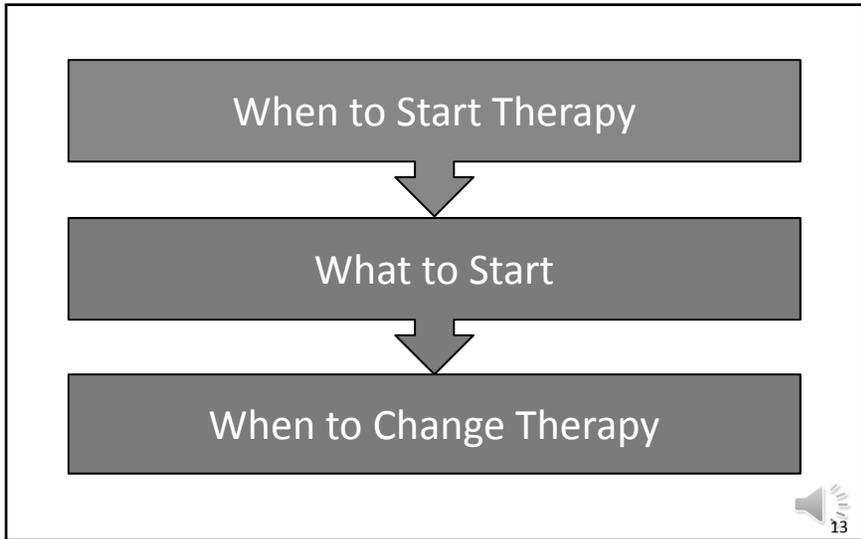
Gras L et al. *J Acquir Immune Defic Syndr*. 2007;45(2):183-192.



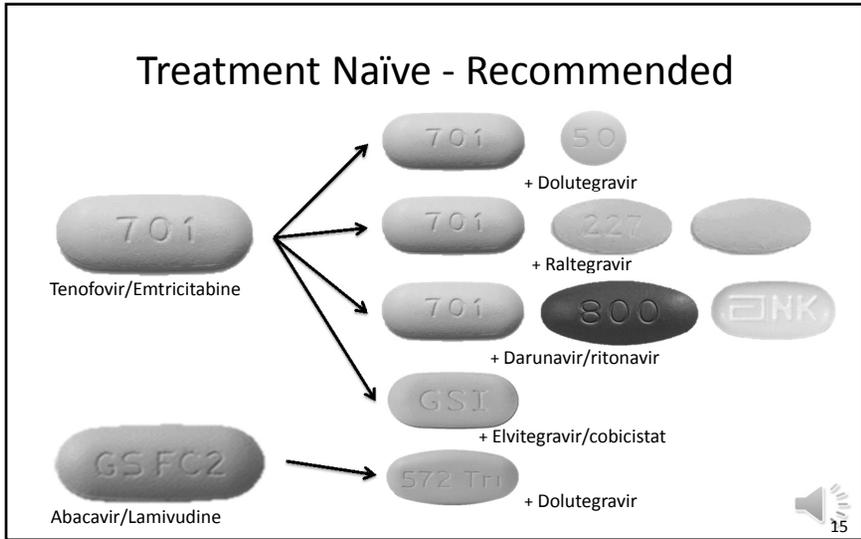
Risk of Early Treatment

- Development of treatment related side effects
- Less time for patient readiness assessment
- Increase total time on medications
 - Greater chance of pill fatigue
 - More long term side effects of medications
- Longer opportunity to develop resistant virus if not adherent to medications





- ### Treatment Naïve - Recommended
- Integrase Inhibitor Based
 - Dolutegravir/abacavir/lamivudine
 - Dolutegravir + tenofovir/emtricitabine
 - Elvitegravir/cobicistat/tenofovir/emtricitabine
 - Raltegravir + tenofovir/emtricitabine
 - Protease Inhibitor Based
 - Darunavir/ritonavir + tenofovir/emtricitabine
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- ### Treatment Naïve - Alternative
- NNRTI Based
 - Efavirenz/tenofovir/emtricitabine
 - Rilpivirine/tenofovir/emtricitabine
 - Protease Inhibitor Based
 - Atazanavir + (cobicistat or ritonavir) + tenofovir/emtricitabine
 - Darunavir + (cobicistat or ritonavir) + abacavir/lamivudine
 - Darunavir/cobicistat + tenofovir/emtricitabine
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Treatment Naïve – Treatment Selection Factors

- Baseline resistance testing and viral load
- Patient anticipated adherence
- Other health conditions
 - Kidney disease, heart disease
 - Pregnancy
 - Hepatitis co-infections
- Side Effects
- Drug interactions
- Patient's daily schedule and meal times



Treatment Experienced

- Resistance testing
- Antiretroviral medication history
 - Side effect history
 - Allergies
 - Adherence/possible resistance
- All treatment naïve factors



What Not to Start

- Mono or Dual Therapy
- Triple NRTI therapy



Not Recommended as Part of a Regimen

- Reyataz + Crixivan
- Videx EC + Zerit / Viread
- Sustiva in first trimester or in women with significant child-bearing potential
- Emtriva + Efavirenz
- Intelence + Unboosted PI
- Intelence + Boosted Reyataz, Lexiva or Aptivus
- Viramune with CD4 outside of recommended range
- Zerit + Retrovir
- Unboosted Prezista, Invirase or Aptivus



When to Start Therapy



What to Start



When to Change Therapy



Reason For Therapy Changes

- Viral Failure
- Side Effects
- Drug Interactions
- Comorbidities
- Reduce Pill Burden
- Pregnancy
- Cost/Insurance



Viral Failure

- Possible Causes
 - Suboptimal adherence
 - Pharmacokinetic issues
 - Possible drug resistance
- New regimen selection is based on cause of regimen failure and remaining antiretroviral options



Can I Go Back To My Old Regimen?

- Resistance/Viral Failure
 - No
- Side Effects, Drug Interactions, Comorbidities
 - Depends on the clinical picture
- Pill burden, Pregnancy, Cost/Insurance
 - Likely



Interruptions in Therapy

- Stop all antiretrovirals at once
 - Spacing them out only leads to resistance
- In patients with hepatitis B, treatment interruptions can lead to a hepatitis flare
- Always refer patient back to their medication provider



Drug Holidays

- If a patient's immune system is strong is it possible to stop medication for a period of time to decrease medication side effects?
- Short answer: No



SMART Study

- 5,472 patients enrolled
 - Half took medications continuously
 - Half took medications till their CD4 count was >350, then stopped till <250
- Results
 - Those who took medication holidays were 2.5x more like to have a clinical event or death



Summary

- All patient should be offered medications regardless of CD4 count
- Treatment regimens should have 3 active medications
- Regimens should be designed to fit the patient
- Interruptions in therapy should be avoided

