Based on Thai Guideline, Asymptomatic HIV จะเริ่มยาต้านไวรัสเมื่อใด?

A. CD4 > 500
B. CD4 < 500
C. CD4 < 350
D. CD4 < 200
E. เมื่อใดก็ได้เมื่อผู้ป่วยพร้อม

Lab ใครบ้างที่ต้องตรวจในผู้ป่วย newly diagnosed HIV?

A. CD4
B. Viral load
C. HBs Ag
D. HCV Ab
E. VDRL
F. CXR
G. LFT
H. Pap smear in women
I. Lipid profiles

A. AZT
B. TDF
C. 3TC, FTC
D. NVP
E. IDV
F. RTV
G. ddi
H. d4T
I. EFV
J. LPV

ยาคู่ใดที่ไม่ใช้ร่วมกัน

A. AZT+d4T
B. AZT+3TC
C. AZT+TDF
D. ddi + d4T
E. FTC+3TC
F. TDF +ddi
G. TDF+3TC

A. AZT
B. d4T
C. TDF
D. NVP
E. EFV
F. LPV/r
G. IDV/r

A. CNS side effect
B. Nephrolithiasis
C. Lipoatrophy
D. Diarrhea
E. Anemia
F. Fanconi syndrome
G. Hepatitis and rash
**GENERAL KNOWLEDGE OF HIV**

**AIDS Mortality Rates: 1996-2001**

![Graph showing mortality rates and ART utilization](image1)


![Graph showing incidence of AIDS and death](image2)

**Trends in Annual Rates of Death from Leading Causes of Death Among Persons 25-44 Years Old, USA, 1982-1998**

![Graph showing trends in annual death rates](image3)

**ARV miracle**

Before antiretroviral therapy, September 2000 ©Partners In Health

After antiretroviral therapy, December 2000 ©Partners In Health
**Intervention for human diseases: per-person survival gains (months)**

Walensky R. JID 2006;194:11-9

**Survival of Person with and without HIV infection**

Lohse N. Ann Intern Med 2007;146:87-95

**Survival of Patients with CD4 Counts ≥500 cells/mm³ for >5 Years is Similar to the General Population**

APROCO and AQUITAINE cohorts


**NA-ACCORD: Increasing Life Expectancy in North American HIV+ Pts on HAART**

- Analysis of 23,730 HIV+ pts in NA-ACCORD, on ART, with recent active data available
  - Estimated life expectancy at age 20 yrs increased in later periods

**Life Expectancy of HIV-Positive Patients**

- Comparison of life expectancy of Athena cohort patients to general population (n=4174)
- Age at week 24, country of birth and stage B symptoms were associated with a higher risk of death
- Expected life years remaining at age 25 was 53.1 (44.9-59.5) for general population and 52.7 for asymptomatic HIV+ patients
- The modeled life expectancy of patient presenting at an older age and women were slightly lower that general population

Adherence to a PI-containing regimen correlates with HIV RNA response at 3 months.

Peterson, et al. 6th Conference on Retroviruses and Opportunistic Infections; 1999; Chicago, IL.

What Degree of Adherence Is Needed?

N = 50 in each group

Fischl et al 8th CROI, 2001 abstract 528

\[ p < 0.01 \]

When to Start: 2012 DHHS Guidelines

Commitment to Adhere ARV

When to Start: 2012 BHIVA Guidelines

<table>
<thead>
<tr>
<th>CD4+ Cell Count</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; 350 cells/mm³</td>
<td>Start ART (1A)</td>
</tr>
<tr>
<td>350-500 cells/mm³</td>
<td>Delay ART</td>
</tr>
</tbody>
</table>

Recommend to start ART

- AIDS-defining illness
- Pregnancy
- HIV-related co-morbidity (HIVAN)
- HBV coinfection
- HCV coinfection
- Non-AIDS malignancy requiring chemotherapy
- Serodiscordant couples
- Primary HIV infection (neurological involvement, AIDS, confirmed CD4<350)

European Guideline 2013

<table>
<thead>
<tr>
<th>Condition</th>
<th>Current CD4 count</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asymptomatic HIV</td>
<td>≤350 C C</td>
</tr>
<tr>
<td>Symptomatic HIV disease</td>
<td>R R</td>
</tr>
<tr>
<td>Primary HIV infection</td>
<td>C C</td>
</tr>
<tr>
<td>Pregnancy</td>
<td>R R</td>
</tr>
<tr>
<td>HIV associated condition</td>
<td></td>
</tr>
<tr>
<td>Neurocognitive impairment</td>
<td>R R</td>
</tr>
<tr>
<td>Hodgkin's lymphoma</td>
<td>R</td>
</tr>
<tr>
<td>HPV associated cancers</td>
<td>R</td>
</tr>
<tr>
<td>Non-AIDS defining cancers</td>
<td>C C</td>
</tr>
<tr>
<td>Autoimmune diseases</td>
<td>C C</td>
</tr>
<tr>
<td>High-risk for CVD or history of CVD</td>
<td>C C</td>
</tr>
<tr>
<td>Chronic viral hepatitis</td>
<td></td>
</tr>
<tr>
<td>HBV requiring treatment</td>
<td>R</td>
</tr>
<tr>
<td>HCV for which anti-HCV treatment is being considered or given</td>
<td>R</td>
</tr>
</tbody>
</table>

When to Start in Adults

<table>
<thead>
<tr>
<th>TARGET POPULATION (ARV-NAIVE)</th>
<th>2010 ART GUIDELINES</th>
<th>2013 ART GUIDELINES</th>
<th>STRENGTH OF RECOMMENDATION &amp; QUALITY OF EVIDENCE</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV+ ASYMPTOMATIC</td>
<td>CD4 &lt;350 cells/mm³</td>
<td>CD4 &lt;350 cells/mm³ (CD4 ≤350 cells/mm³ as a priority)</td>
<td>Strong, moderate-quality evidence</td>
</tr>
<tr>
<td>HIV SYMPTOMATIC</td>
<td>WHO clinical stage 3 or 4, regardless of CD4 cell count</td>
<td>No change</td>
<td>Strong, moderate-quality evidence</td>
</tr>
<tr>
<td>PREGNANT AND BREASTFEEDING WOMAN WITH HIV</td>
<td>CD4 &lt;350 cells/mm³ or WHO clinical stage 3 or 4, regardless of CD4 cell count</td>
<td>Regardless of CD4 cell count or WHO clinical stage</td>
<td>Strong, moderate-quality evidence</td>
</tr>
<tr>
<td>HIV/TB CO- INFECTION</td>
<td>Presence of active TB disease, regardless of CD4 cell count</td>
<td>No change</td>
<td>Strong, low-quality evidence</td>
</tr>
<tr>
<td>HIV/HBV CO- INFECTION</td>
<td>Evidence of chronic active HBV disease, regardless of CD4 cell count</td>
<td>Evidence of severe chronic HBV liver disease, regardless of CD4 cell count</td>
<td>Strong, low-quality evidence</td>
</tr>
<tr>
<td>HIV+ PARTNERS IN SD COUPLE</td>
<td>No recommendation established</td>
<td>Regardless of CD4 cell count or WHO clinical stage</td>
<td>Strong, high-quality evidence</td>
</tr>
</tbody>
</table>

Summary of Changes in WHO Recommendations

When to Start in Adults

<table>
<thead>
<tr>
<th>Clinical Category</th>
<th>CD4</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>AIDS</td>
<td>Any</td>
<td>Treat</td>
</tr>
<tr>
<td>Symptomatic HIV</td>
<td>Any</td>
<td>Treat</td>
</tr>
<tr>
<td>Asymptomatic HIV</td>
<td>&lt;350</td>
<td>Treat</td>
</tr>
<tr>
<td>Pregnancy</td>
<td>Any</td>
<td>Treat, D/C after delivery if CD4&gt;350</td>
</tr>
</tbody>
</table>

2010 Thailand Guidelines: Initiation of ART in the Chronically HIV-Infected Patient

<table>
<thead>
<tr>
<th>Clinical Category</th>
<th>CD4</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>AIDS</td>
<td>Any</td>
<td>Treat</td>
</tr>
<tr>
<td>Symptomatic HIV</td>
<td>Any</td>
<td>Treat</td>
</tr>
<tr>
<td>Asymptomatic HIV</td>
<td>&lt;350</td>
<td>Treat</td>
</tr>
<tr>
<td>Pregnancy</td>
<td>Any</td>
<td>Treat, D/C after delivery if CD4&gt;350</td>
</tr>
</tbody>
</table>

Thailand Guideline 2014?

- DHHS (Treat all CD4)
- WHO (Treat CD4 < 500)
- Conservative (Optional for CD4 350-500)
When to start: 2014 Thailand Guideline

<table>
<thead>
<tr>
<th>Conditions</th>
<th>CD4-cell count</th>
<th>Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV infection regardless of symptoms and co-infection</td>
<td>≤ 500</td>
<td>Recommended (BII)</td>
</tr>
<tr>
<td></td>
<td>&gt; 500</td>
<td>Recommend (AI)</td>
</tr>
</tbody>
</table>

- The following issue should be considered:
  - Asymptomatic: unclear individual benefit but clear public health benefit
  - Patients should be willing and able to commit to Tx, understand the benefit and risks of Tx and importance of adherence.
  - Providers may consider deferring Tx on the basis of clinical and/or psychological factors

Clinical conditions may have benefit with early ART (CD4 > 500 cells/mm³)

<table>
<thead>
<tr>
<th>Individual benefits</th>
<th>Public Health benefits</th>
</tr>
</thead>
<tbody>
<tr>
<td>TB/HIV co-infection (AII)</td>
<td>Serodiscordant couples (AI)</td>
</tr>
<tr>
<td>HIV/HIV co-infection with cirrhosis (AII)</td>
<td>Pregnancy (AI)</td>
</tr>
<tr>
<td>HCV/HIV co-infection with cirrhosis (BII)</td>
<td>TB/HIV co-infection</td>
</tr>
<tr>
<td>HIVAN</td>
<td>Acute HIV infection</td>
</tr>
</tbody>
</table>

Major Targets of Antiretroviral Agents

- RT Inhibitors:
  - NRTI: AZT, ddl, ABC, 3TC, FTC, d4T, TDF
  - NNRTI: NVP, EFV, ETR, RPV
  - PI: ATV, DRV, T20, IDV

- Integrase Inhibitor:
  - RAL, EGV, DTG

- Fusion Inhibitor:
  - AMD3100, T22

- CCR5 Inhibitor:
  - Maraviroc

- Entry Inhibitor:
  - CXCR4, AM0100, T22

Current ARV

<table>
<thead>
<tr>
<th>NRTI</th>
<th>NNRTI</th>
<th>PI</th>
<th>Entry inhibitor</th>
<th>Integrase inhibitor</th>
</tr>
</thead>
<tbody>
<tr>
<td>AZT</td>
<td>NVP</td>
<td>ATV</td>
<td>Fusion inhibitor</td>
<td>RAL</td>
</tr>
<tr>
<td>ddl</td>
<td>EFV</td>
<td>DRV</td>
<td>T20</td>
<td>EGV</td>
</tr>
<tr>
<td>ABC</td>
<td>ETR</td>
<td>FPV</td>
<td>DTG</td>
<td></td>
</tr>
<tr>
<td>3TC</td>
<td>RPV</td>
<td>IDV</td>
<td></td>
<td></td>
</tr>
<tr>
<td>FTC</td>
<td>LVP/Vv</td>
<td></td>
<td>Maraviroc</td>
<td></td>
</tr>
<tr>
<td>d4T</td>
<td>NFV</td>
<td>TDF</td>
<td></td>
<td></td>
</tr>
<tr>
<td>TDF</td>
<td>RTV</td>
<td>TPV</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Antiretroviral therapy

- **HAART**: Highly Active Anti-Retroviral Therapy
- **cART**: Combined Antiviral Therapy
  - 2 NRTI + 1NNRTI
  - 2 NRTI + PI
  - 2 NRTI + Integrase inhibitor

chronic illness programme for the treatment of HIV

- Anti-retroviral Therapy (ART)
  - Treatment of Opportunistic Infections (OIs)
  - Treatment of Hyperlipidemia
- Laboratory Testing
- Voluntary Counseling & Testing
- Positive Prevention
HAART or cART
NNRTI based regimens

- d4T or AZT
- 3TC or FTC
- ddI or ABC or TDF

ARV components Not recommended as initial therapy

<table>
<thead>
<tr>
<th>ARV</th>
<th>Reasons</th>
</tr>
</thead>
<tbody>
<tr>
<td>ABC/ddI</td>
<td>Insufficient data in treatment naive pts</td>
</tr>
<tr>
<td>ABC/TDF</td>
<td>Insufficient data in treatment naive pts</td>
</tr>
<tr>
<td>ddI/TDF</td>
<td>High rate of virologic failure</td>
</tr>
<tr>
<td></td>
<td>Rapid selection of resistance mutations</td>
</tr>
<tr>
<td>ddI + d4T</td>
<td>High incidence of toxicities</td>
</tr>
<tr>
<td>d4T + AZT</td>
<td>Antagonism in vitro and in vivo</td>
</tr>
<tr>
<td>FTC + 3TC</td>
<td>Similar resistance profiles</td>
</tr>
<tr>
<td></td>
<td>Minimal additive antiviral activity</td>
</tr>
</tbody>
</table>

Fixed Combination drugs

- d4T+3TC+NVP= GPO VIR-S
- AZT+3TC+NVP= GPO VIR-Z
- AZT+3TC= Zilarvir
- d4T+3TC= Lastavir
- TDF+FTC= Truvada, Ricovir EM
- LPV+RTV= Lopinavir
- TDF+FTC+EFV= Atevir
- TDF+FTC+EFV= Atripla

Boosted PI

- SQV 3x3
- RTV 6x2 (refrigerate)
- IDV 2x3 (q 8 hr with empty stomach)
- LPV/r
- ATV
- DRV

- SQV/r 1000/100 BID
- IDV/r 400/100 BID
- LPV/r 400/100 BID
- ATV/r 200-300/100 OD
- DRV/r 800/100 OD

Thailand 2014: Guidelines for Initial ARV Regimens

Rationale: One Regimen For All

Preferred 1st line regimen: TDF + 3TC (or FTC) + EFV

- Simplicity: regimen is very effective, well tolerated and available as a single, once-daily FDC and therefore easy to prescribe and easy to take for patients – facilitates adherence
- Harmonizes regimens across range of populations (Adults, Pregnant Women (1st trimester), TB and Hepatitis B)
- Safety in pregnancy
- Efficacy against HBV and less risk of hepatic toxicity with EFV
- EFV is preferred NNRTI for people with HIV and TB (pharmacological compatibility with TB drugs)

Antiretroviral Pregnancy Registry: Birth Defects With First Trimester Exposure

- Enrols ~ 1500 women exposed to ART each yr (80% US)\(^3\)
- 13,507 live births with follow-up data through July 2011
- Overall birth defect prevalence comparable to CDC population-based surveillance data: 2.9 per 100 live births vs 2.72
- No specific birth-defect patterns detected
- In separate small study, no growth or bone abnormalities in infants whose mothers took TDF in pregnancy\(^5\)

ART and Birth Defects in ANRS French Perinatal Cohort

- French national prospective multicenter cohort studying PMTCT strategies in HIV-positive women\(^1\)
- 2.72% of HIV-positive women in France
- 13,114 live births exposed to ART in utero across 17 centres, TB regimens across range of populations (Adults, Pregnant Women (1st trimester), TB and Hepatitis B)
- Findings consistent with meta-analysis of studies of EFV use\(^2\) in pregnancy and data from the US Antiretroviral Pregnancy Registry\(^3\)

<table>
<thead>
<tr>
<th>Defects/Live Births, n (%) of First Trimester Exposures</th>
<th>Overall Birth Defects χ²</th>
<th>P vs EFV</th>
<th>P vs ZDV</th>
</tr>
</thead>
<tbody>
<tr>
<td>EFV</td>
<td>12/1276</td>
<td>1.1 (0.8-1.1)</td>
<td>0.31</td>
</tr>
<tr>
<td>ZDV</td>
<td>18/1276</td>
<td>3.5 (2.2-5.1)</td>
<td>0.001</td>
</tr>
</tbody>
</table>

Specific organ system defects χ²: P = .08


- In EFV first trimester-exposed infants, T risk for neurologic (but not neural tube) defects but not for overall birth defects
- In ZDV first trimester-exposed infants, T risk for both overall birth defects and heart defects

HBV/HIV COINFECTION

HCV/HIV COINFECTION

TDF/XTC* EFV

If patients cannot tolerate NNRTIs

AZT/3TC* ABC/3TC* RPV NVP

ATV/r

XTc= FTC or 3TC

* Preferred STR (single-tablet regimen) or fixed dose combination pill

<table>
<thead>
<tr>
<th>Key 3rd Drug</th>
<th>Dual NRTI</th>
<th>NNRTI</th>
</tr>
</thead>
<tbody>
<tr>
<td>TDF/XTC*</td>
<td>EFV</td>
<td>LPV/r</td>
</tr>
<tr>
<td>AZT/3TC*</td>
<td>ABC/3TC*</td>
<td>RPV</td>
</tr>
<tr>
<td>ATV/r</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

1. The Antiretroviral Pregnancy Registry.
Laboratory Monitoring Schedule:

<table>
<thead>
<tr>
<th>Test</th>
<th>Entry into care</th>
<th>FU before ART</th>
</tr>
</thead>
<tbody>
<tr>
<td>CD4</td>
<td></td>
<td>Q.6 m</td>
</tr>
<tr>
<td>HIV RNA</td>
<td>Optional</td>
<td></td>
</tr>
<tr>
<td>Hepatitis B profile</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hepatitis C</td>
<td></td>
<td></td>
</tr>
<tr>
<td>LFT</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CBC</td>
<td>Q.6 m</td>
<td></td>
</tr>
<tr>
<td>Lipid profile</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fasting BS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>VDRL</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CKR</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pap smear</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**MONITORING HIV**

**Laboratory Monitoring Schedule:**

<table>
<thead>
<tr>
<th>Test</th>
<th>Entry into care</th>
<th>FU before ART</th>
</tr>
</thead>
<tbody>
<tr>
<td>CD4</td>
<td></td>
<td>Q.6 m</td>
</tr>
<tr>
<td>HIV RNA</td>
<td>Optional</td>
<td></td>
</tr>
<tr>
<td>Hepatitis B profile</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hepatitis C</td>
<td></td>
<td></td>
</tr>
<tr>
<td>LFT</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CBC</td>
<td>Q.6 m</td>
<td></td>
</tr>
<tr>
<td>Lipid profile</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fasting BS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>VDRL</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CKR</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pap smear</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Difference due to more failures with RPV vs EFV:

- More virologic failures with RPV vs EFV: 14% vs 8%
  - Differences due to more failures between Wks 48-96 failure rates comparable between Arms from Wks 48-96
  - Development of NRTI mutations more common with RPV vs EFV
  - EFV
drug resistance with ETR

- Discontinuation for AEs more common with RPV vs EFV: 9% vs 4%
Pooled ECHO/THRIVE Analysis: Wk 96 Safety

<table>
<thead>
<tr>
<th>Adverse Event, %</th>
<th>Rilpivirine (n = 686)</th>
<th>Efavirenz (n = 682)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Most common adverse events of interest</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Any neurologic</td>
<td>17 38*</td>
<td>8 27*</td>
</tr>
<tr>
<td>• Dizziness</td>
<td>16 24*</td>
<td>8 13*</td>
</tr>
<tr>
<td>• Any psychiatric</td>
<td>4 15*</td>
<td>7 16*</td>
</tr>
<tr>
<td>Grade 2-4 laboratory abnormality</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Total cholesterol</td>
<td>7 22*</td>
<td>7 18*</td>
</tr>
<tr>
<td>• LDL-C</td>
<td>6 10</td>
<td>6 11</td>
</tr>
<tr>
<td>• AST</td>
<td>6 10</td>
<td>6 11</td>
</tr>
<tr>
<td>• ALT</td>
<td>6 10</td>
<td>6 11</td>
</tr>
</tbody>
</table>

*P < .0001 vs rilpivirine.  
†P < .0000 vs rilpivirine.


Open-Label StAr Trial: RPV/TDF/FTC Noninferior to EFV/TDF/FTC at Wk 48

- RPV/TDF/FTC noninferior to EFV/TDF/FTC in overall population and in pts with baseline HIV-1 RNA > 100,000 c/mL
- RPV/TDF/FTC superior to EFV/TDF/FTC in pts with baseline HIV-1 RNA ≤ 100,000 c/mL


Switching From EFV/TDF/FTC to RPV/TDF/FTC in Suppressed Patients

- Single-arm study of 50 patients virologically suppressed on EFV/TDF/FTC as first regimen for ≥ 3 mos
  - No virologic resistance mutations in study pts
  - No switch to salvage treatment of regimen
- 100% maintained HIV-1 RNA ≤ 50 c/mL at Wk 12 after switch to RPV/TDF/FTC (primary endpoint)
- No events leading to discontinuation after switch
- RPV mean C_{trough} within target range by 2 wks


RPV/TDF/FTC Indications

---------------------------------------------------------------------INDICATIONS AND USAGE---------------------------------------------------------------------

COMPLERA: a combination of 2 nucleoside analog HIV-1 reverse transcriptase inhibitors (emtricitabine and tenofovir disoproxil fumarate) and 1 non-nucleoside reverse transcriptase inhibitor (rilpivirine), is indicated for use as a complete regimen for the treatment of HIV-1 infection in treatment-naïve adult patients with HIV-1 RNA less than or equal to 100,000 copies/mL. (1)

- DHHS guidelines 2013(2)
  - RPV is not recommended in patients with pretreatment HIV-1 RNA > 100,000 copies/mL
  - Higher rate of virologic failures reported in patients with pre-ART CD4+ cell count < 200 cells/mm³ who were treated with RPV + 2 NRTIs.


Efavirenz

- Advantage
  - Long track record
  - High efficacy
  - Convenience
  - Forgiving of missed dose

- Disadvantage
  - CNS adverse effects
  - Risk of resistance with treatment interruption
  - Lower CD4+ cell count increase than with other drug classes
    - Lipids
    - Vitamin D?
**Ripilvirine**

- **Advantage**
  - Once daily
  - Small pill
  - Less lipids
  - Less CNS side effects
  - Low cost

- **Disadvantage**
  - Less effective in HIV RNA > 100,000 c/mL
  - High failure rate in CD4 <200 cells/mm³

**Nevirapine**

<table>
<thead>
<tr>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>No food effect</td>
<td>Higher incidence of rash (SJS, TEN)</td>
</tr>
<tr>
<td>Less lipid effects than EFV</td>
<td>Higher incidence of hepatotoxicity</td>
</tr>
<tr>
<td>Contraindicated in pts with moderate or severe hepatic impairment (Child Pugh B or C)</td>
<td></td>
</tr>
<tr>
<td>Higher risk of hepatotoxicity in treatment naive with high CD4</td>
<td>Less clinical data than EFV</td>
</tr>
</tbody>
</table>

**Risk of NVP Hepatotoxicity by CD4+ Count and Sex**

- Women
  - 1.2% Symptomatic Hepatic Events
  - 0.9% Asymptomatic Hepatic Events

- Men
  - 0.9% Symptomatic Hepatic Events
  - 0.5% Asymptomatic Hepatic Events

**Drug Specific Toxicities**

- **Lamivudine (300mg OD or 3TC 150mg BID)**
  - Lactic acidosis

- **Emtricitabine (200mg)**

- **Tenofovir (TDF 300mg OD)**
  - Renal toxicity
  - Fanconi syndrome, hypokalemia, hypophosphatemia
  - Lactic acidosis
  - Bone loss early

- **Abacavir (ABC 300mg BID or 600mg OD)**
  - Hypersensitivity (HLA-B 5701) in 3-5%, no re-challenge
  - Lactic acidosis

**Management of d4T side effects**

- **Lipoatrophy**: use low dose of d4T
  - change to AZT or TDF

- **Dyslipidemia**: change to AZT or TDF

- **Peripheral neuropathy**: change to AZT or TDF

- **Pancreatitis**: D/C medication change to AZT

- **Lactic acidosis**: D/C medication

- **Stavudine (d4T 30mg BID)**
  - Neuropathy
  - Lipoatrophy
  - Dyslipidemia: hypertriglyceridemia
  - Hepatitis
  - Lactic acidosis
  - Ascending motor weakness: "ascending neuromuscular weakness", some associated with elevated lactate levels resemble Guillain Barré syndrome
  - one case of myositis
Drug Specific Toxicities

- **Zidovudine (AZT 200-300mg BID)**
  - 5% grade III/IV nausea
  - Anemia/leucopenia
  - Headache
  - Myopathy
  - Lactic acidosis
  - Fat atrophy
  - Blue nails

- **Management**
  - Start AZT in healthy patients
  - Follow CBC both short term and long term
  - If anemia change to TDF or ddI or d4T

- **Didanosine (ddI BW< 60 kg, 250mg, BW>60kg, 400 mg OD ac)**
  - Diarrhea (sachet > tablet with buffer >enteric coat), need to be taken on empty stomach
  - Nausea, diarrhea
  - Pancreatitis (rare)
  - Neuropathy especially with d4T
  - Lactic acidosis especially with d4T, contraindicate used with d4T in pregnancy

- **Indinavir (IDV 400-800/r100 BID)**
  - GI: N/V, hyperbilirubinemia
  - Skin disorders: alopecia, dry skin, toenail
  - Nephrolithiasis
  - Renal dysfunction
  - Lipodystrophy
  - Metabolic complications
    - Lipid abnormalities
    - Insulin resistance
    - Osteopenia
  - Need to monitor FBS BUN Cr UA q 6 mo.

Lopinavir/ritonavir

<table>
<thead>
<tr>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coformulated</td>
<td>GI side effect with diarrhea, nausea</td>
</tr>
<tr>
<td>Once or twice daily dosing in treatment naive</td>
<td>Once-daily dosing not recommended in pregnant women</td>
</tr>
<tr>
<td>No food restriction</td>
<td>Lower drug exposure in pregnant women - may need dose increase in 3rd trimester</td>
</tr>
<tr>
<td>Recommended PI in pregnant women</td>
<td></td>
</tr>
<tr>
<td>Greater CD4 cell count increase than EFV</td>
<td>(EFV)</td>
</tr>
</tbody>
</table>

Metabolic Complications

- **Lipoatrophy**
  - facial fat pads lost
  - legs, buttocks, arms prominent
  - subcutaneous veins
  - pseudocachexia

- **Mitochondrial Toxicity**
  - Lipid abnormalities
  - Dysregulation in glucose metabolism
  - Body fat redistribution
  - Bone
Lipoatrophy: Risk Factors

- Almost certainly interrelated
- Antiretroviral therapy
  - Thymidine analogue exposure (d4T > AZT)
  - EFV used
- Host factors
  - Age
- HIV disease factors
  - Duration of illness
  - Severity of illness: AIDS, low CD4+ cell count

ARV-Associated Adverse Effects: Lactic Acidosis/Hepatic Steatosis

- Possibly due to mitochondrial toxicity
- Associated with NRTIs (especially d4T, ddl, AZT)
- Clinical presentation variable: have high index of suspicion
- Lactate >2-5 mmol/dL plus symptoms
- Treatment: discontinue ARVs, supportive care

Risk factors for hyperlactatemia

- Use of d4T + ddl
- Use of either d4T, ddl or AZT
- ddl + hydroxyurea
- ddl + ribavirin
- Treatment > 6 months
- Female gender
- Pregnancy
- Decreased CCr <70 ml/min
- Obesity
- High baseline body mass index

Management of hyperlactatemia

- Hyperlactatemia
  - lactate >5-10 mmol/l: nucleoside analogues withdrawal
  - Tenofovir, abacavir, 3TC regimens
- Lactic acidosis
  - nucleoside analogues withdrawal
  - treatment of metabolic acidosis
  - Cofactors (thiamine, riboflavin, L-carnitine)
  - antioxidants (vitamin C and E, co-enzyme Q10)

ARV-Associated Adverse Effects: Hyperlipidemia

- Elevations in total cholesterol, LDL, and triglycerides
- Associated with all PIs (except ATV), d4T, EFV
- Mechanism unknown
- Consequences uncertain: concern for cardiovascular events, pancreatitis
- Monitor: Chol, Trig, HDL, LDL q 6mo
- Treatment: consider ARV switch; lipid-lowering agents (caution with PI + certain statins)

ARV-Associated Adverse Effects: Hyperglycemia

- Insulin resistance, hyperglycemia, and diabetes associated with all PIs, cARV, thymidine (d4T, AZT) especially with chronic use
- Mechanism not well understood
  - Insulin resistance, relative insulin deficiency
- Consider regular screening via fasting glucose
**ARV and Mitochondrial toxicity**

**Lactic acidosis and Lipodystrophy**

- d4T
- ddl
- AZT
- FTC
- ABC
- TDF

**Lipohypertrophy**

- IDV, RTV
- any bPIs
- ATV

---

**ARV failure**

**Criteria for failure**

- **Virological failure**
- **Immunological failure**
- **Clinical failure**

---

**Clinical failure**

- Occurrence or recurrence of HIV-related events (after at least 3 months on ART, except pulmonary TB)
- Excluding immune reconstitution syndrome
- Late
- Unreliable: some patients demonstrate discordant responses in virologic, immunologic and clinical parameters

---

**Factors associated with immunologic failure**

- CD4 < 200/mm³ when starting ART
- Older age
- Coinfection (e.g. HCV)
- Medication both ARV (AZT, TDF+ddI) and other medication
- Persistent immune activation
- Loss of regenerative potential of immune system

---

**Important of percentage of CD4**

<table>
<thead>
<tr>
<th></th>
<th>White blood cell</th>
<th>% lymphocyte</th>
<th>Absolute lymphocyte</th>
<th>% CD4</th>
<th>Absolute CD4 cell</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>8000</td>
<td>40%</td>
<td>3200</td>
<td>10%</td>
<td>320</td>
</tr>
<tr>
<td></td>
<td>4000</td>
<td>40%</td>
<td>1600</td>
<td>10%</td>
<td>160</td>
</tr>
</tbody>
</table>

---

8/2/2014
Virologic Definitions

- **Virologic suppression**: A confirmed HIV RNA level below the limit of assay detection (e.g., <48 copies/mL).
- **Virologic failure**: The inability to achieve or maintain suppression of viral replication (to an HIV RNA level <200 copies/mL).
- **Incomplete virologic response**: Two consecutive plasma HIV RNA levels >200 copies/mL after 24 weeks on an ARV regimen.

Immunological failure

- **Immunological failure**: no acceptable definition
  - CD4 increase < 50 cells/mm³ after 1 year of treatment
  - CD4 drop > 30% from maximum value or > 3%
  - CD4 drop down below baseline
  - CD4 <350 cells/mm³ after 4-7 years of HAART

Risk of AIDS and non-AIDS complication are increase especially with CD4 < 200 cells/mm³

- No consensus recommendation for immunological failure

In clinically stable patients with suppressed viral load, CD4 count can be monitored every 6–12 months

DHHS Guideline 2011

**Frequent CD4+ Count Monitoring Not Necessary for Pts With CD4+ > 300**

- Retrospective review of VA laboratory database of >25,000 paired VL and CD4+ counts from 1998-2011 unique pts
- Eligible pts had "sequence"; consecutive VL/CD4+ pairs with
  - VL < 200 copies/mL
  - CD4+ count > 300 cells/mm³
  - %CD4+ > 14
  - < 300 days between CD4+ counts
- Analysis of pts with sequences (n=846) who experienced CD4+ "dips" <200 during periods of virologic suppression (n=61)
  - 24 with clinical causes of lymphopenia

- Virologically suppressed pts with CD4+ > 300 extremely unlikely to have CD4+ count dip < 200
- CD4+ testing may be undertaken less frequently in these pts

Expected Goal

Virological response

Virological suppressed

Virological failure

Virological rebound

Persistent low level viremia

Virological Blip

Stopping drugs with different half-lives may lead to periods of monotherapy

HIV STAR study

- Randomized, open-label, multicenter trial

HIV STAR Study: LPV/r With or Without TDF + 3TC Following Failure of First-line NNRTI

SECOND-LINE: LPV/RTV + RAL vs LPV/RTV + NRTIs After First-line VF

- Randomized, open-label, international, multicenter trial

SECOND-LINE: Noninferiority of LPV/RTV + RAL vs LPV/RTV + NRTIs

- Pooled pt data from ACTG A5142, A5202, A5208 of those failing first-line boosted PI regimens found 131/200 (66%) remained on same regimen.
- Various regimen changes: n = 69
- HIV-1 RNA < 400 c/mL at Wk 24 similar between pts who maintained same regimen and those who switched
- Pts with highest resuppression rates were those with higher CD4+ counts at regimen change and those who had ever responded to first regimen
- Suggests better adherence

EARNEST: Second-Line LPV/RTV-Based ART After Initial NNRTI Failure

- Randomized, controlled, open-label, phase III trial
- Baseline demographics (medians): HIV-1 RNA 69,782 copies/mL; CD4+ 71 cells/mm³; time on ART, 4 yrs
- P = .59

VACCINATION IN HIV PATIENTS

EARNEST: Clinical Outcomes at Wk 96

- “Good disease control” at Wk 96 defined as pt alive, no new WHO 4 events from Wks 0-96, CD4+ cell count > 200 cells/µL, and HIV-1 RNA < 10,000 copies/mL or > 10,000 copies/mL without PI resistance mutations

### ARV IN PATIENTS WITH OI

<table>
<thead>
<tr>
<th>Role of ARV</th>
<th>Dosage</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Induction phase</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tenofovir</td>
<td>245 mg PO</td>
<td>1x daily</td>
</tr>
<tr>
<td>Lamivudine</td>
<td>300 mg PO</td>
<td>1x daily</td>
</tr>
<tr>
<td>Efavirenz</td>
<td>200 mg PO</td>
<td>1x daily</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Consolidation phase</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tenofovir</td>
<td>300 mg PO</td>
<td>1x daily</td>
</tr>
<tr>
<td>Lamivudine</td>
<td>300 mg PO</td>
<td>1x daily</td>
</tr>
<tr>
<td>Efavirenz</td>
<td>200 mg PO</td>
<td>1x daily</td>
</tr>
</tbody>
</table>

### Other Considerations

- **Induction phase:** Tenofovir, lamivudine, and efavirenz should be given in combination for induction therapy.
- **Consolidation phase:** Tenofovir, lamivudine, and efavirenz should be continued for consolidation therapy.
- **Monitoring:** Regular monitoring of CD4+ T-cell count and viral load is recommended.
- **Adjustments:** Adjustments to the ARV regimen may be necessary based on the patient's response and side effects.
SAPiT: Optimal Time to Initiate ART in HIV/TB-Coinfected Patients


### Significantly Improved Outcomes With Integrated HIV and TB Treatment

- 56% lower rate of death associated with concurrent ART and TB treatment (early ART)
- Mortality: HR: 0.44 (95% CI: 0.25-0.79; P = .003)
  - Early ART: 5.4/100 person-yrs
  - Sequential ART: 12.1/100 person-yrs

### SAPiT: Increased Survival With Concurrent HIV and TB Treatment

**SAPiT: Early vs Late ART Initiation During Integrated TB/ART Therapy**

- **Early integrated:** ART started within 4 wks of starting TB Rx
- **Late integrated:** ART started within 4 wks of completing TB Rx intensive phase
- 46% lower AIDS/death rate with early integrated Rx in patients with CD4+ count ≥ 50 cells/mm³

**CAMELIA: ART Initiation at Wk 2 vs Wk 8 of TB Therapy in HIV-Coinfected Patients**

- **WHO 2010 guidelines recommend**
  - Initiate HAART in all HIV-infected patients with TB, regardless of CD4+ cell count
  - Initiate TB therapy before HAART, with HAART added as soon as possible
- **CAMELIA:** randomized, open-label trial of HIV-infected patients with newly-diagnosed AFB-positive TB and CD4+ cell count ≥ 200 cells/mm³
- **Compared HAART initiation (d4T + 3TC + EFV) at**
  - Wk 2 (n = 332) vs
  - Wk 8 (n = 329) of TB therapy
- **All patients received standard TB therapy for 6 mos**
- **Baseline median CD4 25 cell/uL and HIV RNA 5.6 log₁₀/mL**

**STRIDE Study (ACTG 5221): Immediate vs Early ART Initiation in TB Patients**

- Stratified by CD4+ cell count
  - CD4+ count ≤ 50 cells/mm³
  - CD4+ count ≥ 50 cells/mm³

**CAMELIA: Survival With Early vs Late Therapy in TB-Coinfected Patients**

- **Factors Independently Associated With Mortality**
  - Late therapy
  - BMI
  - Karnofsky score
  - NTM
  - Rifampicin

- **Significantly higher incidence of IRIS with early vs late HAART**
  - 4.03 vs 1.44 per 100 person-mos, respectively (P < .0001)
ACTG A5164: Improved Outcomes With Immediate ART During Acute OI

- 92% treatment naive
  - Median baseline CD4+ cell count
    25 cells/mm³; HIV-1 RNA 5.07 log₁₀ copies/mL
- OIs with effective antimicrobial therapy only: PCP, bacterial infections, cryptococcal disease, MAC, toxoplasmosis
- Median duration from start of OI treatment to initiation of HAART
  - Immediate group: 12 days
  - Deferred group: 45 days

- Week 48 virologic outcomes similar between groups
- Safety and incidence of IRIS similar between groups

COAT: Increased Mortality With Early ART During CM Induction Therapy

- Significantly lower OS with early vs deferred ART1
  - Enrollment halted early by NIAID
  - Almost 50%

- Mortality associated with
  - Altered mental status at study entry
    (Glasgow Coma Scale score ≤ 12; HR: 2.0; P = .05)
  - Patients with CM WBC counts ≥ 5
    cells/mm³ at randomization (HR: 3.3; P < .05)

- In separate analysis of COAT data, reduced interferon gamma secretion associated with increased risk of IRIS or death2
  - Multivariate analysis of death or CM
    IRIS risk: OR per 2-fold increase
    0.85 (95% CI: 0.854-0.855; P = .054)


ACTG A5164: Immediate vs Deferred ART in Patients With Acute OIs

- Stratified by CD4+ cell count
  - or ≥50 cells/mm³
  - PDI, or other OI

- Immediate Antiretroviral Therapy
  - Initiation within 48 hours of randomization and within 14 days of starting OI treatment (n = 143)

- Deferred Antiretroviral Therapy
  - Initiation between Weeks 4 and 32 (n = 141)

*Patients with TB excluded.

COAT: Early vs Delayed ART in Tx-Naive Pts With Cryptococcal Meningitis

- Optimal timing of ART initiation after diagnosis of CM remains uncertain
  - Early ART associated with increased mortality in recent trials in resource-limited settings3
  - Earlier study showed improved outcomes with delayed versus deferred ART during acute CM4

- COAT study compared 26-week survival in tx-naive pts with first episode of CM who received early vs deferred ART initiation5


 rocker صاحะอกหมกสั่นๆ

- Primary prophylaxis สำหรับเชื้อเหมือน cryptococcosis, penicilliosis, histoplamosis และกระทั่ง MAC โดยไม่ได้ยินช่องทางใดๆที่ไม่มีข้อบังคับ อาจ สามารถให้เฉพาะรายที่ไม่สามารถยืนการรักษาด้วยการใช้ไวรัสได้วิว (optional)

- การนายเวียนเท้าใช้การใช้ยา CM ลื่นๆ— รับ ART หลังรักษา CM เด็ง 2-4 ชั่วโมงก่อน เทียบ Cryptococcal meningitis ได้รับ 4-6 ชั่วโมงก่อนการใช้ CM
**Time to Initiate ART in patients with OIs (after starting OI treatment)**

<table>
<thead>
<tr>
<th>Conditions</th>
<th>Time of initiation ART</th>
</tr>
</thead>
<tbody>
<tr>
<td>TB</td>
<td></td>
</tr>
<tr>
<td>CD4 ≤50</td>
<td>Within 2 wk</td>
</tr>
<tr>
<td>CD4 &gt;50</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Severe*</td>
</tr>
<tr>
<td></td>
<td>Non severe</td>
</tr>
<tr>
<td>Crypto</td>
<td>4-6 wk</td>
</tr>
<tr>
<td>PCP/MAC/Other OI</td>
<td>2-4 wk</td>
</tr>
<tr>
<td>CMV/PML/Cryptosporidiosis</td>
<td>ASAP</td>
</tr>
</tbody>
</table>

*Severe: Disseminated TB, BMI <16, Hb < 10, Karnofski <40
Adherence Is a Key Determinant of PrEP Trial Outcomes

In the large iPrEx, Partners PrEP, and Thai IDU studies, TFV was detected in blood samples of the majority of subjects who remained HIV uninfected during the study.

PrEP Trials Have Shown Efficacy in MSM, Heterosexual Men and Women, and IDUs

**Adherence Is a Key Determinant of PrEP Trial Outcomes**

<table>
<thead>
<tr>
<th>Study</th>
<th>HIV Seroconverters Detection of TFV in Plasma, %</th>
<th>HIV Uninfected Detection of TFV in Plasma, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>iPrEx(1)</td>
<td>51</td>
<td>51</td>
</tr>
<tr>
<td>Partners PrEP(2) TDF/FTC arm</td>
<td>81</td>
<td>81</td>
</tr>
<tr>
<td>Thai IDU(2)</td>
<td>67</td>
<td>67</td>
</tr>
</tbody>
</table>

This difference in TFV detection translated into a relative risk reduction of acquiring HIV: iPrEx: 92% (95% CI: 40% to 99%; P < .001) Partners PrEP TDF/FTC: 90% (95% CI: 56% to 98%; P = .002) Thai IDU: 70% (95% CI: 2% to 91%; P = .04)

PrEP (Like ART) Works When Taken

<table>
<thead>
<tr>
<th>Study</th>
<th>Blood Samples With TFV Detected, %</th>
<th>HIV Protection Efficacy in Randomized Comparison, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Partners PrEP(1)</td>
<td>81</td>
<td>75</td>
</tr>
<tr>
<td>TDF(2)</td>
<td>51</td>
<td>62</td>
</tr>
<tr>
<td>iPrEx(2)</td>
<td>67</td>
<td>64</td>
</tr>
<tr>
<td>Thai IDU(2)</td>
<td>&lt; 30</td>
<td>No HIV protection</td>
</tr>
</tbody>
</table>

2 additional trials of PrEP (FEM-PrEP and VOICE), both conducted among high-risk African women, did not demonstrate protection against HIV; in both trials, PrEP adherence was very low (< 30%)

PrEP Trials to Date: Negative Study

<table>
<thead>
<tr>
<th>Trial</th>
<th>Population/Setting</th>
<th>Intervention</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>FEM-PrEP(3) (N = 2130)</td>
<td>High-risk women in Africa</td>
<td>Daily oral TDF/FTC</td>
<td>Equal numbers of infections in active and control arms</td>
</tr>
<tr>
<td>VOICE(4) (N = 5039)</td>
<td>Women in Uganda, South Africa and Zimbabwe</td>
<td>Daily TDF gel Daily oral TDF and TDF Oral TDF/FTC</td>
<td>None proved to be effective</td>
</tr>
</tbody>
</table>

**(Participants)**


**Participants**

Male circumcision

<table>
<thead>
<tr>
<th>Study</th>
<th>Population and Intervention</th>
<th>No. of incidence HIV infection</th>
<th>Distribution of HIV incidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>ANRS 1265 trial</td>
<td>3128 uncircumcised, HIV neg, 18-24 year-old, reside in Orange Farm and surrounding area</td>
<td>18</td>
<td>20 (0.85 cases per 100 person-years)</td>
</tr>
<tr>
<td></td>
<td>1546 immediate circumcision</td>
<td>1582 delayed circumcision at end of follow-up</td>
<td>49</td>
</tr>
<tr>
<td></td>
<td>Mean follow up 18.1 months</td>
<td></td>
<td>60%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>76%</td>
</tr>
<tr>
<td>Rakai, Uganda</td>
<td>4996 uncircumcised men, HIV neg, 15-49 year-old</td>
<td>2474 immediate circumcision</td>
<td>22</td>
</tr>
<tr>
<td></td>
<td>2522 delayed circumcision for 24 months</td>
<td></td>
<td>45</td>
</tr>
<tr>
<td></td>
<td>Total follow-up time 24 months</td>
<td></td>
<td>51%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>60%</td>
</tr>
</tbody>
</table>

US Timothy Ray Brown, also known as “The Berlin Patient”, the first man to cure AIDS CCR5 Delta32/Delta32 Transplant

Clinical Course and HIV-1 Viremia in Berlin man

Very Early Triple-Drug ART Elicits “Functional Cure” in HIV-Infected Child

- Infant born to an untreated HIV-infected mother at 35 wks gestation via spontaneous vaginal delivery
  - Maternal HIV infection identified during labor via ELISA and Western blot
  - Infant HIV infection confirmed via HIV-1 DNA PCR, HIV-1 RNA analysis of 2 separate samples at 30 and 31 hrs of age
  - ZDV/3TC + NVP (at therapeutic dose) initiated at 31 hrs of age, continued for 7 days
  - ZDV/3TC + LPV/RTV continued from 7 days to 18 mos of age
  - HIV-1 RNA undetectable by Day 30
  - Mother removed patient from care at 18 mos of age

“Functional Cure” Child: Standard HIV-1 Assays Undetectable to Age 26 Mos

- ART regimens: ZDV/3TC + NVP (31 hours – 7 days)
  - ZDV/3TC + LPV/RTV (7 days – 18 months)
- Plasma VL on ART displayed typical biphasic decay from baseline VL 19,812 c/mL
  - VL undetectable by < 30d of age
  - VL remained undetectable though > 80d of age

- Assessments at Mos 24 and 26
  - Western blot negative
  - No HIV-specific CD8+ or CD4+ T-cell responses
  - Standard HIV-1 RNA and HIV-1 DNA undetectable
- By ultrasensitive assays
  - Mos 24: HIV-1 RNA < 50 c/mL
  - Mos 24: HIV-1 DNA < 200 c/mL
  - Mos 28: HIV-1 DNA < 200 c/mL

- Clinical trials of exposed infants treated with ART recommended

Detection of Human Immunodeficiency Virus Type 1 (HIV-1) Infection in the Child.


HIV controller (HIC) and post treatment controller (PTC)

- HIC < 1% of HIV who spontaneously control viremia to undetectable levels (without ARV)
- PTC: interrupting a prolonged antiretroviral therapy initiated close to primary HIV infection are able to control viremia afterwards.

Saéz-Cirion A. PLOS Pathogens 2013;9:e1003211

14 PTC. CD4 and viral load

Saéz-Cirion A. PLOS Pathogens 2013;9:e1003211

Early Treatment of Pts With Acute HIV Infection Restricts Seeding of Reservoirs

- RV254/SEARCH 010: ongoing, prospective, open-label study of subjects seeking voluntary HIV testing (n = 75 with Fiebig stage I-III acute infection)
  - Before ART, HIV reservoir seeding limited
    - Integrated HIV-1 DNA undetectable in PBMCs (92%) and sigmoid colon (98%) of most Fiebig I pts
    - Lower infection frequencies of central memory CD4+ T cells vs other memory cells
  - After ART, decline in HIV reservoir size
    - Integrated HIV-1 DNA undetectable in PBMCs in 90% of pts at 1 yr
    - Reservoir primarily in transitional and effector memory CD4+ T cells
- Suggests very early ART may prevent seeding of reservoirs


Thank you for your attention