Update 2013
HIV Treatment & Prevention

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Professor of Medicine,
Chulalongkorn University; and
HIV-NAT, Thai Red Cross AIDS Research Center
Time from HIV seroconversion to death

N=3823 from 8 cohorts

1079 deaths, 19,671 p-yrs of follow-up

Todd et al. AIDS 2007, 21 (suppl 6):S55–S63
Natural History of HIV Disease Progression

- **HIV Infection**
  - 90%: Typical Progressors (7-12 years)
  - <10%: Rapid Progressors (<3 years)
  - <1%: Long-term Non-progressors

Long-term Non-progressors:
- Normal, Stable CD4+ T cell count
- Viral load <500 copies/ml
## When to start ART by guidelines

<table>
<thead>
<tr>
<th>Guidelines</th>
<th>CD4</th>
<th>Note</th>
</tr>
</thead>
<tbody>
<tr>
<td>IAS-USA 2012</td>
<td>All</td>
<td>If patients ready to start</td>
</tr>
<tr>
<td>DHHS 2012</td>
<td>All</td>
<td>If patients ready to start</td>
</tr>
<tr>
<td>EACS 2011</td>
<td>≤500</td>
<td>Regardless of CD4 for specific settings</td>
</tr>
<tr>
<td>WHO 2010</td>
<td>≤350</td>
<td>And If patients ready to start</td>
</tr>
<tr>
<td>Thai 2010</td>
<td>≤350</td>
<td>If patients ready to start</td>
</tr>
<tr>
<td><strong>WHO 2013</strong></td>
<td>&lt;500</td>
<td></td>
</tr>
<tr>
<td>Thai 2013 (pending)</td>
<td>&lt;500</td>
<td></td>
</tr>
</tbody>
</table>
Three Decades of Learning and the Future

Evidences and developments

- **1981**
  - Few ARVs
  - More toxicity

- **late 1980**
  - More class ARVs
  - More potent – PIs
  - But high pill burden

- **Mid 1990**
  - Three ARVs (HAART)
  - Durable undetectable VL

- **2012**
  - Earlier HAART
  - ↓ non-AIDS death
  - ↓ Transmission
  - ↓ New TB

- **2022**
  - New strategies
  - Long-acting ARV?
  - Cure?

Availability and treatment options

- More new ARVs
- More tolerable
- More OD options
- More FDC options
- Single tablet regimens

- Monthly ARV? Cure?
When to start HAART

Clinical outcomes
No AIDS-complication + No non-AIDS-complication

CD4 cell count

Years After HIV Infection

START trial
CIPRA HT001

500
350
200
HIV Late Presenters (CD4<350) and advanced patients (CD4<200 or AIDS) remain a major challenge worldwide

- **UK**: 30-50% of patients had CD4<200 at baseline
- **USA**: Latino 76%, Black 58% had CD4<350
- **India**: up to 50% had CD4<200, up to 70% had CD4<350
- **Nigeria**: 50% CD4<200, 70% CD4<350
- **Thailand**: 44% CD4<50
- **sub-Saharan Africa**: 40% CD4<350

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1. *Int AIDS Soc. 2010; 13(Suppl 4): P107*
3. *Interdisciplinary Perspectives on Infect Dis 2012*
Incidence of IRIS Following HAART

10-15% in N. America and Europe
20-25% in resource-limited countries

Murdoch et al. AIDS Res Therapy 2007; 4:9
Timing of IRIS

Viral load

CD4

IRIS

Risk Factors
• Low BL CD4 count
• Rapid decline of VL
• Early timing of HAART following OI Rx

Time Following HAART

Weeks

Months

Years

Photo is from -Dhasmana et al. Drugs 2008; 68 (2): 191-208
## Optimal Timing to initiate HAART in Patients with Active OIs

<table>
<thead>
<tr>
<th>Active OIs</th>
<th>When to start</th>
<th>Remarks</th>
</tr>
</thead>
</table>
| Tuberculosis | **CD4 <50**\(^1,2\)  
Within 2 weeks of the Diagnosis  
**CD4 higher**  
By 8-12 weeks of the Diagnosis | **TB meningitis**\(^3\): is less certain  
Treatment at 2 wks had more severe AEs than at 8 wks of TB Rx |
| Cryptococcosis | Less certain | Early Rx (3 days) was associated with 2.85x risk of death vs 10 weeks\(^4\) |
| Other OIs | Within 2 weeks after OI diagnosis | |

What to Start

*Guidelines vs individualization*
Current Antiretroviral Agents

**RT Inhibitors**
- NRTI: AZT, ABC, ddI, d4T, 3TC, FTC
- NNRTI: NVP, EFV, ETV, RPV
- NTRTI: Tenofovir (TDF)

**Protease Inhibitors**
- SQV, rtv, IDV, NFV, AMV, LPV/rtv, ATV, fAMP, DRV

**HIV**
- **DNA**
- **RNA**
- **RT**
- **Integrate**
- **ds DNA**
- **Genomic RNA**
- **Proviral DNA**
- **mRNA**
- **Spliced mRNA**
- **Polyprotein Protein**

**Entry Inhibitors**
- CCR5 inhibitor: Maraviroc (MVC)
- Fusion gp41: Enfuvirtide

**Integrate inhibitors**
- Raltegravir (RAL)
- Elvitegravir
Current Available Antiretroviral Agents 2013

in Developed Countries (Available = 30)

NRTI = 8

Nucleos(t)ide RTIs
1. Zidovudine (ZDV)
2. Didanosine (ddI)
3. Zalcitabine (ddC)
4. Stavudine (d4T)
5. Lamivudine (3TC)
6. Abacavir (ABC)
7. Emtricitabine (FTC)
8. Tenofovir DF (TDF)

NNRTI = 5

Non-nucleoside RTIs
1. Nevirapine (NVP)
2. Delavirdine (DLV)
3. Efavirenz (EFV)
4. Etravirine (ETR)
5. Rilpivirine (RPV)

PI = 10

Protease Inhibitors
1. Saquinavir (SQV)
2. Ritonavir (RTV)
3. Indinavir (IDV)
4. Nelfinavir (NFV)
5. Amprenavir (APV)
6. Lopinavir/r (LPV/r)
7. Atazanavir (ATV)
8. Fosamprenavir (fAPV)
9. Tipranavir (TPV)
10. Darunavir (DRV)

EI = 2

Fusion Inhibitor
• Enfuvirtide (T-20)

CCR5 Antagonist
• Maraviroc (MVC)

Integrase inh = 3

Integrase Inhibitors
• Raltegravir (RAL)
• Dolutegravir*
• Elvitegravir

EI = 2

Integrase Inh = 3

Integrase Inhibitors
• Raltegravir (RAL)
• Dolutegravir*
• Elvitegravir

EI = 2

Boosters
• Ritonavir (RTV)
• Cobicistat* (cobi)

* In expanded access or submitted for regulatory approval
Current Use Antiretroviral Agents 2013
in Developed Countries (current use=17)

NRTI = 5

Nucleos(t)ide RTIs
1. Zidovudine (ZDV)
2. Lamivudine (3TC)
3. Abacavir (ABC)
4. Emtricitabine (FTC)
5. Tenofovir DF (TDF)

NNRTI = 4

Non-nucleoside RTIs
1. Efavirenz (EFV)
2. Etravirine (ETR)
3. Rilpivirine (RPV)
4. Nevirapine (NVP)

PI = 3

Protease Inhibitors
1. Lopinavir/r (LPV/r)
2. Atazanavir (ATV)
3. Darunavir (DRV)
4. Ritonavir (RTV) -booster

EI = 1

CCR5 Antagonist
• Maraviroc (MVC)

Integrase inh = 2

Integrase Inhibitors
• Raltegravir (RAL)
• Dolutegravir*
• Elvitegravir

Booster = 2

Boosters
• Ritonavir (RTV)
• Cobicistat* (cobi)

* In expanded access or submitted for regulatory approval
What to start in Resource-rich settings?

*Three drug combination in Naïve Patients*

2 Nucleoside RT Inhibitors + NNRTI or Boosted PIs

**NtRTI or NRTI**
- TDF
- ABC
- AZT
- d4T

**Cytidine Analog**
- FTC
- 3TC

**NNRTI or Boosted PIs**
- EFV
- Atazanavir/r
- Darunaivir/r
- Raltegravir
Virologic Responses of Commonly Used Third ARV for the Initial HAART

Data from various clinical trials of treatment-naïve patients
% of patients with VL<50 at 96 weeks except STARTMRK at 48 weeks (ITT)

*EFV, ATV/r, DRV/r superiority to LPV/r

ACTG 5142, CASTLE, ARTEMIS = 96 weeks, STARTMRK=48 weeks results

All combined with 2 NRTIs
Current Strategy and Trend
Prescribing a Simplify regimen

Once-daily
Single tablet regimen (STR)

Atripla® (TDF/FTC/EFV)  Stribild® (TDF/FTC/EVG/COBI)
Mylan Generic 3 in 1 (TDF/3TC/EFV) tested

The HIV
Netherlands Australia Thailand
Research Collaboration

Studies / 2012 / Pharmacokinetic Studies

Therapeutic Drug Monitoring (TDM) Studies
HIV-NAT 118

Therapeutic Drug Monitoring of the generic tenofovir/lamivudine/efavirenz tablets in the Thai HIV-infected Patient
This is a prospective, open-label, single arm study that assesses the efficacy and safety of fixed dose combination of TDF/3TC/EFV.

Status: Opened on February 2, 2010. Completed
Enrolled/Target: 100/100
Funding: Matrix Laboratory

Results: The generic FDC of TDF/3TC/EFV was well tolerated and efficacious. Our findings lend support to the use of this generic FDC as first-line antiretroviral therapy in resource limited settings.

For our Thai Setting

What to start?
What to start in Resource-limited settings?

*Three drug combination in Naïve Patients*

2 Nucleoside RT Inhibitors + NNRTI or Boosted PIs

- **NtRTI or NRTI**
  - TDF
  - AZT
  - d4T

- **Cytidine Analog**
  - 3TC
  - FTC

- **NNRTI or Boosted PIs**
  - EFV
  - NVP
Adherence is critical
Potential Concern When Stopping Drugs With Different Half-lives
Life-Threatening !!
*Preventable and Manageable*

Nevirapine associated
Steven-Johnson’s Syndrome (SJS)

*Courtesy of Dr. Pravit, Chulalongkorn Hospital, Bangkok*
A Lady with Very Severe CNS side-effect – couldn’t work and about to give-up her EFV-based HAART

EFV – severe CNS AEs with poor QoL

Currently she is happy with this regimen and has VL<50 for >2 yrs
EFV: Standard doses of Efavirenz associated with a higher exposure in Thais/Asians

Median AUC (h*mmg/L)

- Caucasian Std dose: 2.2
- Asian Std dose: 3
- Asian Lower Dose: 2.1

Ethnic and dosing

Std dose 600 mg/day
Lower dose 400 mg/day

van der Lugt J, and Avinhingsanon A. Asian Biomedicine Feb 2009
Ergotism and bPI is not common in patients who were well VL control and on bPIs.

Thai report
N=23
All had VL<50, CD4 >250
- 20 hospitalization (4-20 days)
- 3 gangrene
- 2 Amputation
- 1 death

bPI – Ergotamine AEs

a HCW case—was prescribed bPI as a PEP regimen

Avihingsanond A. et al in submission 2012
**boosted PI : WARNING**

Serious Drug Interaction

1. **Ergotism**: ergotamine
2. **Rhabdomyolysis**: statins (simvastatin, etc.) Alternatives: pravastatin, fluvastatin and fibrate derivatives
3. **Excessive sedation**: benzodiazepines (diazepam, alprazolam, midazolam,..) except lorazepam
4. **Hypotension**: Ca-blockers (amlodipine, nifedipine, felodipine), beta-blockers
5. **Cushing syndrome, adrenal insufficiency**: with fluticasone
6. **Torsades de Pointes** (prolong QT and ventricular arrhythmia): cisapride, pimozide; ditiazem; antiarrhythmic – flecanide, amiodarone, quinidine etc.
How to monitor properly?
Viral Relapse Following Discontinuation of HAART

Once Start we should not stop HAART

How to detect failure and DR?

Time-course of HAART Failure

Thai NHSO guidelines:
VL q 6 mo, until VL<50, then q 1 yr
CD4: q 6 mo, until CD4 >350, q 1 yr
Virologic Failure
“The inability to achieve or maintain suppression of viral replication”

<table>
<thead>
<tr>
<th>Setting</th>
<th>DHHS 2009</th>
<th>DHHS 2011</th>
<th>WHO 2009</th>
</tr>
</thead>
<tbody>
<tr>
<td>Incomplete suppression after 24 weeks</td>
<td>&gt;400*</td>
<td>&gt;200*</td>
<td>&gt;5000**</td>
</tr>
<tr>
<td>Virologic Rebound</td>
<td>&gt;50</td>
<td>&gt;200***</td>
<td>&gt;5000</td>
</tr>
</tbody>
</table>

*High Baseline VL (>100,000 c/ml) may take longer than low BL VL

**Values of >5 000 copies/ml are associated with clinical progression and a decline in the CD4 cell count

***>200 is associated with evidence of viral evolution and drug-resistance mutation accumulation
<table>
<thead>
<tr>
<th>Study</th>
<th>N</th>
<th>comparators</th>
<th>Sites</th>
<th>Sponsors</th>
<th>End point analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV-STAR</td>
<td>200</td>
<td>TDF/3TC +LPV/r, LPV/r mono</td>
<td>Thailand 10 sites</td>
<td>HIVNAT, NHSO, Swiss cohort</td>
<td>Nov 2011</td>
</tr>
<tr>
<td>SECOND-LINE</td>
<td>550</td>
<td>2NRTI +LPV/r, RAL +LPV/r</td>
<td>All continents 18 countries</td>
<td>Kirby Insitute, Australia</td>
<td>Sept 2012</td>
</tr>
<tr>
<td>ALISA</td>
<td>386</td>
<td>TDF/FTC +LPV/r, TDF/3TC +ATV/r</td>
<td>Africa SA, Tanzania</td>
<td>French NIH</td>
<td>May 2013</td>
</tr>
<tr>
<td>2LADY</td>
<td>450</td>
<td>TDF/FTC +LPV/r, ABC/ddI +LPV/r, TDF/FTC +DRV/r</td>
<td>Africa Burkina Faso, Cammarooun, Senegal</td>
<td>ANRS12169</td>
<td>Sep 2013</td>
</tr>
<tr>
<td>EARNEST</td>
<td>1277</td>
<td>2NRTIs +LPV/r, RAL +LPV/r, LPV/r mono</td>
<td>Africa 5 countries</td>
<td>MRC, EDCTP</td>
<td>Dec 2013</td>
</tr>
</tbody>
</table>

www.clinicaltrials.gov (assessed 22 Apr 2012)
**HIV-STAR Results**

(HIVNAT, TRC-ARC, Thailand initiated trial)

*Patients with baseline GSS ≥ 2 had a better VC rate* at 48 weeks of treatment

- **Mono LPV/r**
  - No. of subjects = 98
  - 61%

- **GSS 1**
  - No. of subjects = 19
  - 79%

- **GSS 2**
  - No. of subjects = 78
  - 83.3% 

*P < 0.05

Number of active ARV(s) in the regimen

SECOND-LINE results

Ritonavir-boosted lopinavir plus nucleoside or nucleotide reverse transcriptase inhibitors versus ritonavir-boosted lopinavir plus raltegravir for treatment of HIV-1 infection in adults with virological failure of a standard first-line ART regimen (SECOND-LINE): a randomised, open-label, non-inferiority study

SECOND-LINE Study Group*

Summary
Background Uncertainty exists about the best treatment for people with HIV-1 who have virological failure with first-line combination antiretroviral therapy of a non-nucleoside analogue (NNRTI) plus two nucleoside or nucleotide analogue reverse transcriptase inhibitors (NtRTI). We compared a second-line regimen combining two new classes of drug with a WHO-recommended regimen.

Methods We did this 96-week, phase 3b/4, randomised, open-label non-inferiority trial at 37 sites worldwide. Adults with HIV-1 who had confirmed virological failure (plasma viral load >500 copies per mL) after 24 weeks or more of first-line treatment were randomly assigned (1:1) to receive ritonavir-boosted lopinavir plus two or three NtRTIs (control group) or ritonavir-boosted lopinavir plus raltegravir (raltegravir group). The randomisation sequence was computer generated with block randomisation (block size four). Neither participants nor investigators were masked to allocation. The primary endpoint was the proportion of participants with plasma viral load less than 200 copies
SECOND-LINE Study

% patients with VL<200 c/ml

Patients failed NNRTI-regimens

Pros:
1. Not required DR test
2. Easy for trained non-medical staffs to deliver care (task shifting)
3. Easy for drug supply and stock
4. RAL is less toxicity than NRTS

Cons: RAL is expensive

Lancet 2013, June 15; 381: 2091–99
Life expectancy can be expanded for 52 years with HAART in patients diagnosed at 25 y-o.

**Life time HIV Care**

The success is highly depend also on the management of the **non-AIDS co-morbidity**.
Life Expectancy approaches normal in a High-income country after HAART

The Netherlands
N = 17,580 person-year
Median CD4 = 480 (24 wks of Dx)
Life expectancy from 25 yo
Men = 52.7 years
Women = 57.8 years

Life expectancy of recently diagnosed asymptomatic HIV-infected patients approaches that of uninfected individuals

van Sighem, Ard; Gras, Luuk; Reiss, Peter; Brinkman, Kees; de Wolf, Frank; on behalf of the ATHENA national observational cohort study
The life expectancy can be near normal with antiretroviral therapy, especially when ART was initiated at CD4 >150 cells.

**Uganda (N=22,315)**

<table>
<thead>
<tr>
<th>Age</th>
<th>Life Expectancy at 30 yo</th>
</tr>
</thead>
<tbody>
<tr>
<td>14–19 y</td>
<td>CD4 &lt;50 = 14 years</td>
</tr>
<tr>
<td>20–24 y</td>
<td>CD4 &gt;150 = 40 years</td>
</tr>
<tr>
<td>25–29 y</td>
<td></td>
</tr>
<tr>
<td>30–34 y</td>
<td></td>
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<tr>
<td>35–39 y</td>
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<tr>
<td>40–44 y</td>
<td></td>
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<tr>
<td>45–49 y</td>
<td></td>
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<tr>
<td>50–54 y</td>
<td></td>
</tr>
<tr>
<td>≥55 y</td>
<td></td>
</tr>
</tbody>
</table>

The table above details the life expectancy overall and by sex among persons receiving combination antiretroviral therapy in Uganda.
Thailand: Age and gender distribution
HIV/AIDS statistic, BOE, MOPH (data up to Nov 2011)
Emerging co-morbidities in HIV

Renal dysfunction
30% of HIV+ patients have abnormal kidney function\(^1\)

Reduced bone mineral density
Increased prevalence 63% of HIV+ patients\(^2\)

Cancer
Increased risk of non-AIDS-defining cancers e.g. anal, vaginal, liver, lung, melanoma, leukemia, colorectal and renal\(^5\)

Cardiovascular disease
75% increase in risk of acute MI\(^4\)

Neurocognitive dysfunction
Impairment present in \(\geq 50\)% HIV+ patients\(^3\)

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Lifetime HIV care
Requires an integrated multidisciplinary approach

- Cardiologist
- Hepatologist
- Plastic surgeon
- Nephrologist
- Neurologist
- Endocrinologist
- Nutritionalist
- Smoking cessation
- HIV physician
- Gynecologist

Adapted From Anna Maria Geretti. London
Biomedical HIV Prevention

What Works and What is underway

Kiat Ruxrungtham
Professor of Medicine
Faculty of Medicine, Chulalongkorn University; and
HIVNAT, Thai Red Cross AIDS Research Center
Opportunities for **Biomedical Preventions**

Prior to exposure

- Male circumcision
- Oral pre exposure prophylaxis (daily PrEP)
- Topical PrEP (daily gels or intra-vaginal rings (microbicides)
- Vaccines

Exposure (pre-coital/coital)

- Oral pre exposure prophylaxis (intermittent PrEP)
- Coitally dependent topical PrEP (microbicides)

Exposure (pre-coital/coital)

- Oral post exposure prophylaxis (PEP)

After infection

- Anti-retroviral therapy
- Immediate treatment of positive partners in discordant couples
- Treatment for prevention in all who test positive for HIV (T4P)

All have a behavioral and structural components

Modified from Shattock et al. IAS 2011 slides
Efficacy of HIV Prevention Strategies From Randomized Clinical Trials

<table>
<thead>
<tr>
<th>Study</th>
<th>Effect Size, % (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>HPTN 052, ART for prevention; Africa, Asia, Americas</td>
<td>96% (73-99)</td>
</tr>
<tr>
<td>Partners PrEP, PrEP for discordant couples; Uganda, Kenya</td>
<td>73% (49-85)</td>
</tr>
<tr>
<td>TDF2, PrEP for heterosexual men and women; Botswana</td>
<td>63% (21-84)</td>
</tr>
<tr>
<td>Medical male circumcision; Orange Farm, Rakai, Kisumu</td>
<td>54% (38-66)</td>
</tr>
<tr>
<td>iPrEX, PrEP for MSMs; Americas, Thailand, South Africa</td>
<td>44% (15-63)</td>
</tr>
<tr>
<td>Sexually transmitted diseases treatment; Mwanza, Tanzania</td>
<td>42% (21-58)</td>
</tr>
<tr>
<td>CAPRISA 004, Microbicide; South Africa</td>
<td>39% (6-60)</td>
</tr>
<tr>
<td>RV144, HIV vaccine; Thailand</td>
<td>31% (1-51)</td>
</tr>
</tbody>
</table>

N= 1,750 heterosexual serodiscordant couples in resource-constrained countries randomized to receive ART early (CD4 350-550 cells/μL) or defer until CD4 < 250 cells/μL.

<table>
<thead>
<tr>
<th>Event Rates</th>
<th>Early ART</th>
<th>Deferred ART</th>
<th>HR</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Transmission Rate per 100 pt-years (95% CI)</td>
<td>0.3 (0.1-0.6)</td>
<td>2.2 (1.6-3.1)</td>
<td>0.11 (0.04-0.32)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Clinical Event Rate per 100 pt-years (95% CI)</td>
<td>2.4 (1.7-3.3)</td>
<td>4.0 (3.5-5.0)</td>
<td>0.59 (0.40-0.88)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

PrEP Studies
Pre-Exposure Prophylaxis
PrEP studies with positive results

- **PARTNER**
  - N = 4747
  - Male, female
  - 82% TDF detected

- **TDF2**
  - N = 1219
  - Male, female
  - 79% TDF detected

- **iPrEX**
  - N = 2499
  - Male (MSM), TG
  - 51% TDF detected

Bars represent the percentage of TDF detected in each study.
PrEP studies with Negative results

FEM-PrEP  2012
VOICE    2013
FEM-PrEP showed failure in preventive efficacy

- N= 2120 African women
- The study showed no HIV protection using daily oral FTC/TDF
- The principal: the lack of adherence to the study medication
  - <30% of study participants having detectable tenofovir in blood samples

Van Damme et al., New England Journal of Medicine 2012
VOICE trial results showed no different in HIV acquisition in women on daily HIV prevention

CROI 2013: VOICE Trial Results on Daily HIV Prevention for Women

March 4, 2013 by San Francisco AIDS Foundation

Highly anticipated results were reported today from the VOICE trial, which looked at the safety and efficacy of daily oral PrEP and drug-containing vaginal microbicide gel in more than 5,000 women in South Africa, Uganda, and Zimbabwe.

Jeanne Marrazzo, MD, MPH, explained to a packed auditorium at the 20th Retrovirus Conference that these approaches did not prevent new HIV infections in this particular study because most participants didn’t actually use them.

When VOICE—short for Vaginal and Oral Interventions to Control the Epidemic—began enrolling women in September 2009, it randomized participants to use one of the following:

1. tenofovir gel
2. placebo gel
3. oral tenofovir tablet
4. oral Truvada (TDF/FTC)
5. oral placebo pill

Only 58% had detectable plasma TDF (low adherence)

“Low adherence was seen among younger, unmarried women who were most at risk for HIV.”

Condom use rate 87%

N = >5000
SF, Uganda, Zimbabwe
New PreP studies

- **Bangkok TDF Study** in PWID (IDUs): the results will be presented at the IAS HIV Pathogenesis conference 2013 at KL, Malaysia in July, and has published in Lancet June 13.
  - N= 2413, IDUs in Bangkok
  - TDF vs placebo

- **IPERGAY**
  - N= 1900 MSM (France, Canada)
  - TDF/FTC vs placebo
Antiretroviral prophylaxis for HIV infection in injecting drug users in Bangkok, Thailand (the Bangkok Tenofovir Study): a randomised, double-blind, placebo-controlled phase 3 trial

Kochit Choopanya, Michael Martin, Pravan Sunthorasami, Udomsak Sangkum, Philip A Mock, Manoj Leelachawalit, Sithisat Chiamwongpaet, Praphan Kitisin, Pitinan Natrujirote, Somyot Kittimunkong, Rutt Chuachowong, Roman J Gvetadze, Janet M McNicholl, Lynn A Paxton, Marcel E Curlin, Craig W Hendrix, Suphak Vanichseni, for the Bangkok Tenofovir Study Group

Summary
Background. Antiretroviral pre-exposure prophylaxis reduces sexual transmission of HIV. We assessed whether daily oral use of tenofovir disoproxil fumarate (tenofovir), an antiretroviral, can reduce HIV transmission in injecting drug users.

Methods. In this randomised, double-blind, placebo-controlled trial, we enrolled volunteers from 17 drug-treatment clinics in Bangkok, Thailand, between February 2007 and January 2009.

Results. 49% overall reduction in HIV incidence (from 0.68 to 0.35 /100 PY) in adherent individuals the reduction was increased to 71%
Future new options for PrEP *monthly injection*! may overcome the low adherence issue.

Long-acting monthly injection ARV under clinical development!

- **GSK744** (integrase inh) *and*
- **TMC278** (NNRTI)
Can we end AIDS epidemic?
Optimism *versus* Reality

It is not a time to question, but it a time to act smartly!
HIV Prevention Strategy

One size can’t fit all, we need smart tailors

- ART
- PrEP
- Male circumcision
- HIV testing
- Microbicide
- Behavior change

Tailored Prevention Package
Can we be the AIDS Free Generation?