30 Years of HIV/AIDS in Thailand: From Screening to Treatment and Prevention

• Introduction to AIDS in Thailand
• Epidemiology of HIV/AIDS in Thailand in 30 years
• Antiretroviral therapy and impact on survival in HIV-infected Thai patients
• Prevention and screening of HIV infection in 2013

Presenters:
• Somnuek Sungkanuparph
• Sasisopin Kiertiburanakul
• Darunee Chotiprasitsakul

Panelists:
• Boonmee Sathapatayavongs
• Kumthorn Malathum
• Siriorn Watcharananan
• Porpon Rotjanapan
• Maria Chitasombat
• Open up your mind
• Refine your attitude
• Doctors:
  We are not judging, we are saving lives.
• Patients:
  They do not need our forgiveness, they do need the benefit of our knowledge.

“A Story of AIDS in Thailand” photo assay by Matthew Williams
Burden of disease in Thailand: changes in health gap between 1999 and 2004

Kanitta Bundhamcharoen*, Patarapan Odton, Sirinya Phulkerd, Viroj Tangcharoensathien

Table 1 Top twenty causes of DALY loss, 2004, Thailand

<table>
<thead>
<tr>
<th>Top 20 ranking in men</th>
<th>Death (x1,000)</th>
<th>YLLs (x1,000)</th>
<th>YLDs (x1,000)</th>
<th>Top 20 ranking in women</th>
<th>Death (x1,000)</th>
<th>YLLs (x1,000)</th>
<th>YLDs (x1,000)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. HIV/AIDS</td>
<td>26.4</td>
<td>634.2</td>
<td>17.7</td>
<td>Stroke</td>
<td>26.1</td>
<td>267.0</td>
<td>48.5</td>
</tr>
<tr>
<td>2. Traffic accidents</td>
<td>23.5</td>
<td>548.6</td>
<td>42.7</td>
<td>HIV/AIDS</td>
<td>11.0</td>
<td>279.5</td>
<td>15.1</td>
</tr>
<tr>
<td>3. Stroke</td>
<td>23.8</td>
<td>282.6</td>
<td>54.0</td>
<td>Diabetes</td>
<td>14.0</td>
<td>183.7</td>
<td>108.8</td>
</tr>
<tr>
<td>4. Alcohol dependence/</td>
<td>1.0</td>
<td>18.1</td>
<td>315.2</td>
<td>Depression</td>
<td>0.0</td>
<td>0.0</td>
<td>191.5</td>
</tr>
<tr>
<td>harmful use</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5. Liver cancer</td>
<td>18.8</td>
<td>277.3</td>
<td>3.1</td>
<td>Ischaemic heart disease</td>
<td>11.5</td>
<td>129.6</td>
<td>10.7</td>
</tr>
<tr>
<td>6. Ischaemic heart disease</td>
<td>13.2</td>
<td>168.4</td>
<td>15.6</td>
<td>Osteoarthritis</td>
<td>0.2</td>
<td>1.2</td>
<td>129.9</td>
</tr>
<tr>
<td>7. COPD</td>
<td>13.5</td>
<td>124.8</td>
<td>58.6</td>
<td>Traffic accidents</td>
<td>5.1</td>
<td>115.4</td>
<td>10.8</td>
</tr>
<tr>
<td>8. Diabetes</td>
<td>8.2</td>
<td>101.6</td>
<td>79.3</td>
<td>Liver cancer</td>
<td>8.7</td>
<td>123.9</td>
<td>1.7</td>
</tr>
<tr>
<td>9. Cirrhosis</td>
<td>8.2</td>
<td>140.5</td>
<td>4.3</td>
<td>Deafness</td>
<td>-</td>
<td>-</td>
<td>110.7</td>
</tr>
<tr>
<td>10. Depression</td>
<td>-</td>
<td>-</td>
<td>136.9</td>
<td>Anaemia</td>
<td>0.0</td>
<td>0.2</td>
<td>109.3</td>
</tr>
</tbody>
</table>
Epidemiology of HIV/AIDS in Thailand in 30 years

Darunee Chotiprasitsakul
1984 first AIDS case

1984-1988, huge numbers of HIV infections and AIDS cases, resulting from multiple transmission routes; IDU, heterosexual, homosexual, and mother-to-child infection

44% of sex workers in Chiang mai were infected with HIV

100 percent condom programme

PMTCT

HAART

Ministry of Public Health, 2004

Millions of infections averted

Figure 1: Adult HIV Prevalence Rate (Ages 15–49), 2011

- <1% (98 countries)
- 1-5% (36 countries)
- 5-10% (4 countries)
- >10% (9 countries)
- NA

UNAIDS. Report on the Global AIDS Epidemic; 2012
Estimated HIV prevalence, ages 15-49

Global epidemiology of HIV infection in men who have sex with men (MSM)
Diagnoses of HIV Infection among Adults and Adolescents, by Transmission Category, 2011—United States and 6 Dependent Areas

N = 50,007

- Male-to-male sexual contact: 62%
- Injection drug use (IDU) – Males: 18%
- Injection drug use (IDU) – Females: 10%
- Male-to-male sexual contact and IDU: 5%
- Heterosexual contact\(^a\) – Males: 3%
- Heterosexual contact\(^a\) – Females: 3%
- Other\(^b\): <1%

Note. Data include persons with a diagnosis of HIV infection regardless of stage of disease at diagnosis. All displayed data have been statistically adjusted to account for reporting delays and missing transmission category, but not for incomplete reporting.

\(^a\) Heterosexual contact with a person known to have, or to be at high risk for, HIV infection.

\(^b\) Includes hemophilia, blood transfusion, perinatal exposure, and risk factor not reported or not identified.
Diagnoses of HIV Infection among Adults and Adolescents, by Sex and Transmission Category, 2011—United States and 6 Dependent Areas

Males
N = 39,495
- Male-to-male sexual contact: 78%
- Injection drug use (IDU): 12%
- Other: 6%
- Less than 1%

Females
N = 10,512
- Heterosexual contact: 86%
- Other: 14%
- Less than 1%

Note. Data include persons with a diagnosis of HIV infection regardless of stage of disease at diagnosis. All displayed data have been statistically adjusted to account for reporting delays and missing transmission category, but not for incomplete reporting.  

* Heterosexual contact with a person known to have, or to be at high risk for, HIV infection.  

* Other includes hemophilia, blood transfusion, perinatal exposure, and risk factor not reported or not identified.
HIV prevalence among MSM in Thailand, 2003-2010

HIV prevalence among female sexual worker in 2010 = 1.8%

National AIDS Prevention and Alleviation Committee (2010)
UNGASS Country Progress Report Thailand
Global epidemiology of HIV infection in injection drug users (IDUs)

HIV Prevalence among IDUs in Thailand, 2009

HIV Prevalence in 2010 from UNAIDS 21.9%

Number of people living with HIV

Annual number of AIDS death

## HIV/AIDS in 2011

<table>
<thead>
<tr>
<th></th>
<th>Global</th>
<th>Thailand</th>
</tr>
</thead>
<tbody>
<tr>
<td>Estimated total population, end 2011</td>
<td>7.0 billion</td>
<td>66.7 million</td>
</tr>
<tr>
<td>Total number of people living with HIV/AIDS in 2011</td>
<td>34.0 million</td>
<td>490,000</td>
</tr>
<tr>
<td>Children under 15 living with HIV/AIDS in 2011</td>
<td>3.3 million</td>
<td>N/A</td>
</tr>
<tr>
<td>New HIV/AIDS infections in 2011</td>
<td>2.5 million</td>
<td>9,700</td>
</tr>
<tr>
<td>Deaths due to AIDS in 2011</td>
<td>1.7 million</td>
<td>23,000</td>
</tr>
<tr>
<td>Estimated adult HIV prevalence</td>
<td>0.8%</td>
<td>1.2%</td>
</tr>
</tbody>
</table>

UNAIDS. Report on the Global AIDS Epidemic; 2012
Antiretroviral Therapy and Impact on Survival in HIV-infected Thai Patients

Somnuek Sungkanuparph, M.D.
Professor of Medicine
Division of Infectious Diseases, Department of Medicine
Faculty of Medicine Ramathibodi Hospital, Mahidol University
Survival of AIDS Patients by First Presenting Opportunistic Infections in Ramathibodi Hospital, Thailand, 1990-1994

Kaplan-Meier Survival Curve

Cryptococcosis

Tuberculosis

Toxoplasmosis

Other OIs

PCP

Effect of Antiretroviral Therapy

Virological response

Immunological response

Clinical response
• less illnesses
• improved weight
• better well being
• back to work
• better quality of life

Viral load vs. Time

CD4 vs. Time

Limit of detection

Somnuek Sungkanuparph – ISAAR 2013
Mortality and Frequency of HAART among HIV-infected Patients in the United States

Survival Rate and Risk Factors of Mortality Among HIV/Tuberculosis-Coinfected Patients With and Without Antiretroviral Therapy

Weerawat Manosuthi, MD,* Suthat Chottanapand, MD,* Supeda Thongyen, BSc.N,* Achara Chaovavanich, MD,* and Somnuek Sungkanuparph, MD†

Received ART, n = 411

Not received ART, n = 592

$P < 0.001$

(J Acquir Immune Defic Syndr 2006;43:42–46)
Survival Rate of HIV-infected Patients with Cryptococcosis in Thailand

Survival Rate of HIV-infected Patients with Cryptococcosis in Thailand

Proportion of patients without death from cryptococcosis

Study time (months)

Received ART

Not Received ART

$P < 0.001$

Received ART

No ART

No ART-censored

Received ART-censored

Evolution of Antiretroviral Therapy

Survival from age 25 years

- Population controls (HIV-negative)
- Current HAART (2006-2010)
- Late HAART (2000-2005)
- Early HAART (1997-1999)

Pre-HAART (1995-1996)

Age, years
0 25 30 35 40 45 50 55 60 65 70

Probability of Survival
0 0.25 0.5 0.75 1
More than 14 million people are estimated to be in need of treatment with antiretrovirals (ARVs), but less than half are on treatment.

### Access to Antiretroviral Therapy

<table>
<thead>
<tr>
<th>Region</th>
<th>Percent on ARVs as of the end of 2009</th>
</tr>
</thead>
<tbody>
<tr>
<td>Latin America/Caribbean</td>
<td>50%</td>
</tr>
<tr>
<td>Sub-Saharan Africa</td>
<td>37%</td>
</tr>
<tr>
<td>East/South/Southeast Asia</td>
<td>31%</td>
</tr>
<tr>
<td>Europe/Central Asia</td>
<td>19%</td>
</tr>
<tr>
<td>Middle East/North Africa</td>
<td>11%</td>
</tr>
</tbody>
</table>

Percent on ARVs as of the end of 2009 (of those in need of antiretroviral treatment in low- and middle-income countries)

Note: Globally less than half of people in need were on treatment as of the end of 2010.
ART coverage (%) in Patients with CD4 < 350 cells/mm$^3$

ART Scaling-up and AIDS Deaths

When to Start Antiretroviral Therapy

- Preservation of limited ART options
- Avoid drug toxicity
- Avoid risk of resistance if adherence is inadequate (and transmission of resistant viruses)
- Save cost

Delayed ART
When to Start Antiretroviral Therapy

Balance Now Favors Earlier ART

- Preservation of limited ART options
- Avoid drug toxicity
- Avoid risk of resistance if adherence is inadequate (and transmission of resistant viruses)
- Save cost

- Increase long-term survival
- Increase potency, durability, simplicity, safety of current ART
- More subsequent ART options
- Decrease toxicity with earlier ART
- Decrease risk of uncontrolled viremia at all CD4 count levels
- Decrease transmission

Delayed ART

Early ART
When to Start Antiretroviral Therapy
Balance for Thailand 2013

- Preservation of limited ART options
- **Avoid drug toxicity**
- Avoid risk of resistance if adherence is inadequate (and transmission of resistant viruses)
- **Save cost**

- Increase long-term survival
- Increase potency, durability, simplicity, safety of current ART
- More subsequent ART options
- Decrease toxicity with earlier ART
- Decrease risk of uncontrolled viremia at all CD4 count levels
- Decrease transmission

*Delayed ART*  \[\triangle\]  *Early ART*
Lipodystrophy Syndrome in Thai Patients

Association between *HLA-B*4001 and Lipodystrophy among HIV-Infected Patients from Thailand Who Received a Stavudine-Containing Antiretroviral Regimen

Wittaya Wangsomboonsiri, Surakameth Mahasirimongkol, Soranun Chantarangsu, Sasisopin Kiertiburanakul, Angkana Charoenyingwattana, Surat Komindr, Chupong Thongnak, Taisei Mushiroda, Yusuke Nakamura, Wasun Chanratita, and Somnuek Sungkanuparph

Departments of 1Medicine and 2Pathology, Faculty of Medicine Ramathibodi Hospital, 3Pharmacogenomics project under collaboration between Thailand Center of Excellence for Life Sciences, Mahidol University, Bangkok, 4Center for International Cooperation, and 5Medical Genetic Section, Department of Medical Sciences, Ministry of Public Health, Nonthaburi, Thailand; and 6Research Group for Pharmacogenomic, RIKEN, Center for Genomic Medicine, Tokyo, Japan
<table>
<thead>
<tr>
<th>Categories</th>
<th>Number of Patients</th>
<th>Proportion %</th>
</tr>
</thead>
<tbody>
<tr>
<td>National Health Security</td>
<td>85,994</td>
<td>80.34</td>
</tr>
<tr>
<td>Social Security Insurance</td>
<td>12,451</td>
<td>11.63</td>
</tr>
<tr>
<td>No Insurance</td>
<td>5,285</td>
<td>4.94</td>
</tr>
<tr>
<td>Government Employee</td>
<td>2,072</td>
<td>1.94</td>
</tr>
<tr>
<td>Others</td>
<td>916</td>
<td>0.86</td>
</tr>
<tr>
<td>Refugee</td>
<td>324</td>
<td>0.30</td>
</tr>
<tr>
<td>All</td>
<td>107,042</td>
<td>100</td>
</tr>
</tbody>
</table>
Current Antiretroviral Agents

HIV Medication Chart

Nucleoside/Nucleotide Analogue Reverse Transcriptase Inhibitors (NRTI)
- Emtriva* (emtricitabine, FTC)
- Epivir* (lamivudine, 3TC)
- Retrovir* (zidovudine, AZT, ZDV)
- Videx EC (didanosine, ddl)
- Viread (tenofovir, TDF)*
- Zerit* ( stavudine, d4T)
- Ziagen* (abacavir, ABC)

Protease Inhibitors (PI)
- Aptivus (tipranavir, TPR)
- Crixivan (indinavir, IDV)
- Invirase (saquinavir hard gel capsules, SQV)
- Kaletra* (lopinavir/ritonavir, LPV/r)
- Lexiva ( fosamprenavir, FPV)
- Norvir* (ritonavir, RTV)
- Prezista (darunavir, DRV)

Fixed Dose Combinations
- Atripla (TDF+FTC+EFV)
- Complivir (AZT plus 3TC)
- Epzicom (ABC plus 3TC)
- Trizivir (AZT plus 3TC plus abacavir)
- Truvada (TDF+FTC)

Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTI)
- IntENCIL (etravirine, ETV)
- Rescriptor (delavirdine, DLV)
- Sustiva* ( efavirenz, EFV)
- Viramune* ( nevirapine, NVP)

Entry Inhibitors
- Fuzeon (enfuvirtide, T-20)
- Selzentry (maraviroc, MVC)

Integrase Inhibitors
- Isentress (raltegravir, RAL)

All pills shown in actual size.

Medication brand names appear in bold. Generic names and commonly used abbreviations appear in parentheses.

* Also available in liquid form.
Guidelines for Antiretroviral Therapy in HIV-1 Infected Adults and Adolescents: The Recommendations of the Thai AIDS Society (TAS) 2008


1 Faculty of Medicine Ramathibodi Hospital, Mahidol University, Bangkok
2 Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok
3 Faculty of Medicine, Chulalongkorn University, Bangkok
4 Chonburi Hospital, Chonburi
5 Faculty of Medicine, Chiang Mai University, Chiang Mai
6 Faculty of Medicine, Khon Kaen University, Khon Kaen
7 Bamrasnaradura Infectious Diseases Institute, Ministry of Public Health, Nonthaburi
8 Faculty of Medicine, Srinakarinwirot University, Nakhon-Nayok
9 Vichaiyut Hospital, Bangkok, Thailand; and the president of the TAS
10 HIV-NAT, Thai Red Cross AIDS Research Centre, Bangkok

* Both share equal contribution as senior authors
Practice Guideline

Thai national guidelines for antiretroviral therapy in HIV-1 infected adults and adolescents 2010

Somnuck Sungkanuparph\textsuperscript{a}, Wichai Techasathit\textsuperscript{b}, Chitlada Utaipiboon\textsuperscript{c}, Sanchai Chasombat\textsuperscript{d}, Sorakij Bhakeecheep\textsuperscript{e}, Manoon Leechawengwongs\textsuperscript{f}, Kiat Ruxrunghatham\textsuperscript{g,h}, Praphan Phanuphak\textsuperscript{g,h}, for The Adults and Adolescents Committee of the Thai National HIV Guidelines Working Group

\textsuperscript{a}Faculty of Medicine Ramathibodi Hospital, Mahidol University, Bangkok 10400; \textsuperscript{b}Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok 10700; \textsuperscript{c}Global AIDS Program, Thailand MOPH-U.S. CDC Collaboration, Nonthaburi 11000; \textsuperscript{d}Bureau of AIDS, TB, and STIs, Department of Disease Control, Ministry of Public Health, Nonthaburi 11000; \textsuperscript{e}National Health Security Office, Bangkok 10210; \textsuperscript{f}Thai AIDS Society, Bangkok 10310; \textsuperscript{g}Faculty of Medicine, Chulalongkorn University, Bangkok 10330; \textsuperscript{h}HIV-NAT, Thai Red Cross AIDS Research Centre, Bangkok 10330, Thailand
Thai national guidelines for antiretroviral therapy in HIV-1 infected adults and adolescents 2010

Table 1. Indications for initiation of antiretroviral therapy (ART).

<table>
<thead>
<tr>
<th>Clinical Presentation</th>
<th>CD4+ T-cell counts (cells/mm³)</th>
<th>Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>AIDS-defining illness*</td>
<td>Any value</td>
<td>Treat</td>
</tr>
<tr>
<td>HIV-related Symptomatic**</td>
<td>Any value</td>
<td>Treat</td>
</tr>
<tr>
<td>Asymptomatic</td>
<td>&lt;350</td>
<td>Treat</td>
</tr>
<tr>
<td>Asymptomatic</td>
<td>≥350</td>
<td>Defer treatment; follow up clinical status and monitor CD4+ T-cell count every 6 months</td>
</tr>
<tr>
<td>Pregnancy</td>
<td>Any value</td>
<td>Treat, Discontinue ART after delivery if pre-treatment CD4+ T-cell count is ≥350 cells/mm³</td>
</tr>
</tbody>
</table>

*as described in the 1993 revised classification system for HIV infection and expanded surveillance case definition for AIDS among adolescents and adults [24] and with penicillosis, which is considered as AIDS-defining illness in Thailand [25]. **oral candidiasis, pruritic papular eruptions (PPE), unexplained fever or diarrhea > two weeks, >10% unexplained weight loss in 3 months, or herpes zoster involved > two dermatomes.
Thai national guidelines for antiretroviral therapy in HIV-1 infected adults and adolescents 2010

Table 2. Recommended preferred and alternative first ART regimens.

<table>
<thead>
<tr>
<th>NRTIs</th>
<th>NNRTIs</th>
<th>PIs</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Preferred</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AZT + 3TC</td>
<td>EFV(4)</td>
<td><strong>Preferred</strong></td>
</tr>
<tr>
<td>TDF + 3TC/FTC(1)</td>
<td>NVP(5)</td>
<td>(if patient cannot tolerate NNRTIs)</td>
</tr>
<tr>
<td><strong>Alternative</strong></td>
<td></td>
<td><strong>Alternative</strong></td>
</tr>
<tr>
<td>ABC + 3TC(2)</td>
<td>+</td>
<td>ATV/r</td>
</tr>
<tr>
<td>d4T + 3TC(3)</td>
<td></td>
<td>DRV/r</td>
</tr>
<tr>
<td>ddI + 3TC</td>
<td></td>
<td>SQV/r</td>
</tr>
</tbody>
</table>

All ARVs in the above table are listed in alphabetical order. (1) TDF should be used in caution in patients with abnormal creatinine clearance and in elderly patients. TDF + 3TC/FTC is recommended in patients with HBV co-infection [2]. (2) ABC can cause hypersensitivity reactions and should not be used with NVP. (3) d4T, if used, should be replaced with another NRTI after 6-12 months. (4) It cannot be used in the first trimester of pregnancy. (5) NVP should be used with caution in females with CD4+ T cell counts >250 cells/mm³.

S. Sungkanuparph, et al. Asian Biomedicine Vol. 4 No. 4 August 2010; 515-528
# Prevalence of HBV and HCV Infection in Thai HIV-infected Patients

<table>
<thead>
<tr>
<th>Residential areas</th>
<th>Number of patients</th>
<th>Co-infection with HIV</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>HBV</td>
<td>HCV</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>No.</td>
<td>Prevalence/100 (95% CI)</td>
<td>No.</td>
<td>Prevalence/100 (95% CI)</td>
</tr>
<tr>
<td>Bangkok*</td>
<td>311</td>
<td>29</td>
<td>9.3 (6.3-13.1)</td>
<td>28</td>
<td>9.0 (6.1-12.7)</td>
</tr>
<tr>
<td>Provincial areas*</td>
<td>218</td>
<td>17</td>
<td>7.8 (4.6-12.2)</td>
<td>13</td>
<td>6.0 (3.2-10.0)</td>
</tr>
<tr>
<td>- Central</td>
<td>111</td>
<td>9</td>
<td>8.1 (3.8-14.8)</td>
<td>7</td>
<td>6.3 (2.6-12.6)</td>
</tr>
<tr>
<td>- North</td>
<td>27</td>
<td>2</td>
<td>7.4 (0.9-24.3)</td>
<td>2</td>
<td>7.4 (0.9-24.3)</td>
</tr>
<tr>
<td>- Northeast</td>
<td>47</td>
<td>4</td>
<td>8.5 (2.4-20.4)</td>
<td>3</td>
<td>6.4 (1.3-17.5)</td>
</tr>
<tr>
<td>- South</td>
<td>7</td>
<td>2</td>
<td>28.6 (3.7-71.0)</td>
<td>1</td>
<td>14.3 (0.4-57.9)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>529</td>
<td>46</td>
<td>8.7 (6.4-11.4)</td>
<td>41</td>
<td>7.8 (5.6-10.4)</td>
</tr>
</tbody>
</table>

* No difference of prevalence of HBV or HCV infection between Bangkok and Provincial area, chi-square = 2.48, p value = 0.115

HBV Drug Resistance in HIV-infected Patients Receiving ART with Lamivudine (but not Tenofovir)

- ART had been rapidly scaled up in Thailand prior to availability of TDF.
- 84 HBV/HIV co-infected patients who had HIV RNA < 50 copies/ml with 3TC-containing ART (without TDF) in 2008.
- Median duration of ART = 45.5 months; median CD4 = 352 cells/mm³.
- Prevalence of 3TC resistance was 22.6% (19/84 patients).
- From multivariate analysis, duration (month) of 3TC use was associated with 3TC resistance [OR=1.045; 95% CI, 1.001-1.092, p=0.046].

<table>
<thead>
<tr>
<th>Drugs</th>
<th>HBV drug resistance mutations detected</th>
<th>Number of patients</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lamivudine</td>
<td>L80V/I, L180M/A181T, M204V, V173L</td>
<td>19</td>
<td>100%</td>
</tr>
<tr>
<td>Telbivudine</td>
<td>M204V/I, N236T</td>
<td>18</td>
<td>95%</td>
</tr>
<tr>
<td>Entecavir</td>
<td>L180M, A181T/V</td>
<td>16</td>
<td>84%</td>
</tr>
<tr>
<td>Adefovir</td>
<td>N236T, A181T/V</td>
<td>16</td>
<td>84%</td>
</tr>
<tr>
<td>Tenofovir</td>
<td>-</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

Treatment Failure

- Virological failure
- Immunological failure
- Clinical failure

CD4
HIV-RNA

Time

Criteria for failure

Somnuek Sungkanuparph – ISAAR 2013
Risk of Disease Progression/Death for Discordant Responders

Viral control may not be enough: there may be a significant immune component of successful therapy

Causes of Treatment Failure

- Poor Potency
  - Wrong Dose
- Host Genetics
- Insufficient Drug Level
- Poor Absorption
- Rapid Clearance
- Poor Activation
- Drug Interactions

- Viral Replication in the Presence of Drug
- Resistant Virus
- Treatment Failure

- Social/Personal Issues
- Regimen Issues
- Toxicities
## Resistance-associated RT Mutations: Y181C, M184V, Y188L

### Nucleoside and Nucleotide RT Inhibitors

<table>
<thead>
<tr>
<th>Drug</th>
<th>Resistance Interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td>zidovudine (AZT)</td>
<td>No Evidence of Resistance</td>
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<tr>
<td>didanosine (ddI)</td>
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<tr>
<td>lamivudine (3TC)/emtricitabine (FTC)</td>
<td>Resistance</td>
</tr>
<tr>
<td>stavudine (d4T)</td>
<td>No Evidence of Resistance</td>
</tr>
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<td>abacavir (ABC)</td>
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</table>

### Non-nucleoside RT Inhibitors

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<tr>
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<tr>
<td>efavirenz (EFV)</td>
<td>Resistance</td>
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</tbody>
</table>
# Common HIV Drug Resistance Pattern

## After Failing d4T/3TC/NVP: Case 2

Resistance-associated RT Mutations: Y181C

<table>
<thead>
<tr>
<th>Nucleoside and Nucleotide RT Inhibitors</th>
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</tr>
</tbody>
</table>
Common HIV Drug Resistance Pattern
After Failing d4T/3TC/NVP: Case 3

Resistance-associated RT Mutations: M184V

<table>
<thead>
<tr>
<th>Nucleoside and Nucleotide RT Inhibitors</th>
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</tbody>
</table>
### Common HIV Drug Resistance Pattern

**After Failing d4T/3TC/NVP: Case 4**

HIV RNA 23,600 copies/mL

Resistance-associated RT Mutations: K103N, Y181C, M184V, T215Y

<table>
<thead>
<tr>
<th>Nucleoside and Nucleotide RT Inhibitors</th>
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<tr>
<td>zidovudine (AZT)</td>
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</tr>
<tr>
<td>didanosine (ddI)</td>
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<td>Resistance</td>
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<thead>
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<td>efavirenz (EFV)</td>
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</tbody>
</table>
Common HIV Drug Resistance Pattern
After Failing d4T/3TC/NVP: Case 5

HIV RNA 51,700 copies/mL


<table>
<thead>
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</table>

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<td>efavirenz (EFV)</td>
<td>Resistance</td>
</tr>
</tbody>
</table>
Common HIV Drug Resistance Pattern
After Failing d4T/3TC/NVP: Case 6

Resistance-associated RT Mutations: K103N, F116Y, Q151M

<table>
<thead>
<tr>
<th>Nucleoside and Nucleotide RT Inhibitors</th>
<th>Resistance Interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td>zidovudine (AZT)</td>
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<tr>
<td>didanosine (ddl)</td>
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</tr>
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<td>Possible Resistance</td>
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<td>nevirapine (NVP)</td>
<td>Resistance</td>
</tr>
<tr>
<td>efavirenz (EFV)</td>
<td>Resistance</td>
</tr>
</tbody>
</table>
Common HIV Drug Resistance Pattern
After Failing d4T/3TC/NVP: Case 7

HIV RNA 121,700 copies/mL


<table>
<thead>
<tr>
<th>Nucleoside and Nucleotide RT Inhibitors</th>
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</tr>
</thead>
<tbody>
<tr>
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</tr>
<tr>
<td>efavirenz (EFV)</td>
<td>Resistance</td>
</tr>
</tbody>
</table>
Options for a Second-Line Antiretroviral Regimen for HIV Type 1–Infected Patients Whose Initial Regimen of a Fixed-Dose Combination of Stavudine, Lamivudine, and Nevirapine Fails

Somnuek Sungkanuparph,¹ Weerawat Manosuthi,² Sasisopin Kiertiburanakul,¹ Bucha Piyavong,¹ Noppanath Chumpathat,² and Wasun Chantratita¹

¹Faculty of Medicine Ramathibodi Hospital, Mahidol University, Bangkok, and ²Bamrasnaradura Infectious Diseases Institute, Ministry of Public Health, Nonthaburi, Thailand

(See the editorial commentary by Gallant on pages 453–5)

Drug Resistance after Failure of Initial Antiretroviral Therapy in Resource-Limited Countries

Joel E. Gallant
Division of Infectious Diseases, Johns Hopkins University School of Medicine, Baltimore, Maryland
HIV Drug Resistance and Time to Detection of Treatment Failure

- CD4 COUNT
- VIRAL LOAD
- VIROLOGIC FAILURE
- IMMUNOLOGIC FAILURE
- CLINICAL FAILURE

HIV Drug Resistance

Losina E et al, 15th CROI 2008, #823
### Table 5. Recommended laboratory monitoring after initiation of ART.

<table>
<thead>
<tr>
<th>Laboratory tests</th>
<th>Recommended time for the test</th>
<th>Note</th>
</tr>
</thead>
<tbody>
<tr>
<td>CBC, CD4+ T-cell count</td>
<td>at 6 and 12 months</td>
<td>every 6 months</td>
</tr>
<tr>
<td>Plasma VL</td>
<td>First regimen: at 6 and 12 months</td>
<td>every 12 months (every 6 months is preferred)</td>
</tr>
<tr>
<td></td>
<td>The next regimens: at 3 and 6 months</td>
<td>every 12 months</td>
</tr>
<tr>
<td>FBS</td>
<td>at 6 and 12 months</td>
<td>every 6 months</td>
</tr>
<tr>
<td>ALT</td>
<td>at 6 and 12 months</td>
<td>every 6 months</td>
</tr>
<tr>
<td>Creatinine*</td>
<td>at 6 and 12 months</td>
<td>every 6 months</td>
</tr>
<tr>
<td>Lipid profile (TC, TG, LDL, HDL)</td>
<td>at 6 and 12 months</td>
<td>every 6 months</td>
</tr>
<tr>
<td>Urinalysis</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>CXR</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Pap smear</td>
<td>at 12 months</td>
<td>every 12 months</td>
</tr>
</tbody>
</table>

*for calculation of creatinine clearance.
## Will HIV DR Testing Improve the Survival?

### Multivariate Cox analysis of risk factors for death

<table>
<thead>
<tr>
<th>Groups</th>
<th>HIV DR Testing</th>
<th></th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Yes</td>
<td>No</td>
<td></td>
</tr>
<tr>
<td>Overall</td>
<td>HR 0.69</td>
<td>Reference</td>
<td>0.017</td>
</tr>
<tr>
<td>95% CI: 0.51-0.94</td>
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<tr>
<td>Prior to initiation of ART</td>
<td>HR 0.25</td>
<td>Reference</td>
<td>0.170</td>
</tr>
<tr>
<td>95% CI: 0.03-1.84</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prior to change regimens in ART-experienced patients</td>
<td>HR 0.60</td>
<td>Reference</td>
<td>0.002</td>
</tr>
<tr>
<td>95% CI: 0.43-0.82</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prior to change regimens in triple-class ART-experienced patients</td>
<td>HR 0.61</td>
<td>Reference</td>
<td>0.022</td>
</tr>
<tr>
<td>95% CI: 0.40-0.93</td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>

### Additional Considerations:
- Adequate sample size?
- Adequate follow-up duration?
- Other outcomes: AIDS-defining illness?

When to Use HIV Drug Resistance Testing

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Primary/acute</strong></td>
<td>Recommend</td>
<td>Recommend</td>
<td>Recommend</td>
<td>—</td>
</tr>
<tr>
<td><strong>Post-exposure</strong></td>
<td>—</td>
<td>—</td>
<td>Recommend*</td>
<td>—</td>
</tr>
<tr>
<td><strong>prophylaxis</strong></td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td><strong>Chronic and</strong></td>
<td>Recommend</td>
<td>Recommend</td>
<td>Recommend</td>
<td>?</td>
</tr>
<tr>
<td><strong>treatment naïve</strong></td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td><strong>Failure</strong></td>
<td>Recommend</td>
<td>Recommend</td>
<td>Recommend</td>
<td>Recommend</td>
</tr>
<tr>
<td><strong>Pregnancy</strong></td>
<td>Recommend</td>
<td>Recommend</td>
<td>Recommend</td>
<td>—</td>
</tr>
<tr>
<td><strong>Pediatric</strong></td>
<td>—</td>
<td>Recommend</td>
<td>Recommend</td>
<td>—</td>
</tr>
</tbody>
</table>

*Especially if exposure to someone receiving antiretroviral drugs is likely or if prevalence of drug resistance in untreated patients ≥ 5% (European: ≥ 10%).

Causes of Treatment Failure

- Social/Personal Issues
- Regimen Issues
- Toxicities

Poor Adherence

- Insufficient Drug Level
- Poor Potency
- Wrong Dose

Host Genetics

- Poor Absorption
- Rapid Clearance
- Poor Activation

Drug Interactions

Viral Replication in the Presence of Drug

- Resistant Virus

Treatment Failure

Transmission
Emergence of HIV-1 drug resistance mutations among antiretroviral-naïve HIV-1-infected patients after rapid scaling up of antiretroviral therapy in Thailand

Somnuek Sungkanuparp1*, Chonlaphat Sukasem2, Sasispin Kiertiburanakul1, Ekawat Pasomsub2 and Wasun Chanratita2

Abstract

Background: After rapid scaling up of antiretroviral therapy in HIV-1-infected patients, the data of primary HIV-1 drug resistance in Thailand is still limited. This study aims to determine the prevalence and associated factors of primary HIV-1 drug resistance in Thailand.

Methods: A prospective observational study was conducted among antiretroviral-naïve HIV-1-infected Thai patients from 2007 to 2010. HIV-1 subtypes and mutations were assayed by sequencing a region of HIV-1 pol gene. Surveillance drug resistance mutations recommended by the World Health Organisation for surveillance of transmitted HIV-1 drug resistance in 2009 were used in all analyses. Primary HIV-1 drug resistance was defined as the presence of one or more surveillance drug resistance mutations.

Results: Of 466 patients with a mean age of 38.8 years, 58.6% were males. Risks of HIV-1 infection included heterosexual (77.7%), homosexual (16.7%), and intravenous drug use (5.6%). Median (IQR) CD4 cell count and HIV-1 RNA were 176 (42-317) cells/mm³ and 68,600 (19,525-220,330) copies/mL, respectively. HIV-1 subtypes were CRF01_AE (86.9%), B (8.6) and other recombinants (4.5%). The prevalence of primary HIV-1 drug resistance was 4.9%. Most of these (73.9%) had surveillance drug resistance mutations to only one class of antiretroviral drugs. The prevalence of patients with NRTI, NNRTI, and PI surveillance drug resistance mutations was 1.9%, 2.8% and 1.7% respectively. From logistic regression analysis, there was no factor significantly associated with primary HIV-1 drug resistance. There was a trend toward higher prevalence in females (odds ratio 2.18; 95% confidence interval 0.896-5.304; p = 0.086).

Conclusions: There is a significant emergence of primary HIV-1 drug resistance in Thailand after rapid scaling up of antiretroviral therapy. Although HIV-1 genotyping prior to antiretroviral therapy initiation is not routinely recommended in Thailand, our results raise concerns about the risk of early treatment failure in patients with primary HIV-1 drug resistance. Interventions to prevent the transmission of HIV-1 drug resistance and continuation of surveillance for primary HIV-1 drug resistance in Thailand are indicated.
Emergence of HIV-1 drug resistance mutations among antiretroviral-naïve HIV-1-infected patients after rapid scaling up of antiretroviral therapy in Thailand

Ramathibodi Hospital, 2007-2010, N=466

is HIV cure possible?
Sterilising cure: the Berlin patient

Yuki et al., International Workshop on HIV and Hepatitis Resistance, Sitges, June 2012
The Boston patients...allogeneic stem cell Tx for lymphoma

HIV-1 DNA (copies/10^6 PBMC)

100% donor granulocyte chimerism

Viral outgrowth assay negative day +652

100% donor lymphocyte chimerism

Viral outgrowth assay negative day +1266

Henrich et al., IAC Washington DC 2012
Virus persists in all patients on cART

Strategies for cure

- Eliminate latently infected cells
- Eliminate residual virus replication
- Enhance HIV-specific immunity
- Make cells “resistant” to HIV

Sharon R Lewin
Director, Infectious Disease Unit, Alfred Hospital
Professor, Department of Medicine, Monash University
Co-head, Centre for Virology, Burnet Institute, Melbourne, Australia

16th Bangkok International Symposium on HIV Medicine, Bangkok, January 2013
Early ART Intervention Restricts the Seeding of the HIV Reservoir in Long-lived Central Memory CD4 T Cells

Jintanat Ananworanich*1,2,3,4, C Vandergeeten5, N Chomchey1,2, N Phanuphak1,2, V Ngauy6, R-P Sekaly5, M Robb7, N Michael7, J Kim1,7, N Chomont5, and RV254/SEARCH 010 Study Group

1SEARCH, Bangkok, Thailand; 2The Thai Red Cross AIDS Res Ctr, Bangkok; 3HIVNAT, Bangkok, Thailand; 4Faculty of Med, Chulalongkorn Univ, Bangkok, Thailand; 5Vaccine and Gene Therapy Inst, Port St Lucie, FL, US; 6Armed Forces Res Inst of Med Sci, Bangkok, Thailand; and 7US Military HIV Res Prgm, Silver Spring, MD

Background: HIV infection of central memory CD4 T cells (T_{CM}) is a major cause of HIV persistence and an obstacle to HIV cure. Acute HIV infection (AHI) represents a window of opportunity to intervene to limit reservoir seeding.

Methods: 47 subjects with Fiebig stages I to III were enrolled (stage I: NAT+, p24-, 3rd generation EIA-; stage II: p24+, 3rd gen EIA-; stage III: 3rd gen EIA+/WB-). Total and integrated HIV DNA was measured in peripheral blood mononuclear cells (PBMC) (n = 47) and sigmoid colon (n = 21) by real-time PCR (detection limit 3 copies/10^6 cells). HIV DNA was determined in CD4 T cell populations of a subset who had leukapheresis. Subjects initiated ART at a median of 2 (IQR 1-3) days from baseline. Mann-Whitney U test was used to determine differences in HIV DNA between Fiebig stages and Spearman's rank test was used to assess correlation between reservoir localization at weeks 0 and 24.
**Results:** At baseline, Fiebig stages (subjects) were I (19), II (3), and III (25). Median (IQR) total peripheral blood mononuclear cell (PBMC) HIV DNA content was lower in Fiebig I (7, 0-32) than Fiebig II (2191, 96-4042) and Fiebig III (289, 40-1062), *p* = 0.0002. All Fiebig I subjects had undetectable integrated DNA compared with 33% and 52% of Fiebig II and III subjects, respectively. In 3 Fiebig I and 4 Fiebig II/III subjects undergoing leukapheresis, most integrated HIV DNA was seeded in CD4 T cells, and not monocytes, B or CD8 T cells. Importantly, the 3 Fiebig I subjects had no detectable integrated DNA in T\textsubscript{CM}, T\textsubscript{TM}, and T\textsubscript{EM}. Among 4 Fiebig II-III subjects, all showed low infection in T\textsubscript{CM} with median integrated DNA copies/10\textsuperscript{6} cells of 446 (342-774) for T\textsubscript{CM}, 2830 (987-6485) for T\textsubscript{TM} and 1898 (780-3461) for T\textsubscript{EM}. After 24 weeks of ART, HIV integrated DNA was dramatically reduced in all with 100% Fiebig I (n = 11), 67% Fiebig II (n = 3), and 72% Fiebig III (n = 18) having undetectable levels. The localization of the reservoir at week 0 predicts the localization after treatment (Correlation coefficient: 0.89, *p*-value <0.0001). In sigmoid colon (8 Fiebig I, 11 Fiebig II/III), median HIV integrated DNA copies/10\textsuperscript{6} cells were 0 in Fiebig I, 9263 in Fiebig II, and 149 in Fiebig III, *p* = 0.01. After 24 weeks of ART, 100% Fiebig I (n = 4) and 67% Fiebig II/III (n = 9) had undetectable HIV integrated DNA.

**Conclusions:** Fiebig I subjects exhibited extremely low reservoir size with no detected HIV integrated DNA in PBMC and memory CD4 T cell subsets before and after ART. Early ART intervention restricted the seeding of the HIV reservoir in long-lived T\textsubscript{CM}. 
Prevention and Screening of HIV Infection in 2013

Sasisopin Kiertiburanakul, MD, MHS
Associate Professor
Department of Medicine
Faculty of Medicine Ramathibodi Hospital
Mahidol University

Medicine Grand Round, Ramathibodi Hospital (April 17, 2013)
HIV Prevention
Which HIV Prevention Method Do You Know?

- Microbicides
- Vaccine
- Clean needle
- Mother-to-child transmission prevention
- Screening and treatment of STDs
- Male circumcision
- Condom
- Antiretroviral drugs
- HIV counseling and testing
- HIV counseling and testing
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><strong>ART for prevention;</strong> HPTN 052, Africa, Asia, Americas</td>
<td>96 (73-99)</td>
</tr>
<tr>
<td><strong>PrEP for discordant couples;</strong> Partners PrEP, Uganda, Kenya</td>
<td>73 (49-85)</td>
</tr>
<tr>
<td><strong>PrEP for heterosexual men and women;</strong> TDF2, Botswana</td>
<td>63 (21-84)</td>
</tr>
<tr>
<td><strong>Medical male circumcision;</strong> Orange Farm, Rakai, Kisumu</td>
<td>54 (38-66)</td>
</tr>
<tr>
<td><strong>PrEP for MSMs;</strong> iPrEX, Americas, Thailand, South Africa</td>
<td>44 (15-63)</td>
</tr>
<tr>
<td><strong>Sexually transmitted diseases treatment;</strong> Mwanza, Tanzania</td>
<td>42 (21-58)</td>
</tr>
<tr>
<td><strong>Microbicide;</strong> CAPRISA 004, South Africa</td>
<td>39 (6-60)</td>
</tr>
<tr>
<td><strong>HIV vaccine;</strong> RV144, Thailand</td>
<td>31 (1-51)</td>
</tr>
</tbody>
</table>

What is Treatment as Prevention?

- Use of ARVs to reduce the risk of passing HIV to others
- Public health or community benefits from the use of ART to decrease onward HIV transmission
- Secondary benefit of ART
- Rational: ARVs reduce viral load and thus reduces infectiousness
HPTN 052 Enrollment


106 (6.1%)
HPTN 052

Immediate ART
Initiate ART at CD4 cell count 350-550 cells/mm$^3$ (n = 886 couples)

Delayed ART
Initiate ART at CD4 cell count ≤250 cells/mm$^3$* (n = 877 couples)

*Based on 2 consecutive values ≤250 cells/mm$^3$

- Primary efficacy endpoint: virologically linked HIV transmission
- Primary clinical endpoints: WHO stage 4 events, pulmonary TB, severe bacterial infection and/or death
- Couples received intensive counseling on risk reduction and use of condoms

DSMB recommended release of results as soon as possible following April 28, 2011, review; follow-up continues but all HIV-infected partners offered ART after release of results

Results: HPTN 052

Total HIV transmission events: 39
(4 in immediate arm and 35 in delayed arm; $P < 0.0001$)

Linked transmissions: 28

Unlinked or TBD transmissions: 11

Immediate arm: 1

Delayed arm: 27

$P < 0.001$

Factors Associated with Linked Transmissions

- All transmissions occurred prior to starting ART
- 82% of transmissions occurred in African patients
- 64% transmissions from female to male partners

<table>
<thead>
<tr>
<th>Variable</th>
<th>HR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment, immediate vs delayed</td>
<td>0.04</td>
<td>0.01-0.28</td>
</tr>
<tr>
<td>Baseline CD4 count, per 100 cells/mm³ decrease</td>
<td>1.24</td>
<td>1.00-1.54</td>
</tr>
<tr>
<td>Baseline HIV RNA, per 1 log₁₀ copies/mL increase</td>
<td>2.85</td>
<td>1.51-5.41</td>
</tr>
<tr>
<td>Baseline condom use, 100% vs &lt;100%</td>
<td>0.33</td>
<td>0.12-0.91</td>
</tr>
<tr>
<td>Sex of infected partner, male vs female</td>
<td>0.73</td>
<td>0.33-1.65</td>
</tr>
</tbody>
</table>

Pre-exposure Prophylaxis

- PrEP
- New HIV prevention method in which people who do not have HIV infection take a pill daily to reduce their risk of becoming infected
- Part of a comprehensive HIV prevention strategy that includes safer sex practices, such as consistent and correct condom use, regular HIV testing and risk reduction counseling*

# PrEP Trials to Date

<table>
<thead>
<tr>
<th>Trial</th>
<th>Population/Setting</th>
<th>Intervention</th>
<th>Reduction in HIV infection rate, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPRISA¹</td>
<td>High-risk women in South Africa</td>
<td>▪ Coitally applied vaginal TDF gel</td>
<td>39</td>
</tr>
<tr>
<td>iPrEx²</td>
<td>MSM, transgender women, 11 sites in US, South America, Africa, Thailand</td>
<td>▪ Daily oral TDF/FTC</td>
<td>44</td>
</tr>
<tr>
<td>Partners PrEP³</td>
<td>Serodiscordant couples in Africa</td>
<td>▪ Daily oral TDF</td>
<td>Women: 71; men: 63</td>
</tr>
<tr>
<td></td>
<td></td>
<td>▪ Daily oral TDF/FTC</td>
<td>Women: 66; men: 84</td>
</tr>
<tr>
<td>TDF2⁴</td>
<td>Heterosexual males and females in Botswana</td>
<td>▪ Daily oral TDF/FTC</td>
<td>62 (underpowered to detect differences between sexes)</td>
</tr>
<tr>
<td>FEM-PrEP⁵</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></td>
<td></td>
<td></td>
<td>▪ Study stopped for lack of efficacy</td>
</tr>
</tbody>
</table>

Pre-Exposure Prophylaxis Initiative (iPrEx): Fully Enrolled as of December 2009

11 sites; n = 2499 participants
100 subjects with emergent HIV infection
- 36 in FTC-TDF group vs. 64 in placebo group
- Relative reduction of 44% (95% CI 15 to 63; \(P=0.005\))

Figure 2. Kaplan–Meier Estimates of Time to HIV Infection (Modified Intention-to-Treat Population).

VOICE: Oral TDF, Oral TDF/FTC, Vaginal TFV Gel as PrEP in African Women

- Phase IIB placebo-controlled trial of >5000 women in South Africa, Uganda, and Zimbabwe
- Daily oral TDF, daily oral TDF/FTC, daily vaginal TFV 1% gel
  - DSMB stopped daily oral TDF arm and daily vaginal gel arm, both for lack of efficacy; daily oral TDF/FTC arm continued
  - 334 infections seen across 5 arms; 22 infected at enrollment

### Primary efficacy results (mITT)

<table>
<thead>
<tr>
<th></th>
<th>TDF* (n = 1007)</th>
<th>Oral placebo* (n = 1003)</th>
<th>Oral placebo (n = 1007)</th>
<th>TFV Gel (n = 1007)</th>
<th>Gel placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infections, n</td>
<td>52</td>
<td>35</td>
<td>61</td>
<td>60</td>
<td>61</td>
</tr>
<tr>
<td>Infections/100 PY</td>
<td>6.3</td>
<td>4.2</td>
<td>4.7</td>
<td>4.6</td>
<td>5.9</td>
</tr>
</tbody>
</table>

### Protective efficacy vs placebo

<table>
<thead>
<tr>
<th></th>
<th>HR (95% CI)</th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1.49 (0.97-2.30)</td>
<td>1.04 (0.7-1.5)</td>
<td>0.85 (0.6-1.2)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>P value</td>
<td>0.07</td>
<td>&gt;0.2</td>
<td>&gt;0.2</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Censored when sites took women off TDF and TDF placebo. Total n = 1009

Marrazzo J et al. CROI 2013. Abstract 26LB.
Questions That Arise From These Data

- Why were there differences between these studies and the other TDF-based studies?
- Adherence?
- Penetration of drug in vaginal tissue?
- Degree of HIV exposure?
- Genital inflammation?
Data on effectiveness of PrEP, especially in women, are inconsistent.

ARVs should be provided to HIV-negative people only when all eligible HIV-positive patients are receiving ART.

Lead to worsening of HIV epidemic, PrEP users might reduce their use of higher-efficacy HIV prevention tools.

Causing drug resistance.

Unaffordable.

**FDA is requiring Truvada’s manufacturer to collect certain post-marketing data to help evaluate the drug’s use for a PrEP indication in real-world practice.**

Medical Male Circumcision

- Biologically plausible
- Ecological and observational studies
- Meta-analysis\(^1\)
  - General populations 0.56 (95% CI 0.44-0.70)
  - High-risk populations 0.29 (95% CI 0.20-0.41)
- Prospective study
  - In Rakai, Uganda: a randomised trial\(^2\)
  - Study in Kisumu, Kenya\(^3\)
  - 50-60% reduction in HIV acquisition

Medical Male Circumcision

- No substantial protective effect for female partners
- 1 time intervention provides life-long partial protection against HIV and other sexually transmitted infections
- Since 2007, WHO and UNAIDS have recommended voluntary medical male circumcision (VMMC)
  - By the end of 2011, >1.3 million VMMC had been performed
- Population impact of VMMC
- Uganda: 27% (95% CI 10-40%) reduction in HIV incidence in non-Muslim men (1999 vs 2004-2011)*

HIV Prevention in Thailand in 2013

- **Antiretroviral strategies**
  - Mother to child transmission
  - Antiretroviral therapy: treatment as prevention
  - Pre-exposure prophylaxis??
  - Microbicides??

- **Non-antiretroviral prevention strategies**
  - Barrier
  - Treat sexual transmitted diseases
  - Medical male circumcision??
  - Clean needle?
  - HIV testing!?
HIV Screening
Case

- 56 years old man, government officer
- 9/2009: anorexia, fatigue and weight lost 12 kg. in 2 months
- HBsAg positive, AST 162, ALT 96 U/L
- 10/2009: refer to hepatologist
  - Anti-HBs negative, HBeAg positive
  - HBV VL >110,000,000 IU/mL
- AFP 6.56 ng/mL, anti-HCV negative
- U/S upper abdomen: mild liver parenchymatous changes without focal mass
Case

- 3/2010: start entecavir
- 11/2010: HBV VL 119 IU/mL
- 2/2011: more weight lost 5 kg., itching over extremities
  - PE: oral thrush, PPE
- HIV infection was diagnosed by dermatologist
- 3/2011: low-graded fever, dry cough, fatigue, nausea, vomiting, and headache for 2 weeks
Why Should We Do HIV Screening?

- Prevention strategies that incorporate universal HIV screening have been highly effective
  - Screening blood donors
  - Screening pregnant women
- Relative lack of progress in preventing sexual transmission of HIV
- Persons who are aware of their HIV infections substantially reduce sexual behaviors that might transmit HIV after they become aware they are infected*

Why Should We Do HIV Screening?

- HIV infection is a serious health disorder that can be diagnosed before symptoms develop
- HIV can be detected by reliable, inexpensive, and noninvasive screening tests
- Infected patients have years of life to gain if treatment is initiated early, before symptoms develop
- Costs of screening are reasonable in relation to the anticipated benefits

### Characteristics

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>n</th>
<th>(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, median year (range)</td>
<td>35.5</td>
<td>(15.8-72.3)</td>
</tr>
<tr>
<td>Male gender, n (%)</td>
<td>126</td>
<td>(57.0)</td>
</tr>
<tr>
<td>Risk of HIV acquisition, n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heterosexual</td>
<td>141</td>
<td>(63.8)</td>
</tr>
<tr>
<td>Homosexual/bisexual</td>
<td>12</td>
<td>(5.4)</td>
</tr>
<tr>
<td>Intravenous drug users</td>
<td>8</td>
<td>(3.6)</td>
</tr>
<tr>
<td>Unknown</td>
<td>60</td>
<td>(27.2)</td>
</tr>
</tbody>
</table>

### Reasons for HIV serology testing, n (%)

<table>
<thead>
<tr>
<th>Reasons</th>
<th>n</th>
<th>(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preoperative screening</td>
<td>91</td>
<td>(41.2)</td>
</tr>
<tr>
<td>Suspicion of HIV infection by physicians</td>
<td>71</td>
<td>(32.0)</td>
</tr>
<tr>
<td>Antenatal care screening in pregnant women</td>
<td>22</td>
<td>(10.0)</td>
</tr>
<tr>
<td>Self voluntary testing</td>
<td>22</td>
<td>(10.0)</td>
</tr>
<tr>
<td>Confirmation</td>
<td>9</td>
<td>(4.1)</td>
</tr>
<tr>
<td>Partner had positive HIV serology</td>
<td>6</td>
<td>(2.7)</td>
</tr>
</tbody>
</table>
### CD4 Cell Count Levels in Newly Diagnosed HIV-infected Patients in Ramathibodi Hospital

<table>
<thead>
<tr>
<th></th>
<th>2006</th>
<th>2009</th>
<th>P-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV prevalence</td>
<td>242/23987 (1%)</td>
<td>291/31920 (0.9%)</td>
<td>0.242</td>
</tr>
<tr>
<td>Number of study patients</td>
<td>220</td>
<td>224</td>
<td></td>
</tr>
<tr>
<td>Number of tested</td>
<td>141</td>
<td>125</td>
<td></td>
</tr>
<tr>
<td>Median CD4, cells/mm³</td>
<td>221</td>
<td>176</td>
<td>0.259</td>
</tr>
<tr>
<td>Interquartile range</td>
<td>77-386</td>
<td>43-362</td>
<td></td>
</tr>
<tr>
<td>Min, max</td>
<td>6, 1284</td>
<td>2, 1178</td>
<td></td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>260 (233)</td>
<td>239 (232)</td>
<td></td>
</tr>
<tr>
<td>CD4 &lt;200 cells/mm³</td>
<td>68 (48.2%)</td>
<td>66 (52.8%)</td>
<td>0.457</td>
</tr>
<tr>
<td>CD4 200-350 cells/mm³</td>
<td>30 (21.3%)</td>
<td>25 (20%)</td>
<td>0.798</td>
</tr>
<tr>
<td>CD4 &gt;350 cells/mm³</td>
<td>43 (30.5%)</td>
<td>34 (27.2%)</td>
<td>0.554</td>
</tr>
</tbody>
</table>
CD4 Counts at ART Initiation in Asia

Recommended HIV Testing in Thailand

- Having signs and symptoms of HIV/AIDS
- Having or ever have sexual activity without protection
- Persons with tuberculosis
- Persons with STDs
- IDUs who shares needle
- Pregnant women and her husband
- Babies born to HIV positive women
- HCWs after occupational exposure with a risk for HIV acquisition
- Sexual assailant and sexually assaulted victims
- Before married and plan to have a baby

MOPH. Thai Guideline 2010.
Recommended for Repeated HIV Testing in Thailand

- Men who have sex with men and having HIV risk continuously
  - At least 2 times/year, until having a positive result
- Having HIV risk exposure but have a negative result within 3 months after exposure
  - Repeat in the next 2 weeks and/or 3 months
- Having HIV risk behavior continuously
  - Repeat once a year

MOPH. Thai Guideline 2010.
ZERO NEW HIV INFECTIONS.
ZERO DISCRIMINATION.
ZERO AIDS-RELATED DEATHS.