IPREX implications for Thailand

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Silom Community Clinic
Thailand MOPH – US CDC Collaboration
US Centers for Disease Control and Prevention
IPREX implications for Thailand

Thailand MOPH - US CDC Collaboration
Silom Community Clinic
1) Research
2) Programmatic
IPREX implications for Thailand
Silom Community Clinic

1) Research
- Willingness to participate in chemoprophylaxis trial
- Sex planning and sex spacing and intermittent chemoprophylaxis
- Pharmaco-economics
Sex frequency among 823 HIV-negative MSM in Bangkok Thailand ("On how many days in the past week did you have sex?")

van Griensven et al, 2010
Sex planning among 823 HIV-negative MSM in Bangkok Thailand ("On the last day you had sex, was the first sex on that day planned?")

van Griensven et al, 2010
Sex frequency and number of doses needed for different pre-exposure prophylaxis regimens among men who have sex with men (MSM) in Bangkok, Thailand

Frits van Griensven*, Warunee Thienkrua, Wichuda Sukwicha, Wipas Wimonsate, Supaporn Chaikummao, Anchalee Varangrat and Philip Mock

From the Thailand Ministry of Public Health – US Centers for Disease Division of HIV/AIDS Prevention, Centers for Disease Control *and Prevention, Atlanta, GA, USA
Results

• Of 823 MSM (mean age 28.3 years, range 19-58 years) 33.3% reported to have had sex on one day in the past week, 15.9% on two days, 7.3% on three days, and 6.9% on four days or more
• No sex in the past week was reported by 36.6%
• The estimated number of PrEP doses for event-driven pre-post-exposure dosing in this cohort would be 1872 per week or 910 per 100 PPM
• The estimated number of PrEP doses for time-event-driven bi-weekly standing plus post-exposure dosing 2748 per week or 1,336 per 100 PPM
• The number of PrEP doses needed for time-driven daily dosing would be 5761 per week or 2,800 per 100 PPM
ADAPT
HPTN 067
WE CAN CHANGE
Intermitent PrEP (iPrep)

- HPTN 067: the “ADAPT Study” at Silom Clinic
  - “Alternative Dosing to Augment Pill Taking Study”
  - Phase II, Randomized, Open-Label, Pharmacokinetic and Behavioral Study of the Use of Intermittent Truvada
  - 3-armed study:
    - 1) daily dosing (time driven)
    - 2) pre-post sexual exposure dosing (exposure driven)
    - 3) bi-weekly standing plus post exposure dosing (hybrid dosing)
  - N=360, High risk MSM n=180 Bangkok; high risk heterosexual women n=180, Capetown, South Africa
  - Primary endpoint: Adherence and coverage, by pharmacokinetics and self reports of risk behavior and pill taking (EDM device)
  - 6 weeks run in of DOT to set individual drug level in blood and hair
  - Sexual risk behavior, risk compensation, risk disinhibition, self-control, self-esteem
  - 6 weeks DOT, 24 weeks of f/u on therapy, post 4 week exit visit: total 36 weeks; enrollment 8 months
  - Start March 2011
Safety and adherence to intermittent Truvada for HIV pre-exposure prophylaxis (PrEP) in Kenya and Uganda

<table>
<thead>
<tr>
<th></th>
<th>Kenya (MSM/FSW)</th>
<th>Uganda (DC)</th>
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<tbody>
<tr>
<td><strong>DAILY ADHERENCE RATE Median [IQR]</strong></td>
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<tr>
<td>Overall unadjusted</td>
<td>83% [63-92]</td>
<td>96% [93-100]</td>
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<tr>
<td>Adjusted – Upper</td>
<td>92% [79-99]</td>
<td>97% [93-100]</td>
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<tr>
<td>Adjusted – Lower</td>
<td>82% [63-92]</td>
<td>96% [93-100]</td>
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<tr>
<td><strong>INTERMITTENT ADHERENCE RATE Median [IQR]</strong></td>
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<tr>
<td>Overall unadjusted</td>
<td>68% [63-78]</td>
<td>80% [71-86]</td>
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<tr>
<td>Fixed doses</td>
<td>55% [28-88]</td>
<td>91% [77-98]</td>
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<tr>
<td>Post-coital doses</td>
<td>26% [14-50]</td>
<td>45% [20-63]</td>
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<tr>
<td>Post-coital doses within 2hrs (self report and sexual events per SMS)</td>
<td>105% [57-175]</td>
<td>103% [62-133]</td>
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</table>

*Table 3.* Adherence rates for daily and intermittent groups. Adjusted upper accounts for extra openings and extra tablets taken out. Adjusted lower excludes curiosity openings.
CAPRISA 004

Effectiveness & safety of vaginal microbicide 1% tenofovir gel for prevention of HIV infection in women

Quarraisha & Salim S Abdool Karim

on behalf of the

CAPRISA 004 Trial Group
Methods

• Proof of concept double-blinded, randomized, placebo-controlled trial

• Enrolled high risk HIV uninfected women reporting two coital acts in past 30 days – known high risk populations from pre-trial feasibility studies

• Endpoint driven trial (92 HIV endpoints)

• HIV infection is primary safety & effectiveness endpoint:
  – HIV negative: 2 negative rapid HIV tests
  – HIV endpoint: PCR+ in 2 separate blood specimens
    Positive Western blot

• Intent-to-treat analysis except for adherence analysis
# Effectiveness of Tenofovir Gel in Preventing HIV Infection

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<thead>
<tr>
<th></th>
<th>Tenofovir</th>
<th>Placebo</th>
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<tr>
<td># HIV infections</td>
<td>38</td>
<td>60</td>
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<tr>
<td>Women-years (# women)</td>
<td>680.6 (445)</td>
<td>660.7 (444)</td>
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<tr>
<td>HIV incidence (per 100 women-years)</td>
<td>5.6</td>
<td>9.1</td>
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Incidence rate ratio: 0.61 (CI: 0.4 to 0.94); p = 0.017

39% lower HIV incidence in tenofovir gel group
HIV infection rates in the tenofovir and placebo gel groups: Kaplan-Meier survival probability

![Graph showing Kaplan-Meier survival probability with two lines, one for tenofovir and one for placebo. The graph indicates a lower probability of HIV infection in the tenofovir group compared to the placebo group across different follow-up periods.]

<table>
<thead>
<tr>
<th>Months of follow-up</th>
<th>6</th>
<th>12</th>
<th>18</th>
<th>24</th>
<th>30</th>
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<tr>
<td>Cumulative HIV endpoints</td>
<td>37</td>
<td>65</td>
<td>88</td>
<td>97</td>
<td>98</td>
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<tr>
<td>Cumulative women-years</td>
<td>432</td>
<td>833</td>
<td>1143</td>
<td>1305</td>
<td>1341</td>
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<tr>
<td>HIV incidence rates (Tenofovir vs Placebo)</td>
<td>6.0 vs 11.2</td>
<td>5.2 vs 10.5</td>
<td>5.3 vs 10.2</td>
<td>5.6 vs 9.4</td>
<td>5.6 vs 9.1</td>
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<tr>
<td>Effectiveness (p-value)</td>
<td>47% (0.069)</td>
<td>50% (0.007)</td>
<td>47% (0.004)</td>
<td>40% (0.013)</td>
<td>39% (0.017)</td>
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In the shadow of Caprisa

Oral or Topical ARV PrEP?

Strong push for evaluation of rectal microbicides, e.g., TDF gel, possibly in combination with oral formulations
IPREX implications for Thailand
Silom Community Clinic

1) Research
- Sub-study of rectal cleansing
- Willingness to participate trial of rectal gel
- Study of lubricant use

- Feed into phase II/III studies of dosing, acceptability, feasibility and efficacy of
  - rectal 1% tenofovir gel
  - Combination use of rectal and topical formulations of tenofovir
MTN 017 (Microbicide Trial Network)

- Phase II, multi-site, randomized, six sequence, three period, open label crossover study of adherence and pharmacokinetics of oral and rectal formulations of tenofovir
  - Arms: 1) oral; 2) rectal; 3) both
  - 120 MSM
  - Bangkok, Thailand; Lima, Peru; 2 US Sites
  - Possibly roll-over into Phase IIB, III efficacy trial
### Rectal Microbicide Timeline*

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<td>microbicides</td>
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*An approximation based on 1% tenofovir

Slide: courtesy of Dr Ian McGowan
IPREX implications for Thailand

• PrEP
  – No roll out
  • Continuing concerns
    – Viral resistance
    – Safety
    – Costs
    – Behavioral disinhibition or compensation
    – Dependency
    – Access: controlled/market/programmatic
    – Grey and black markets
IPREX implications for Thailand

• PrEP
  – Adherence is poor
    • MSM don’t like to take pills to avoid negative consequences
    • MSM like to take pills to experience positive consequences
    • MSM don’t like to use condoms and gel because they interfere with sexual excitement, decrease sexual sensation and feelings of intimacy and unity
IPREX implications for Thailand

• PrEP
  – Programmatic implementation (ignoring possible emergence of grey and black markets, prescribers etc.)
  • Only for those at the highest behavioral risk for whom condoms, behavioral modification and partner reduction are no feasible options
    – Young MSM experimenting and exploring their sensuality, sexuality and sexual behavior (15 years and up)
    – Young entering male sex workers (15 years and up)
Proportion HIV uninfected in the Bangkok MSM Cohort Study, 2006-2010

30% infected after 4 years
18 – 21 year old
HIV and TP prevalence and incidence among VCT clients
September 30, 2005 – June 16, 2009

- HIV prevalence significantly increased by age
- HIV and TP incidence significantly decreased by age
IPREX implications for Thailand

• PrEP
  • Young MSM experimenting and exploring their sensuality, sexuality and sexual behavior
    – Limited knowledge and awareness
    – Limited perception of risk
    – Limited negotiation skills
    – Physically inexperienced
    – Challenging youth culture demanding performance and rewarding sexual pleasure and delectation
    – High background HIV prevalence and incidence (acute infection)

% HIV infected

Source: Bureau of Epidemiology, Ministry of Public Health, Thailand
IPREX implications for Thailand

• PrEP
  • Young entering male sex workers
    – May have more or less overlap with young MSM by geographic region, e.g., Chiang Mai versus Pataya
    – Limited knowledge and awareness
    – Limited perception of risk
    – Limited negotiation skills
    – Physically inexperienced
    – Social pressure: need to deliver/achieve, family, social environment, social self and lifestyle
    – Drug use: stimulant, mind-altering and erectile drugs
    – High turnover rate, relatively short duration of exposure
    – High HIV prevalence equivalent to high HIV incidence
Bridging risk and adherence
IPREX implications for Thailand

• PrEP Program
  • Two six months (short) demonstration pilot projects of daily PrEP to prevent HIV infection among young MSM and young entering male sex workers
    – Daily Truvada PrEP
    – Intensive adherence training for self-therapy (condition 1)
    – Intensive adherence training for dyads, buddy observed therapy (BOTPREP) (condition 2)
      » Weekly for 1 month
      » Monthly for 4 months
    – Intensive educational, motivational, empowering sexual and drug use risk reduction training program
      » Weekly for 2 months
      » Monthly for 4 months
IPREX implications for Thailand

• PrEP Program
  • Demonstration pilot projects of daily PrEP
    – Weekly visits for HIV infection evaluation
      » Drug resistance
    – Monthly KAP behavioral and adherence assessments
      » Comprehension
      » Motivation
      » Sexual and drug use behavior
      » Risk compensation
      » Pill burden
    – Monthly pill count, adherence evaluation
    – Assessment of drug burden en side effects
    – Pre-post study bone density evaluation
IPREX implications for Thailand

• PrEP Program
  • Demonstration pilot projects of daily PrEP
    – n = 500 per group (250 dyads; Total = 1000 (500 MSM and 500 MSW))
    – 2 condition comparative design or cross-over 2x2 design
    – Compare to historical HIV incidence
    – Location Bangkok and Chiang Mai (Pata ya....?)
    – Partnerships
      » WHO, UNAIDS, USAID, AVAC, Gates, GAP, EU
      CDC, FHI, MOPH, BMA, SWING, RSAT, Pee Man, SCC, M Plus
    – Costs: 180.000 truvada pills a 1 US$ = 180000
      » Total ~ 1 million US$