The iPrEx Trial: A Case Study

Pedro Goicochea, MSc, MA
Gladstone Institute of Virology and Immunology
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Outline

• 2004: Community Consultations and Controversies I
• 2007: Trial Implementation and Expansion
• April 23rd, 2010: iPrEx Announcement of Study Results and Controversies II
• 2011: iPrEx OLE and Controversies III?
What is PrEP?

• Pre Exposure Prophylaxis or PrEP is the use of antiretroviral medications (ARVs) used to treat people living with HIV, to prevent HIV acquisition
• Two ARVs have been tested for efficacy to be used as PrEP:
  – Tenofovir
  – Emtricitabine + tenofovir
• PrEP could be topical (gel) and oral (pill)
2004 : Community Consultations and Controversies I

When Jorge met Bob

• 2004
  – 11th Conference on Retrovirus and Opportunistic Infections (CROI)
  – PrEP trial in men who have sex with men (MSM)
  – Community Advisory Board (CAB) in Lima, Peru
Community Consultations

- 2005, assessing feasibility:
  - CAB San Francisco Department of Public Health
  - 9 focus groups (FGD) with MSM community members on HIV prevention research
  - Peruvian Ministry of Health/Office of AIDS
  - Peruvian College of Physicians
  - Universidad Peruana Cayetano Heredia School of Medicine (UPCH SoM)
  - Input from Peruvian IRB and University of California San Francisco, Committee on Human Research (UCSF CHR)

Community Consultations and Controversies I (cont.)

- 2005, controversies I
  - August: Protocol receives Notice of Grant Award
  - Community:
    - Why PrEP in Peru?
  - Community forum I – Impacta
  - Community forum II – UPCH SoM
Community Consultations (cont.)

• 2006, preparations
  – 13th CROI: switched from TDF to FTC/TDF
  – Marketing and branding
    • 18 FGD inquiring for:
      – Willingness to participate
      – Strategies for recruitment and retention
      – Study name

Community Consultations (cont.)

• i  = iniciativa
• Pr = Profilaxis Pre
• Ex = Exposición
• iPrEx = a new HIV prevention technology
2007: Trial Implementation and Expansion

iPrEx Implementation & Expansion

2007: iPrEx the Andean PrEP trial

- **Design:**
  - Phase IIB proof of concept
  - 1400 MSM 1:1 to FTC/TDF or placebo
  - Follow up 18 mos.
- **Objectives:**
  - Assess daily use of FTC/TDF once a day for:
    - Adverse events
    - HIV incidence
- **Sites:**
  - Peru: Lima and Iquitos
  - Ecuador: Guayaquil
iPrEx Implementation & Expansion (cont.)

2008: iPrEx goes global

- Design:
  - Phase III efficacy and safety
  - 3000 MSM 1:1 to FTC/TDF or placebo
- Sites:
  - Peru: Lima and Iquitos
  - Ecuador: Guayaquil
  - South Africa: Cape Town
  - USA: San Francisco, Boston
  - Brazil: Sao Paulo, Rio de Janeiro
  - Thailand: Chiang Mai

iPrEx Implementation & Expansion (cont.)

- Followed on Drug for:
  - HIV seroconversion
  - Adverse Events (especially renal & liver)
  - Metabolic Effects (Bone, Fat, Lipids)
  - HBV Flares among HBsAg+
  - Risk Behavior & STIs
  - Adherence
  - If infected
    - Drug Resistance
    - Viral load
    - Immune responses & CD4 Count
iPrEx Implementation & Expansion (cont.)

- HIV Testing Monthly
- Pre- and Post-test counseling
- Condoms (15 or more)
- STI testing if any symptoms, monthly
- STI screening for all every 24 weeks
- Partner treatment
- PEP if recently exposed
- HBV vaccine

April 23rd, 2010: iPrEx Announcement of Study Results and Controversies II
Global iPrEx Study Results

• Data Safety Monitoring Board Meeting November 2009
  – Stop enrollment by December 2009
  – Primary analysis completed by August 2010
• Results presented to the sponsors (US National Institutes of Health and the Bill & Melinda Gates Foundation) in September of 2010

Fully enrolled as of December 2009

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<td>Participants</td>
<td>2,499</td>
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Participants 2499

A reduction of 44%

Placebo Group 64 HIV Infections
Truvada Group 36 HIV Infections
iPrEx Results Announcement, Controversies II

Original Article

Preexposure Chemoprophylaxis for HIV Prevention in Men Who Have Sex with Men

Editorials

Oral Preexposure Prophylaxis for HIV — Another Arrow in the Quiver?

iPrEx Results Announcement, Controversies II (cont.)

Centers for Disease Control and Prevention

MMWR

Morbidity and Mortality Weekly Report

Interim Guidance: Preexposure Prophylaxis for the Prevention of HIV Infection in Men Who Have Sex with Men
iPrEx Results Announcement, Controversies II (cont.)

Treatment as prevention for HIV

June 5, 2011, was the 30th anniversary of the first reports of AIDS patients with an immune disorder in the US. The Centers for Disease Control and Prevention publication, “Morbidity and Mortality Weekly Report,” in the past three decades, HIV/AIDS has become a global pandemic that has claimed the lives of millions worldwide. The epidemic has changed dramatically since its early years, with new treatments and prevention strategies offering hope for the future.

Efficacy of Daily Oral FTC/TDF PrEP

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<th>Efficacy</th>
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<tr>
<td>iPrEx</td>
<td>MSM</td>
<td>42%</td>
<td>18-60%</td>
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<tr>
<td>Partners PrEP</td>
<td>Men</td>
<td>83%</td>
<td>49 to 94%</td>
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<tr>
<td></td>
<td>Women</td>
<td>62%</td>
<td>19 to 82%</td>
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<tr>
<td>TDF2</td>
<td>Men</td>
<td>80%</td>
<td>25 to 97%</td>
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<td></td>
<td>Women</td>
<td>49%</td>
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<td>FemPREP</td>
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PrEP Demonstration Projects

2011: iPrEx OLE and, Controversies III?
iPrEx

will continue a second phase: the Open Label Extension

The primary aims:

- Will pill-taking increase if people are provided Truvada (no placebo) and know it can be effective if taken consistently?
- What will happen to risk practices if people are provided Truvada?
- Collect more safety data over a longer period of time
Participants enrolled in the first phase will be offered an **additional 18 months** of study participation.

All participants will get **counseling, condoms, and testing** for sexually transmitted infections.
All eligible participants will be provided Truvada for **18 months**

HIV + participants **will be followed** throughout the course of this phase
Personal Reflections

- There are very valid arguments on these different positions: i.e. drug resistance, implementation feasibility, costs, logistics, accessibility and other prevention competing priorities; however:
  - Not very many critical positions were discussed regarding CAPRISA 004 trial results
  - Not very many critical comments related to Partners PrEP or TDF2 study results, higher efficacy though
  - Critical positions are related to potential “behavioral desinhibition” of MSM not of heterosexual men and women
  - The discussion is being polarized between treatment and prevention when both are part of the same interest, to prevent infections to occur

Questions