

Oral Pre-Exposure Prophylaxis (PrEP): Status of Science & Implementation

John-Mark Schacht

April 26, 2011



Objectives...

- Review of the CDC's FOA 12-1201 and PrEP
- Highlight data and results from key PrEP-related clinical trials
- Explore continuing and planned PrEP-related clinical trials
- Review key points from CDC's PrEP Interim Guidance
- Review status of FDA review of Truvada ® for HIV-prevention prophylaxis

CDC FOA PS12-1201 & PrEP...

Support PrEP services to MSM at high risk for HIV consistent with the CDC's PrEP Interim Guidance

Funds may not be used for PrEP medications, but may be used to support:

- Planning how to effectively incorporate PrEP into Px education & services
- PrEP-related educational materials
- Development & delivery of risk-reduction activities associated with PrEP
- Communication activities related to PrEP
- Evaluation of PrEP-related activities

Pre-Exposure Prophylaxis (PrEP):
a working definition...

The use of ARVs in various
mediums and in specific dosing
schedules to reduce the risk of
HIV infection

Oral PrEP: study drugs of choice

Tenofovir Disoproxil Fumarate (TDF)

- Manufactured by Gilead Sciences under the brand: Viread ®

Emtricitabine (FTC)

- Also by Gilead, under the brand: Emtriva ®

TDF & FTC have been studied for use as PrEP, in part, due to:

- ✓ Lengthy serum bioavailability: forgives potential dosing irregularities, reduces risk of drug/drug-class resistance
- ✓ Relatively low toxicity profiles

Combos & Cocktails...

- TDF + FTC: by Gilead, under the brand: Truvada ®
- TDF + FTC + EFV (Efavirenz), by Gilead/Bristol-Myers Squibb: Atripla ®

Clinical Trials 101...

- **Phase I:** small cohorts (20 – 80 pp), assessing safety, safe dosing ranges, examine side-effects, assess study methodology
- **Phase II:** medium cohorts (100 – 300 pp), assessing efficacy & safety, rigorous controls, e.g. randomization, double-blinding
- **Phase III:** large cohorts (1,000 – 3,000 pp), seeking confirmation of Phase II results, continued safety monitoring, comparisons to similar treatments, may or may not be controlled
- **Phase IV:** “post marketing” to further study safety & risks, benefits, optimal uses

PrEP Research Highlights...

- iPrEX
- Partners PrEP
- TDF2 (CDC 4940)
- FMI FEM PrEP
- MTN 003 VOICE

iPrEX: The Pre-Exposure Prophylaxis Initiative (2007 - 2011)

- Phase III, randomized, double-blinded, assessing safety & efficacy of once-daily TDF/TFC
- Enrolled 2,499 adult MSM & transwomen (MTF transgender) at high-risk for HIV acquisition in Peru, Brazil, Ecuador, Thailand, South Africa and the U.S.
- Participants received a comprehensive risk-reduction package, including condoms, intensive behavioral counseling, adherence counseling, HIV testing and testing & treatment for STIs

iPrEX Results... November 2010...

- TDF/FTC determined safe & well-tolerated for use in study populations
- TDF/FTC provided an average of 44% additional protection against HIV infection in the context of a comprehensive prevention strategy
- Among participants who maintained adherence of $\geq 90\%$, HIV infection risk reduced by 73%
- Among participants who achieved adherence of $< 90\%$, HIV infection risk reduced by about 21%

Partners PrEP

2008

- Phase III, double-blinded, assessing safety & efficacy of daily TDF or TDF/FTC in HIV negative partners
- Enrolled 4,758 heterosexual sero-discordant couples in Kenya & Uganda
- Participants received comprehensive HIV prevention services: safer-sex counseling, condoms, HIV testing, testing/Tx for STIs

Partners PrEP: Preliminary Results...July 2011

- **62% fewer HIV infections among recipients of TDF; 73% fewer HIV infections among recipients of TDF/FTC**
- **Study drugs determined safe & well-tolerated by participants**
- **Adherence very high: > 97% of dispensed doses taken; > 95% of participants retained in study**
- **Following release of these results, all study participants have been randomized to either TDF or TDF/FTC; use of placebo discontinued**
- **Final results expected in 2013**

TDF2 (C D C 4940)

2007

- **Phase III, randomized, double-blinded study of safety & efficacy of once daily TDF/FTC in heterosexually active young men & women to prevent HIV infection**
- **Enrolled 1200 men & women, aged 18-29 years, in Botswana**
- **Participants received comprehensive HIV prevention services: safer-sex counseling, male & female condoms, HIV testing, testing/Tx for STIs**
- **Results 2011: TDF/FTC reduced risk of HIV infection by an average of 63% in both men & women**

PrEP-related disappointments... 2011...

FMI FEM PrEP

Phase III safety & efficacy study of daily oral TDF/FTC in 3,900 women, in Kenya, South Africa & Tanzania.

The study was discontinued, early, due to lack of evidence of efficacy.

MTN 003 VOICE

Phase IIB safety & efficacy study of daily oral TDF/FTC and TDF and 1% TDF gel in 5,000 women in Malawi, South Africa, Uganda & Zimbabwe. **The study arms for TDF, both oral and 1% gel, were discontinued, early, due to lack of evidence of efficacy.** The TDF/FTC arm continues with results anticipated in 2013.

Continuing & Planned PrEP-related studies

- iPrEX O L E
- CDC 4370
- ANRS Ipergay
- PrEP Demonstration Projects

iPrEX Open Label Extension (O L E)

2011

- Same study sites and participants (drug arm) as iPrEX
- Assessing: long-term efficacy & safety, adherence behaviors, drug resistance, bone mineral density and fat distribution (lipodystrophy), impact on hepatitis (HBV) infection
- Study to run for 72 weeks (1.4 years)
- Results anticipated: 2013

CDC 4370

2005

- Phase II/III, randomized, double-blind study of safety & efficacy of once daily TDF in injection drug users (IDUs) to prevent HIV infection
- Enrolling 2,400 male & female IDUs in Bangkok, Thailand
- Results expected: 2012

ANRS Ipergay

Agence Nationale pour Recherche sur le SIDA

2012

- Phase I, randomized, double-blind study to evaluate feasibility of a phase III study for safety & efficacy
- Seeks to evaluate the use of TDF/FTC intermittently (if/when sexually active, before and/or after sex, etc.) in MSM and transgender women in France and Canada
- Results anticipated: 2014– 2015

PrEP Demonstration Projects

- Florida DOH, MDCHD, U of M: Provider Survey: PrEP & nPEP
- San Francisco DPH & Miami STD Clinic PrEP Demonstration Project

Interim Guidance: Pre-exposure
Prophylaxis for the Prevention of HIV
Infection in Men Who Have Sex With Men
(CDC MMWR Vol. 60, No. 3, January 2011)

Before initiating PrEP... determine eligibility...

- Document negative HIV antibody/antigen test(s)
- Test for acute HIV infection should patient present symptoms
- Confirm that patient is at substantial, ongoing, high risk for HIV infection
- Conduct appropriate kidney function assays
- Screen for HBV infection; vaccinate against HBV if susceptible; treat active HBV infection
- Screen and treat for other STIs, as needed

Initiating PrEP...

- Prescribe Truvada ® (TDF [300 mg] + FTC [200 mg]) to be taken daily
- Prescribe no more than a 90-day supply, renewable only after HIV testing confirms patient remains HIV negative
- Provide risk-reduction and PrEP medication adherence counseling and condoms
- If active HBV infection is diagnosed, consider using TDF/FTC for HBV Tx as well as PrEP for HIV prevention

PrEP follow-up...

- Continue to test for HIV, every 2 – 3 months
- Evaluate & support PrEP medication adherence at each follow-up visit, more often if inconsistent adherence is identified
- Every 2 – 3 months, assess risk behaviors and provide risk-reduction counseling and condoms. Assess STI symptoms and, if present, test and treat for STIs
- 3 months after initiation, then yearly while on PrEP medication perform appropriate kidney function serology

PrEP discontinuance...

- Conduct HIV testing to confirm presence or absence of HIV infection
- If HIV positive, order & document results of resistance/susceptibility assay and establish linkage to HIV care
- If HIV negative, link to risk-reduction support services
- If active HBV was diagnosed at initiation of PrEP, consider appropriate medication for continued Tx of HBV

Gilead Sciences, The Federal Food
& Drug Administration, and
Gilead's Supplemental New Drug
Application (sNDA)

...a timeline...

- **December 2011: Gilead submitted a sNDA to FDA requesting approval for the use of Truvada ® for PrEP against HIV infection among MSM and transgender women**
- **February 2012: FDA grants priority review status to Gilead's sNDA**
- **May 10, 2012: FDA will convene its Antiviral Drugs Advisory Committee, to include Gilead's sNDA and opportunities for public comment**
- **The FDA has set a target review date for Truvada ® for PrEP of June 15, 2012**

Questions?

Comments...

PrEP informational resources...

**Interim Guidance: Pre-exposure Prophylaxis for the
Prevention of HIV Infection in Men Who Have Sex
With Men**

(CDC MMWR Vol. 60, No. 3, January 2011):

www.cdc.gov/hiv/prep/

CDC PrEP Fact Sheet:

<http://www.cdc.gov/hiv/prep/pdf/PrEPfactsheet.pdf>

CDC PrEP Clinical Trials Fact Sheet:

http://www.cdc.gov/hiv/prep/pdf/PrEP_TrialsFactSheet.pdf

Webinar Evaluation

- Before leaving today's webinar, please take a moment to complete the evaluation in the polling section (to the right of your screen)
- Your feedback is extremely important to us and will help improve on current and future trainings
- The more feedback the better!

Contact Information

John-Mark Schacht

Intervention Specialist

John-Mark_Schacht@doh.state.fl.us

Bureau of HIV/AIDS, Prevention Section

Florida Department of Health

4052 Bald Cypress Way, Bin A-09

Tallahassee, FL 32399

(850) 245-4336

Visit us online at:

www.wemakethechange.com

www.preventhivflorida.org

www.facebook.com/preventhivflorida

www.twitter.com/PreventHIVFL

