Px Wire: A Quarterly Update on HIV Prevention Research

AVAC
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AVAC's Take

As this issue of *Px Wire* went to press, the US Food and Drug Administration (FDA) announced its approval of daily oral TDF/FTC for PrEP. This is the first ARV to be approved for HIV prevention in HIV-negative adults. Approval came a week after peer-reviewed publication of the data from FEM-PrEP, TDF-2 and Partners in Prevention trials in the *New England Journal of Medicine* (available at *www.nejm.org*). It is an exciting and challenging development we'll be tracking closely in the months and years to come. In this issue we review global PrEP developments, and present an infographic summarizing progress towards beginning to end the AIDS epidemic. We've also included a list of prevention research-related sessions at AIDS 2012. Enjoy!

Global PrEP Developments

The US FDA approval of Gilead Science Inc.'s application for an HIV prevention indication for daily oral TDF/FTC (brand name Truvada) is a landmark development for the US and the global landscape. (For the latest updates visit *www.prepwatch.org*.)

In addition to FDA approval, many steps related to TDF/FTC as PrEP are being taken in different countries. For now, there is no single master plan. Instead, trial data are being interpreted differently across countries and regions, creating a need for advocates to push for clarity on plans and milestones.

Regulatory and guidance activity

The World Health Organization has said that it plans to release "rapid advice" on PrEP and that this document will encourage interested countries to launch demonstration projects. A comprehensive WHO guidance document on the use of ARVs for prevention and treatment in both HIV-negative and -positive individuals is expected in 2013.

Gilead reports that the company is in ongoing discussions with the European Medicines Agency (EMA) but has not finalized plans for filing for a prevention indication for TDF/FTC. Even if approval is sought and granted, EU member states will still need to develop national policies and introduction plans.

The EMA recently closed the comment period on a paper on regulatory aspects of pre-clinical and clinical development of the full range of oral and topical PrEP strategies.

Demonstration Projects in the United States

STUDY	NUMBER	DURATION	LOCATION
NIAID PrEP MSM Demo	500 MSM	12 months	Miami, San Francisco
Los Angeles PATH*	600 MSM and transgender women	11 months	Los Angeles
CCTG*	400 MSM	24 months	Long Beach, Los Angeles, San Diego
East Bay Consortium*	Young MSM of color	Data not available	East Bay Area, CA

(*California HIV/AIDS Research Program funded)
Demonstration projects are being discussed for Kenya, Nigeria, South Africa, Uganda and other US cities. In addition, ongoing and planned PrEP open-label and feasibility studies will provide information on how to optimize programming. Look for details at *www.avac.org/pxrd* as they become available.

In mid-June the Southern African HIV Clinicians Society Consensus Committee issued guidelines aimed at clinicians on the use of PrEP using TDF/FTC among MSM at risk of HIV infection. Some advocates have raised the question of if and when similar guidance might be developed for heterosexual populations. For now, there is no clarity on the timeline for such a process. Gilead has not yet filed for a PrEP indication with South Africa's regulatory body, the Medicines Control Council (MCC).

Comprehensive US Public Health Service (PHS) guidelines for PrEP in the US are expected in late 2012 or early 2013. They will be posted for public comment prior to publication. These will update and expand on the interim guidance issued for gay men and MSM in early 2011.

Some groups have chosen a slower approach. The British HIV Association and the British Association for Sexual Health and HIV have stated that, based on available data, PrEP for HIV prevention should only be prescribed in the context of a clinical trial until more data are available. The UK Medical Research Council is planning an open-label study to investigate adherence, behavior change and acceptability in British MSM using TDF/FTC as PrEP.

Ensuring access: A prerequisite for PrEP

PrEP using daily oral TDF/FTC is a potentially powerful prevention tool. It is also complicated to explain and demanding to use, given that it requires consistent pill-taking, regular HIV testing and

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ACHIEVING THE END

For the first time, the end of the global AIDS epidemic is within reach. Recent breakthroughs in HIV prevention research have created unprecedented opportunities to curb new HIV infections, save lives and set the world on a path towards eliminating HIV transmission.

AVAC
Global Advocacy for HIV Prevention

DELIVER | PROVEN TOOLS FOR IMMEDIATE IMPACT

TREATMENT AS PREVENTION

DATA

96%

reduction in HIV transmission within serodiscordant couples.

CONCEPT

[PRESENT]
Treatment is prevention — preserving health and providing highly-effective prevention.

[PAST]
Treatment preserves health.

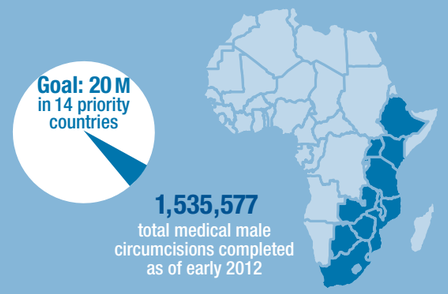
TREATMENT GAP

6.6 million people on treatment

15 million people in need of treatment

34 million people living with HIV

VOLUNTARY MEDICAL MALE CIRCUMCISION



1,535,577
total medical male circumcisions completed as of early 2012

DEMONSTRATE | AND ROLL OUT NEW HIV PREVENTION OPTIONS

PRE-EXPOSURE PROPHYLAXIS

DATA

ON DAILY ORAL TDF/FTC

42%
reduced risk in men who have sex with men

75%
reduced risk in heterosexual couples

Effectiveness of PrEP is dependent on adherence.

REGULATORY PATH

July 2012 – US FDA approves TDF/FTC for HIV prevention in HIV-negative adults

July 2012 (expected) – WHO issues rapid advice on TDF/FTC as PrEP

2013 and beyond – WHO guidance on use of ARVs; regulatory review in additional countries

Regulatory review processes needed or are underway in many other countries worldwide.

DEMO PROJECTS

4
PrEP demonstration projects planned or underway in MSM and transgender women in the US

0
PrEP demonstration projects ongoing in countries outside the US in other populations. At least four are under discussion.

MICROBICIDES

1% TENOFOVIR GEL

39%

In 2010 the CAPRISA 004 trial showed 39% reduced risk of HIV infection. In 2011 the VOICE trials showed no effect. Data from the CAPRISA 008 and FACTS 001 trials could be available in 2014.

RECTAL GEL

Safe and acceptable to women and men in the US (MTN 007)

MTN 017, Phase II safety and adherence study of tenofovir gel for rectal use and oral TDF/FTC in MSM and transgender women. Scheduled to start January 2013.

DAPIVIRINE RING

THE RING STUDY (IPM 027)
Phase III safety and efficacy study in 1,650 women. Results expected early 2015.

ASPIRE (MTN 020)
Phase III safety and efficacy study in 3,476 women. Results expected early 2015.

COMBINE

DEVELOP | LONG-TERM SOLUTIONS NEEDED TO END THE EPIDEMIC

VACCINES

RV144 AND THE P5

31.2%
efficacy overall, with higher efficacy at 12 months after immunization.

First vaccine trial to show protection against HIV in humans.

In 2012, follow-up research yielded clues about how the vaccine affected risk of HIV infection.

Pox-Protein Public Private Partnership (P5) formed in 2011 to develop vaccine strategy similar to the one tested in RV144; efficacy trials of this strategy planned in Thailand and South Africa to begin in 2016.

HVTN 505

DOES THE DNA/AD5 VACCINE PROTECT AGAINST HIV?

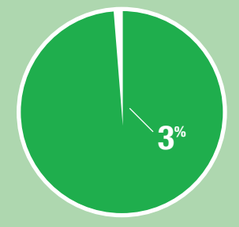
Efficacy data are expected by 2014.

ANTIBODY RESEARCH

100'S OF ANTI-HIV ANTIBODIES DISCOVERED SINCE 2009

Scientists have studied blood samples from people living with HIV and identified potent broadly neutralizing antibodies (bNAbs). Studying the structure of these bNAbs and the way that they attach to the virus has provided clues to guide vaccine design. Right now it is not clear how to design a vaccine that generates mature, potent bNAbs. This important work is ongoing.

CURE



ONLY 3% OF AIDS RESEARCH FUNDING IS DEVOTED TO AIDS CURE RESEARCH.

End

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acceptance of potential side effects. No one knows, at this stage, the best designs for programs that maximize benefit and minimize risk to individuals. This is where "demonstration" or "pilot" projects come in. Such projects are planned in a range of settings (see table on p.1), and the data they generate will be critically important to guiding any further scale-up.

TDF/FTC also has to be available and affordable as treatment before TDF/FTC as PrEP can be considered as a public health intervention. Availability depends on many factors including drug price, inclusion in national formularies and registration status. In Peru, one of the countries where the iPrEx PrEP trial took place, TDF/FTC registration for treatment is still pending. Registration has been filed in Ecuador, another iPrEx country. AVAC partners Epicentro and IRMA are mobilizing a coalition to track regional registration and access issues.

Gilead says that there are plans in place to file a prevention indication for TDF/FTC in multiple countries following FDA review. AVAC will work with partners to track drug access for prevention and treatment in key countries. If you'd like to be involved —please be in touch!

Recently Released

HIV Prevention Research + Development Database, PxRD is a comprehensive source on biomedical HIV prevention clinical trials, *www.avac.org/pxrd*.

Research Literacy Database, AVAC's Research Literacy Database provides a searchable resource of educational materials for many audiences, *www.avac.org/researchliteracy*.

Not to be Missed

The International AIDS Conference will take place July 22-27 in Washington, DC. Some of the many HIV prevention activities are highlighted below—for a comprehensive roadmap, visit *www.avac.org/aids2012*. Let us know about your event at *avac@avac.org*.

Sunday, July 22

- *Start Making Sense: Weighing the Evidence on Hormonal Contraception and HIV,* Mini Room 4, 9:00-11:00
- *Bridging the Worlds of Science, Community and Policy: Communicating HIV Prevention Research,* Mini Room 2, 11:15–13:15
- *Pre-exposure Prophylaxis (PrEP) for HIV Prevention: Maximizing Success*, Mini Room 9, 13:30-15:30
- *Rectal Microbicides: Making HIV Prevention Gel,* Mini Room 8, 15:45–17:45

Monday, July 23

- *Research for New HIV/AIDS Prevention Technologies: Community Perspectives,* Mini Room 8, 7:00-8:30
- *Getting Real about Getting to the End of AIDS,* Session Room 2, 18:30–20:30
- *Global Call For Action For VMMC: Communications and Advocacy for Maximum Public Health Impact,* Session Room 8, 18:30–20:30

Tuesday, July 24

- *The Role of Vaccines in Ending the Epidemic,* Mini Room 6, 18:30-20:30
- *Microbicides: The Road Ahead,* Mini Room 5, 18:30–20:30

Wednesday, July 25

- *Advancing the Integration of HIV and Sexual and Reproductive Health: An Interactive Dialogue,* Session Room 6, 18:30–20:30
- *Paving the Way to an AIDS-Free Generation: The Role of Female Condoms in Comprehensive HIV Prevention,* Mini Room 5, 18:30–20:30

Thursday, July 26

- *Choice Matters: Expanding the Method Mix of ARV-based Prevention for Women in 2012 and Beyond,* Mini Room 7, 18:30–20:30
- *New Products, New Paradigms: Combination Products for Women,* Mini Room 1, 18:30–20:30

Follow AVAC at AIDS 2012 on Twitter *(@hivpxresearch)* and Facebook. If you're in DC, visit us and partners at the Partners in Prevention Research booth (#367) in the Global Village and at the AVAC booth (#70) in the Exhibition Hall.

About AVAC

Founded in 1995, AVAC is a non-profit organization that uses education, policy analysis, advocacy and a network of global collaborations to accelerate the ethical development and global delivery of HIV biomedical prevention options as part of a comprehensive response to the pandemic.

To receive regular updates via email sign up at *www.avac.org/mailinglists*.

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