
AVAC's Take

Reporting back on the XVII International AIDS Conference (3-8 August) in Mexico City could take the entire issue of *Px Wire*—and then some! In this publication, we present you with a few of our strongest impressions of how HIV prevention research figured at the world's largest AIDS gathering. These—and others we haven't included—will doubtless prompt action, questions, advocacy and additional research in the two years before the conference reconvenes in Vienna in 2010.

Three new prevention trials—described in *At a Glance*—were launched in the last three months, all of which are studying vaginal and/or oral ARVs for HIV prevention. Topical ARV formulations are generally referred to as microbicides, and oral ARV prevention is known as PrEP. But the boundaries are far from distinct, and we think it's time for new language: "Oral/Vaginal ARV-based" prevention. Microbicides can also be used rectally and when studies of ARV-based candidates look at this usage, we'll expand the category even further.

As always, we'd love to hear from you! Send any comments to pxwire@avac.org. ■

Data Dispatch: PAVE 100 trial a no-go; Women weigh in on male circumcision for prevention; Mexico City debrief

In July, the US National Institutes of Health (NIH) announced that it would not move forward with the much-discussed PAVE 100 vaccine trial, a planned efficacy trial of a prime-boost strategy that was examined and re-examined in light of the disappointing data from the STEP vaccine trial.

The vaccine strategy to be tested in PAVE 100 was developed by the NIH Vaccine Research Center (VRC) and included an adenovirus-vector based component that was similar, though not identical, to the candidate tested in STEP. When the STEP candidate failed to show efficacy—and also appeared to increase susceptibility to HIV in some recipients—PAVE 100 was first delayed and then scaled back from its original proposal. An NIH announcement in July stated that the redesigned version would not go forward.

As *Px Wire* went to press, the story evolved yet again. Following up on a possibility raised in his July decision about PAVE 100, Anthony Fauci, head of NIH's NIAID, gave the green light to a "smaller, leaner, meaner" trial known, for now, as HVTN 505, which will test the VRC strategy's ability to control viral load, and to garner critical information and ideas for future vaccine research. Now, the US HIV Vaccine Trials

Network must develop and obtain approval for a protocol, and much community consultation is needed to ensure that there's understanding of and input into this trial.

After any clinical trial generates a compelling finding, the most important question is: what does it mean in the real world? And when it comes to male circumcision, there are a number of essential questions—including what does it mean for women and women's ability to negotiate if, when and how sex happens?

WHO/UNAIDS recommends male circumcision as a useful strategy for reducing HIV-negative men's risk of infection via vaginal sex. This approval rests on the evidence generated by three randomized clinical trials in different settings (Kenya, Uganda, South Africa), all of which suggest that medical male circumcision reduces men's risk of infection by at least 50 percent.

This question of implications for women was taken up in June, at a two-day consultation that brought together nearly 40 civil society stakeholders, the majority of whom were women living with HIV from sub-Saharan Africa. This session was organized by AVAC and directly preceded a WHO expert consultation on the same topic.

Meeting attendees articulated concerns about the strategy, particularly as it would impact men's risk behaviors, shared sexual decision-making, spending allocations for women-focused HIV prevention, and stigma and blame directed at HIV-positive women. Addressing these concerns is an essential part of any attempt to introduce male circumcision for HIV prevention.

Continues on back

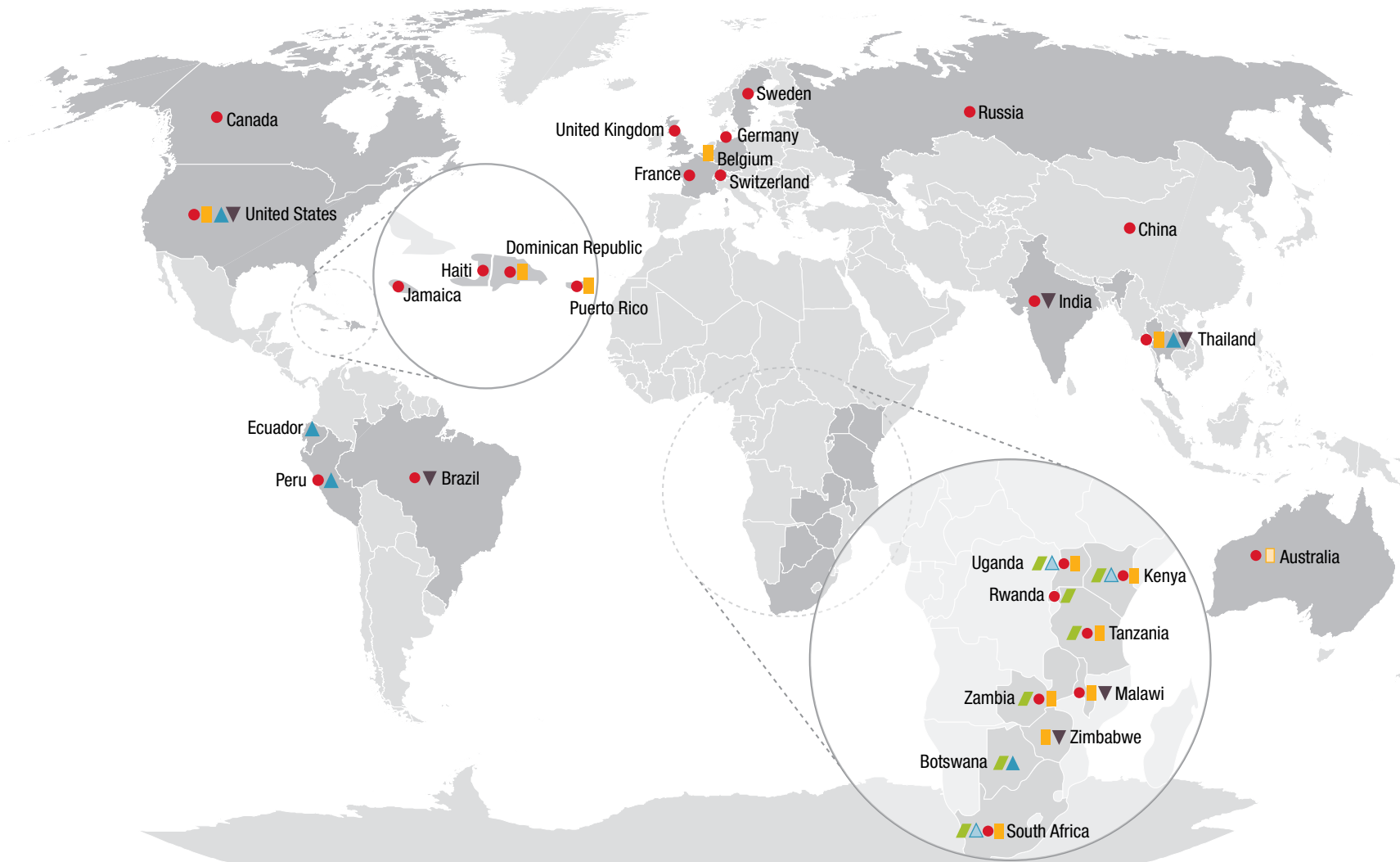
At a Glance: New Clinical Trials

The microbicide VivaGel, owned by Starpharma, entered an NIH-sponsored phase I trial in Australia. The study will look at absorption over time and the level of antiviral activity against HIV and HSV-2.

MTN 001, a phase II trial comparing oral tenofovir (TDF as PrEP) and the vaginal gel formulation of the drug (TDF microbicide gel) kicked off in Uganda, South Africa and the United States. The 21-week NIH-sponsored study measures adherence and drug absorption of both formulations, and will help researchers better understand how to design future prevention studies with tenofovir.

A phase III trial, Partners PrEP, was launched to compare oral TDF with the oral combination of TDF and FTC (emtricitabine) for HIV prevention amongst serodiscordant couples in Kenya and Uganda. Results from this Gates-funded trial are expected in 2012.

ONGOING TRIALS OF NEW PREVENTION OPTIONS WORLDWIDE












- □ Australia
- Belgium
- ▲ Botswana
- ▼ Brazil
- Canada
- China
- □ Dominican Republic
- ▲ Ecuador
- France
- Germany
- Haiti
- ▼ India
- Jamaica
- ▲ □ Kenya
- ▼ Malawi
- Peru
- □ Puerto Rico
- Russia
- Rwanda
- ▲ □ South Africa
- Sweden
- Switzerland
- □ Tanzania
- ▲ ▼ Thailand
- ▲ □ Uganda
- United Kingdom
- ▲ ▼ United States
- □ Zambia
- ▼ Zimbabwe

● VACCINES	■ MICROBICIDES	▲ PRE-EXPOSURE PROPHYLAXIS	▲ HSV-2 TREATMENT	▼ PARTNER TREATMENT
● New	■ New	▲ New	▲ New	▼ New

HIV PREVENTION RESEARCH: A COMPREHENSIVE TIMELINE OF EFFICACY TRIALS*

2007	2008	2009	2010	2011	2012+
<p>FHI Phase III trial of the vaginal microbicide Cellulose Sulfate gel for the prevention of HIV infection in women (Nigeria)</p> <p>Trial stopped early—January 2007 Results announced July 2007</p>	<p>Phase III trial of acyclovir for the reduction of HIV infection in high-risk, HIV-negative, HSV-2 seropositive individuals (Peru, South Africa, US, Zambia, Zimbabwe)</p> <p>Results announced February 2008</p>	<p>Phase III trial of a prime-boost (ALVAC-AIDSVAX) combination preventive HIV vaccine (Thailand)</p>	<p>Large-scale efficacy trial of a once-daily dose of oral tenofovir+emtricitabine to prevent HIV infection in heterosexual men and women (Botswana)</p>	<p>Phase III trial of community mobilization, mobile testing, same-day results, and post-test support for HIV (South Africa, Tanzania, Thailand, Zimbabwe)</p>	<p>Large-scale efficacy trial to determine the effectiveness of two different HIV prevention strategies; once-daily oral tenofovir and once-daily oral tenofovir+emtricitabine in serodiscordant heterosexual couples (Kenya, Uganda)</p>
<p>CONRAD Phase III trial of the vaginal microbicide Cellulose Sulfate gel for the prevention of HIV infection in women (Benin, India, South Africa, Uganda, Zimbabwe)</p> <p>Trial stopped early January 2007 Results announced July 2007</p>	<p>Large-scale trial to evaluate the safety of male circumcision and its potential protective effect for HIV-negative female partners of HIV-positive circumcised males (Uganda)</p> <p>Trial stopped enrollment and surgeries in December 2006. Results announced February 2008</p>	<p>Phase II/IIb trial of the vaginal microbicides BufferGel and 0.5% PRO 2000/5 gel for the prevention of HIV infection in women (Malawi, South Africa, Tanzania, US, Zambia, Zimbabwe)</p>	<p>Large-scale efficacy trial of a once-daily dose of oral tenofovir+emtricitabine to prevent HIV infection in high-risk men who have sex with men (Ecuador, Peru, South Africa, US)</p>		<p>Phase III trial to determine the effectiveness of two antiretroviral treatment strategies in preventing the sexual transmission of HIV in HIV-serodiscordant couples (Brazil, India, Malawi, Thailand, US, Zimbabwe)</p>
<p>Phase III trial of the female diaphragm to prevent HIV infection in women (South Africa, Zimbabwe)</p> <p>Results announced July 2007</p>	<p>Phase III trial of the vaginal microbicide Carraguard for the prevention of HIV infection in women (South Africa)</p> <p>Results announced February 2008</p>	<p>Phase III trial of the vaginal microbicide PRO 2000 for the prevention of HIV infection in women (South Africa, Tanzania, Uganda)</p>	<p>Phase IIB trial of the vaginal microbicide tenofovir gel for the prevention of HIV infection in women (South Africa)</p>		
<p>Test-of-concept trial of Merck's adenovirus preventive HIV vaccine candidate—STEP study (Australia, Brazil, Canada, Dom. Rep., Haiti, Jamaica, Peru, Puerto Rico, US)</p> <p>Trial halted immunizations, September 2007. Follow-up and data collection continue.</p>	<p>Phase II trial to test the clinical and behavioral safety of a once-daily dose of oral tenofovir among HIV-negative men who have sex with men (US)</p>	<p>Large-scale efficacy trial of a once-daily dose of oral tenofovir to prevent HIV infection in injecting drug users (Thailand)</p>			
<p>Test-of-concept trial of Merck's adenovirus preventive HIV vaccine candidate—Phambili (South Africa)</p> <p>Trial halted enrollment and immunizations, September 2007. Follow-up and data collection continue.</p>	<p>Study of different risk-reduction interventions for HIV vaccine trials—Project UNITY (US)</p>	<p>Phase III trial of HSV-2 suppression in serodiscordant couples (Botswana, Kenya, Rwanda, South Africa, Tanzania, Uganda, Zambia)</p>			

	VACCINE		CERVICAL BARRIER METHOD
	PRE-EXPOSURE PROPHYLAXIS (PrEP)		PARTNER TREATMENT
	HERPES SIMPLEX VIRUS 2 (HSV-2) TREATMENT/SUPPRESSION		BEHAVIORAL
	MICROBICIDE		TRIAL COMPLETED OR STOPPED
	MALE CIRCUMCISION		

To view this timeline online with trial details please visit www.avac.org/timeline-website/.

* The trial end-dates listed in this table are estimates. Due to the nature of clinical trials the actual dates may change. AVAC will continue to monitor the trials' progress and will update the timeline accordingly.

If you have any questions or comments regarding the information presented here please email avac@avac.org.



Data Dispatch continued from p.1

Recently released

- AVAC's "*Anticipating the Results of PrEP Trials*," (August 2008) calls for increased action from governments, global health institutions, donors, researchers, and advocates to prepare for initial results—expected as early as 2009—from PrEP trials. (Download at www.prepwatch.org.)
- "*Sustaining the HIV Prevention Research Agenda*," (August 2008) is the annual report from the HIV Vaccines and Microbicides Resource Tracking Working Group, and looks at funding for the array of experimental biomedical prevention strategies. (Download at www.hivresourcetracking.org.)

Coming Up

- In mid-October, Cape Town will play host to the AIDS Vaccine Conference, an annual gathering of researchers, funders and advocates to discuss the state of the field, new research discoveries and priorities for the year ahead. AVAC, along with multiple partners, will be hosting a special pre-conference session, "The Road Ahead: Addressing Critical Issues in AIDS Vaccine Research." The session will address a range of issues including research ethics in a post-STEP world, gender issues in vaccine and HIV prevention research, and key priorities for the field. For more information on this session and the conference visit www.avac.org/aidsvaccine08.htm.
- The PrEP committee of the CHAMP Prevention Research Advocacy Working Group invites the HIV/AIDS community in the United States to join in achieving a state of community preparedness. For information on mobilizing contact Josh Thomas at josh@champnetwork.org. ■

Not to be Missed

October 13: The Road Ahead: Addressing Critical Issues in AIDS Vaccine Research, *Cape Town, SA*

October 13-16: AIDS Vaccine 2008, *Cape Town, SA*

October 17-21: 2008 National Gay Men's Health Summit, *Seattle, WA*

November 19-21: 2008 National Summit on HIV Diagnosis, Prevention, and Access to Care, Forum for Collaborative HIV Research, *Arlington, VA*

December 1: World AIDS Day

The women health activists attending the meeting concluded with the drafting a statement on male circumcision's implications for women, presented at the following WHO consultation. (Download the statement in PowerPoint at www.avac.org/pdf/mc_statement.pdf.)

Mexico City—a selective set of quick takes:

• **Tx as Px—the growing buzz:** The phrase "treatment as prevention" turned up in plenty of speakers' remarks, even as the definition and the feasibility of the concept remained in debate. The thumbnail sketch: that treatment for HIV-positive people will lower infectiousness and that some of the same drugs might be used by HIV-negative people as an HIV risk-reduction strategy known as pre-exposure prophylaxis, or PrEP, and to prevent parent-to-child transmission during pregnancy and delivery. Can a one-two-three punch of antiretrovirals for both positive and negative people work? Are the health systems that are racing and struggling to meet the demand for ARV treatment in developing countries on track to expand to meet these "treatment as prevention" demands? These questions must be answered before this catch-phrase catches on.

• **PrEP demands action now:** There are no results from efficacy trials of PrEP—these are at least a year out—but there's plenty of work that must be done now, as was discussed at an AVAC-convened satellite session in which panelists responded to a range of different scenarios for trial outcomes. (Download satellite report at www.avac.org/pdf/prep_sat_080308.pdf).

In a session on community engagement with HIV research, Thai Treatment Action Group leader Karyn Kaplan reminded the audience of continued community concerns about the ongoing trial in Thai injection drug users.

• **More to consider as male circumcision moves forward:** Jam-packed sessions on male circumcision for HIV prevention provided updates on rates of risk behavior in participants from the completed efficacy trials, additional discussions of the implications for women, impact models and evidence on the durability of the protective effect out to 42 months in the volunteers in the Kenyan trial. ■

About AVAC



AVAC seeks to create a favorable policy and social environment for accelerated ethical research and eventual global delivery of new HIV prevention options as part of a comprehensive response to the pandemic.

101 West 23rd St. #2227 • New York, NY 10011 USA
Telephone +1 212.367.1279 • www.avac.org

To subscribe to or download *Px Wire* visit www.pxwire.org.