

Webinar #2 in our 2016 series

#### **Community Perspectives from CROI 2016**

#### Wednesday, April 6, 2016 | 2:30 pm - 4 pm ET

#### SPEAKERS:

#### Kate Borloglou

Jessica Salzwedel

Lisa Diane White

deputy director, SisterLove, Inc.

CAB member, The Well Project

program coordinator, AVAC

IN PARTNERSHIP WITH:

thewellproject





Together, we can change the course of the HIV epidemic...one woman at a time.

#onewomanatatime

#thewellproject

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### About The Well Project

- Non-profit organization with a mission to change the course of the HIV/AIDS pandemic through a unique and comprehensive focus on women and girls
- Leverages technology to improve health outcomes and increase quality of life for women and girls living with HIV
- Focus is to provide accessible and comprehensive #information, #community support, and #advocacy building
- Access our resources and join our community at <u>www.thewellproject.org</u>



#### About WATCH!

- WATCH! Women's Advocacy and Treatment Coalition on HIV is an ongoing HIV treatment advocacy and capacity-building webinar series
- The 2016 WATCH! series will take place throughout the year, and will include 5-6 webinars
- For certification, participants must participate in live webinar or view recording, take a pre- and post-test, and final evaluation survey (end of series)
- Webinars will be recorded and can be accessed up to one month after they take place



### Webinar Details

- Webinar will last approximately 90 minutes with Q&A at end
- Use live chat box on left side to enter questions while someone is talking; questions will be put in queue
- If you are listening to webinar via your phone, please enter second audio pin to connect your phone to computer \* (3-digit number)#
- Participants' lines will be muted until the Q&A
  - To unmute your phone, press \*6, or click on microphone icon at the top of your screen (if using computer microphone)
  - To mute, use your phone "mute" button



### Webinar Agenda



**Treatment Advocacy,** Kate Borloglou, Community Advisory Board, The Well Project, Community Scientific Subcommittee, AIDS Clinical Trials Group (ACTG)



**Pre-Exposure Prophylactics Research Updates from CROI 2016,** Lisa Diane White, Deputy Director, SisterLove, Inc.



**Ring, Injectables & Cure Research Updates from CROI 2016,** Jessica Salzdewel, Program Coordinator, AVAC



Moderator, Krista Martel, Executive Director, The Well Project



#### **Poll Question**

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- The annual Conference on Retroviruses and Opportunistic Infections (CROI) brings together top researchers from around the world to share the latest studies, developments, and best research methods in the ongoing battle against HIV/AIDS and related infectious diseases.
- Global model of collaborative science and the premier international venue for bridging basic and clinical investigation to clinical practice in the field of HIV
- CROI 2016 was held from February 22-25 in Boston, MA
- CROI 2017 to take place February 13-17 in Seattle, WA
- <u>Community Educator scholarships</u> available each year
- Visit <u>www.croiconference.org</u> for more info

#### The Well Project Update from CROI 2016



HIV/hepatitis C co-infection

· Reaching treatment goals

HIV and the brain

- Highlights from AIDS 2014: an Interview with Judy Auerbach
- Update from the 3rd International Workshop on HIV & Women
- Update from the 4th International Workshop on



#### **Treatment Advocacy**

Kate Borloglou The Well Project, ACTG Community Science Sub-Committee April 6, 2016

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### What Is an Advocate?

#### Advocate (n.): A person who **publicly supports** or recommends a particular cause or policy

- Focus of treatment advocacy:
  - Optimizing the quality of care and treatment
  - Increasing the access of care and treatment

### The Many Forms of Advocacy



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#### **Treatment Advocacy**

- Individual advocacy
- Blogger for The Well Project's, A Girl Like Me
- Community Advisory Board for The Well Project
- Ryan White Planning Counsel with local health department
- Community Advisory Board with Ohio State University AIDS Clinical Trials Unit
- Community Scientific Subcommittee with AIDS Clinical Trials Group



### **Treatment Advocacy**

- AIDS Clinical Trials Group (ACTG)
  - Community Scientific Subcommittee
    - Women's Health Inter-Network Scientific Subcommittee
    - Neurology Collaborative Science Group
    - Study Protocol Review Teams



### What Are Clinical Trials?

# *Clinical trial:* Describes many different types of **research studies on human subjects**



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### What is a Clinical Trial?

- A research study with human volunteers
- Designed to answer specific health questions
- Interventional trials test if a new intervention is safe and effective for people to use
  - Interventions can be drugs, devices, techniques, behavioral, or social
- **Observational trials** gather information about health issues from groups of people without any intervention



#### **Poll Question**

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#### Stages of Treatment Trials

Most common type of clinical trial in HIV is a **treatment** or **drug trial**; four stages (phases) of treatment trials:

#### Phase I: Is the drug <u>safe</u>?

- Tests drug in small number of participants (usually <100) to find a safe dose, determine how the drug is eliminated, document side effects
- Usually short (a few days to a few weeks)
- Phase II: Is the drug safe and <u>effective</u>?
  - Tests drug in larger number of participants (usually 100-300) to see if it works
  - May test different doses to find the best one
  - Continues to evaluate drug safety over a longer period of time
  - Usually lasts 6 months 1 year



#### Stages of Treatment Trials

#### Phase III: Is the drug safe and effective in larger groups of people for longer periods of time?

- Tests drug in very large group of participants (typically 1,000 3,000)
- Gathers more information about drug's safety, effectiveness by comparing it to an existing intervention or no intervention over long-term use
- Generally lasts 2-5 years following participants for 1-2 years
- Phase IV or Post-Marketing studies: What are the <u>long-term</u> <u>results</u> of using the drug?
  - Use of the drug in real-life circumstances
  - Done after U.S. Food and Drug Administration (FDA) approval
  - Gets more information about drug's best use
  - Further examines long-term side effects
  - Examines acceptability and actual use



#### Stages of Treatment Trials

- Company submits study data to the drug regulation authority (FDA in the U.S.) for approval once drug has completed first three phases of research
- Because need for HIV treatments is so great, drug can get accelerated approval if it offers something new or meets a need for people living with HIV
  - Accelerated approval may put special restrictions on how drug can be used
- Even with accelerated approval, drug company must continue doing long-term research on the drug for it to get full approval



### The Need for Studies of Women Living with HIV

- In the U.S., about 1 in 4 people living with HIV is a woman
- Almost 8 in 10 U.S. women living with HIV are African American or Latina
- Globally, women made up about half of all people living with HIV in 2013
- But in many HIV studies...

# Only 1 in 10 people being studied is a woman





### Need for Studies of Women Living with HIV

- Because HIV drugs may act differently in women's bodies, studies need to be designed to answer questions for women:
  - Specific drug doses for women
  - Possible differences in lab tests (CD4 cells, viral load)
  - How infections and gynecological conditions affect women living with HIV
  - What side effects are likely to affect women
- Only way to get this information is for *more women living with HIV to participate in clinical trials*

#### The REPREIVE Trial Tests a Strategy to Prevent Heart Disease in HIV

**Randomized Trial to Prevent Vascular Events in HIV** 



REPRIEVE is the **first** large-scale randomized clinical trial to test a strategy for preventing heartrelated disease among people living with HIV.









#### **REPRIEVE Trial Overview**

- The REPRIEVE trial tests whether treatment with **pitavastatin** an FDA approved statin medication lowers heart disease risk in HIV
- 6500 participants with HIV will be randomly assigned to take **pitavastatin or placebo** once daily



 At some sites, a CT substudy of REPRIEVE is offered; substudy participants have pictures of the heart taken at study entry and at 24 months



# Sex-specific mechanisms of cardiovascular disease risk and risk reduction within the REPRIEVE Trial

- An important goal of REPREIVE is to examine how factors unique to women - such as female hormones- affect heart disease risk
- The study will also teach us whether pitavastatin lowers heart disease risk in women as well as it lowers risk in men



#### Women's Recruitment Campaign

- A supplemental aim of the women's objective is to design, implement and evaluate the efficacy of an education-based awareness campaign to enhance enrollment of female participants into REPRIEVE
- Increasing enrollment of women into REPREIVE will allow us to answer clinically relevant questions about sex-specific health outcomes in women with HIV







### Pre-Exposure Prophylactics Research Updates from CROI 2016

Lisa Diane White SisterLove, Inc. April 6, 2016

Sister ove, Inc.



SisterLove, Inc.



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- **SisterLove, Inc.:** A women's HIV and Reproductive Justice and Human Rights non-profit.
- SisterLove, Inc. Mission: To eradicate the impact of HIV and sexual and reproductive oppressions upon all women and their communities in the U.S. and around the world



Sister ove, Inc. SisterLove, Inc.

**Lisa Diane White**, MPH is the Deputy Director of SisterLove, Inc. and joined the team in April, 2004. She has over 26 years of experience in Women's Health issues and other health education programs and services. Lisa Diane works to build collaborations for biomedical HIV prevention research education including Pre- and Post-Exposure Prophylactics, vaccine research, microbicides and clinical trial access.





# What is Pre-Exposure Prophylaxis (PrEP) for HIV prevention?

- The use of antiretroviral medication to prevent exposure to HIV
- TDF/FTC [an antiretroviral containing tenofovir (TDF) and emtricitabine (FTC) that is sold under the brand name Truvada]
  - Approved by U.S. FDA for PrEP in 2012



#### Key Developments

# What are key developments/conclusions from PrEP effectiveness and demonstration projects so far?

- No significant side effects observed in any trials of tenofovir-based PrEP
- Adherence is essential
  - Each trial that found benefit also found that people with high levels of adherence had high levels of protection
  - Lower adherence was associated with low or no protection
- PrEP is highly protective in both men and women



### Key Developments

- People with high rates of HIV risk behaviors can be highly adherent to PrEP
- Serodiscordant couples (one person living with HIV and one HIV-negative individual) can use PrEP as a "bridge" when person living with HIV begins ART or if (s)he chooses not to take ART
  - Can also be used for safer conception



### Key Developments

- Individual cases of HIV drug resistance have been observed in trials to date
  - Resistance could emerge if a person acquired HIV while on PrEP and continued taking PrEP during the time before diagnosis
- These cases appear to have occurred in participants who were living with HIV and in the "window period" of early infection when they began taking PrEP
  - They tested HIV-negative on the trials' screening tests
  - Reinforces importance of regular testing for anyone initiating or taking PrEP



#### Key Developments

- Most of what is known about oral PrEP relates to daily oral TDF/FTC – thus far this is the only form approved and recommended for use by regulatory bodies
- Because of differences in drug absorption in vaginal (20 days) and rectal tissue (7 days), data from MSM cannot be extrapolated to women—and vice versa



### PrEP Updates from CROI

#### **HIV Prevention Trials Network (HPTN) 073**

- Designed to assess initiation, acceptability, safety, feasibility of PrEP for black MSM
  - <u>Not</u> designed to evaluate efficacy of PrEP for HIV prevention
- Enrolled 238 HIV uninfected BMSM in Washington D.C., Los Angeles, and Chapel Hill, NC
- Participants offered Truvada and counseling to support PrEP use
- PrEP was utilized by 178 men
- 5 men became HIV positive, two of whom discontinued PrEP
- A subset of participants will be recruited for qualitative interviews about PrEP facilitators and barriers



### PrEP Updates from CROI

# Scope and risk of clinical complications of PrEP – bone mineral density

- Follow up analysis of iPrEx OLE clinical trial of PrEP assessed bone mineral density (BMD) during PrEP use and after discontinuation
- 498 participants were enrolled and median age was 25, 11% identified as trans, 43% smoked, 81% drank alcohol
- A DXA sub-study of bone mineral density was offered was conducted at 7 study sites
- Bone scans were conducted at baseline and every 24 weeks during PrEP and placebo use, and 24 weeks after stopping use



### PrEP Updates from CROI

#### Scope and risk of clinical complications of PrEP – BMD

- Data analyzed by level of PrEP adherence (as measured by levels of tenofovir in blood samples)
- The retained co-hort experienced longer exposure to PrEP (1.2 years vs. 1.5 years if they enrolled in OLE)
- <u>BMD declined in this group</u>
  - Loss of bone marrow can increase your risk for fractures
  - Participants experienced complete recovery of BMD after stopping PrEP, usually within 6 months
- Guidance about when to start and stop PrEP is important to maximize benefits and minimize BMD side effects


### PrEP Updates from CROI

#### Scope and risk of clinical complications of PrEP – renal function

- In another iPrEx OLE analysis, greater cumulative exposure to TDF-FTC PrEP was associated with greater renal function decline
  - Average decline: 5.6% from baseline in those with daily dosing
  - For those with a baseline creatinine clearance of <90 mL/min, there was a 27% chance of falling to <70 mL/min over the first year</li>
    - 60-90 is a mild decline in kidney function
  - This risk was greater in those over 40 years of age
    - Kidney function naturally declines with age
- Creatinine is a waste product from the breakdown of muscle tissue measured by doctors as a test of kidney function
  - Filtered through the kidneys and excreted in urine
  - As renal function declines, creatining clearance goes down



### PrEP Updates from CROI

#### Scope and risk of clinical complications of PrEP – renal function

- Tenofovir-based pills for PrEP have, on average, a small and not clinically significant effect, on renal function, that is reversible after PrEP discontinuation
- Researchers are still questioning how much renal monitoring is necessary to ensure safety with PrEP since findings over the last two years suggest that toxicity is very rare
- Current CDC guidelines suggest monitoring renal function every 6 months while on PrEP, with consideration for more careful attention for those:
  - Aged >40
  - With lower baseline renal function



### PrEP Updates from CROI

#### Scope and risk of clinical complications of PrEP – STIs

- Two CROI abstracts looked at rates of sexually transmitted infections (STIs) among those taking PrEP
- Rates were high and more frequent screenings detected more STIs
  - In one study, 21% of clients had an STI in the 6 months prior to beginning PreP
    - After being on PrEP, 13% had a new STI at 3-month follow up; 15% had a new STI at 9-month follow up
- Future work needs to assess optimal timing/cost-benefit of more frequent STI screening at each 3 month visit among PrEP users



### Ring, Injectables & Cure Research Updates from CROI 2016

Jessica Salzwedel AVAC April 6, 2016





### Who is AVAC?

AVAC works to accelerate the ethical development and global delivery of HIV prevention tools as part of a comprehensive and integrated response to the epidemic. Through education, policy analysis, advocacy and a network of global collaborations, we mobilize and support efforts to:





## What We'll Discuss

- Microbicide Ring Studies
- Long Acting Injectables
  - Prevention
  - Treatment
- Cure Research





#### Clinical Trial Evidence for HIV Prevention Options (February 2016)





### **Poll Question**

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## Dapivirine Vaginal Microbicide Ring

- "Microbicide" refers to substances that could be used in the vagina and/or rectum to reduce risk of HIV infection via sexual exposure
  - There are no microbicides currently licensed
  - Daily oral PrEP is the only currently available prevention tool that women can use to reduce risk of HIV without partner negotiation
  - Women need multiple options for HIV prevention because one size never fits all (just like birth control methods)
- Results from two Phase 3 trials studying the 4-week slow-release dapivirine vaginal ring were released at CROI 2016



## **Dapivirine Vaginal Ring**

	The Ring Study	ASPIRE
Objectives	Long-term safety and efficacy	Safety and effectiveness
Enrollment	Total: 1959 women ages 18-45 years	Total: 2629 women ages 18-45 years
Linoiment	Active arm: 1307 Placebo arm: 652	Active arm: 1313 Placebo arm: 1316
All participants receive a comprehensive HIV-1 prevention package		
Timeline	Started April 2012 Scheduled end Dec. 2016	Started August 2012 Completed June 2015

### Primary Effectiveness Results

The Ring Study	ASPIRE
• <b>31%</b> relative reduction	• 27% relative reduction
in HIV-1 incidence	in HIV-1 incidence
overall	overall
• 37% reduction among	<ul> <li>56% statistically</li> </ul>
women older than 21	significant reduction
years of age	among women older
	than 21 years of age



### Now What?

- Ring Study in South Africa now providing all women still on trial with dapivirine ring for remainder of their participation; seeking similar approval in Uganda
- NIAID (NIH institute) planning to support HOPE study, openlabel extension (OLE) for ASPIRE participants as well as a study of ring and PrEP in women ages 16-21
- IPM planning OLE study (DREAM) to provide former Ring Study participants access to ring and understand how women may use it when they know it can safely offer protection
- IPM preparing to submit for regulatory approval in late 2016/early 2017; earliest possible approvals in late 2017 and access in 2018

## Image: the well projectLong Acting Injectablesthe well project(LAI)





### LAI Antiretrovirals (ARVs)

	What are they?	What could they do?	Key facts
A STREET	ARVs given via injection that stay in the blood for long periods of time, need to be dosed every few months	In HIV-positive people, LAI ARVs could simplify treatment and change the way ARVs are delivered	Trials of LAI ARVs start with an oral lead-in phase to establish safety and tolerability
	Single-drug LAI PrEP regimens are being evaluated using injections every 8-12 weeks Two-drug LAI treatment are being evaluated using injections every 4-8 weeks	In HIV-negative people, the same ARVs could be long- acting PrEP This could ease adherence and make it simpler for some people to take, although issues of regular testing to monitor for HIV infection need to be addressed, as they do for all PrEP strategies	The drugs used as injectables have unique properties that allow them to be formulated into doses suitable for injection (many common ARVs cannot be used in this way) Trials designed to test for efficacy and possible regulatory approval for both treatment and prevention are expected to launch in 2016/7



Objectives	Safety and efficacy and dosing schedule	
Enrollment	HIV-positive individuals 18+ years Naïve to ART CD4+ greater than 200/cells	
Design	<ul> <li>Phase 2b, 2:2:1 randomized to receive either:</li> <li>400mg injection of cabotegravir + 600 mg IM rilpivirine every 4 weeks</li> <li>600mg injection of cabotegravir + 900mg IM rilpivirine every 8 weeks</li> <li>30mg +ABC/3TC oral daily</li> </ul>	
Results	Both 4- and 8-week intervals were able to maintain viral load <50 copies/mL Upcoming analysis at week 48 will determine dose moving into Phase 3 study	





Objective	Safety and Tolerability of Intramuscular CAB
Enrollment	Low-risk, healthy men 18-65 years
Design	Phase IIa placebo-controlled 5:1 Randomization 30 days, 30mg daily oral lead-in phase 800mg cabotegravir injection every 12 weeks
Results	Cabotegravir oral and LAI were both well tolerated; 8-week dosing being considered Participants preferred 12-week dosing vs. daily oral



### **Cure Research**





### HIV Cure Research-TLR 7 Agonist

Objectives	Safety and Efficacy Dosing Schedule
Study Design	<ul> <li>4 arm placebo-controlled trial of various oral doses</li> <li>Placebo</li> <li>GS 968 0.1mg/kg</li> <li>GS-9620 .05mg/kg</li> <li>GS-9620 .15mg/kg</li> <li>Rectal challenge → 65 day viremia → ART suppression 467 days → 19 TLR 7-Agonist → Treatment Interruption</li> </ul>
Enrolled Population	11 SIV+ Rhesus macaques (non-elite controllers)
Results	Treatment with up to 19 doses was well tolerated No viral blips between doses 11-19 2 of the 9 animals remained aviremic (below detection) for 3 months after treatment stopped



## HIV Cure Research-TLR 7 Agonist

### What is the real life meaning?

- 65 days is generally when non-human primates and humans reach their viral set point
  - The viral set point will be used to determine if there was a reduction in the reservoir
- Many macaques are natural controllers of the virus so it's important to make sure they do not control the virus without medication
- 3 active arms were able to shrink the reservoir
- 2 macaques did not rebound and did not have detectable virus in blood and lymph nodes



### **FRESH Cohort**

### the**well**project

- Study overview
  - 699 young women from Kwa-Zulu Natal enrolled since 2013
  - As of September 2015, 32 women diagnosed within the first 15 days of infection
  - Biweekly clinic visits and 3-hour education/ vocational training
- Dr. Ndhlovu, University of Kwazulu Natal, demonstrated that:
  - HIV-specific CD8 cells develop quickly but are prone to cell death
  - HIV-specific CD8 cells fight HIV and play a role in determining the viral set point early in infection
  - Once HIV-specific CD8 cells die, they do not return in number after ART-driven viral suppression



## The Well Project 2016 Survey



Your Voice Counts! The Well Project 2016 User Survey

Now open! Please provide your input and help us improve our programs and better serve the needs of women and girls living with HIV!

https://www.surveymonkey.com/r/TWPSurvey2016





### The Well Project Resources

The Well Project fact sheets on topics covered in this webinar:

- Update from CROI 2016
- PrEP for Women
- <u>Microbicides</u>
- <u>Understanding Clinical Trials</u>
- Lessons from GRACE: A US Study Focused on Women Living with HIV
- How to Be an Advocate for Yourself and Others
- <u>A Place at the Table: Having a Voice in HIV Planning and Decision</u> <u>Making</u>

Get connected with our community! <a>www.facebook.com/thewellproject</a> & <a>www.twitter.com/thewellproject</a>



## **Additional Resources**

- <u>SisterLove</u>
- <u>AVAC</u>
- <u>Positive Women's Network USA</u>
- <u>ACTG</u>
- <u>REPRIEVE</u>
- HIVE Online
- Black Treatment Advocates Network (BTAN)
- PxROAR (AVAC Advocates Network)



### **Oral PrEP Resources**

### Oral PrEP resources/links:

- AVAC's PrEP basics
- HPTN webinar on Study 073
- HPTN press release on Study 073
- AVAC overview of HPTN 073
- <u>NATAP overview of HPTN 073</u>

### Oral PrEP CROI webcasts

- IPrEX OLE bone mineral density (PrEP)
- <u>IPreX OLE renal function and STIs</u> (PrEP)
- <u>IPrEX OLE renal function and STIs</u> (<u>PrEP</u>)
- <u>STI data from community-based PrEP</u>
- <u>STI detection among PrEP users</u>





- The CUREiculum
- Project Inform HIV Cure Glossary of Terms
- Latte 2 CROI Webcast
- ECLAIR CROI Webcast
- FRESH Cohort Poster at CROI
- Bruce Walker's Cure Plenary at CROI



### Thank You!

# Questions & Answers

The Q & A will come from the questions submitted to the presenters through the chat box during the webinar session.