MSD'S ONGOING EFFORTS IN HIV BIOMEDICAL PREVENTION



13 October 2019 PrEP in Europe Conference - Warsaw

MSD began efforts in HIV prevention R&D in1986



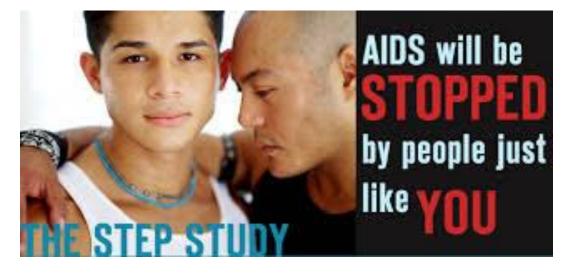
Rewriting Life

Merck's Mission: An AIDS Vaccine

With a hugely ambitious new research program, the pharmaceutical giant has revived the hunt for a vaccine to prevent AIDS. Will others follow?

by Jon Cohen

Mar 1, 2002





HIV & AIDS - sharing knowledge, changing lives

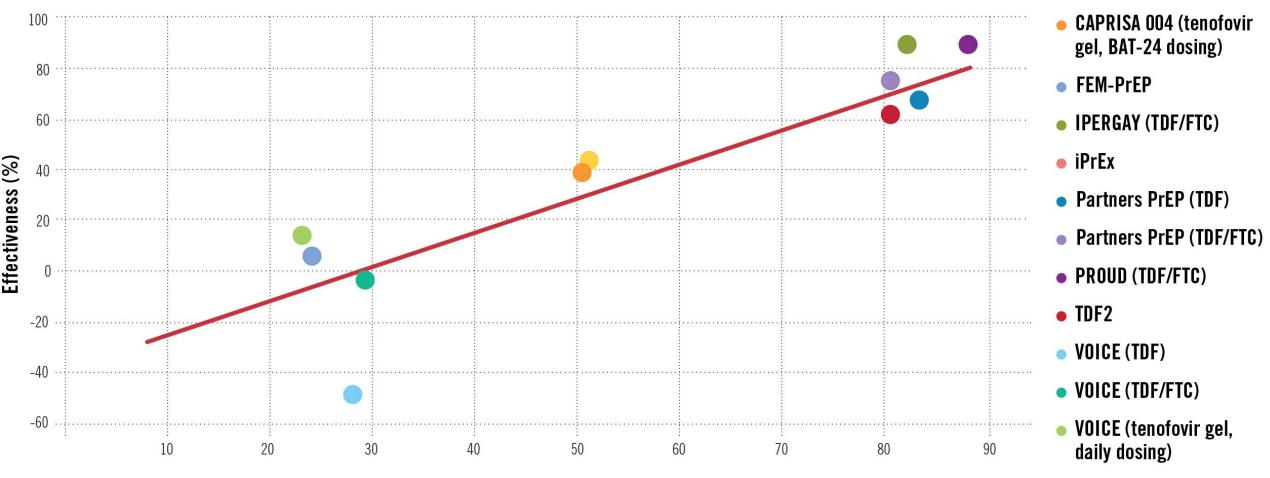
The search for an HIV prevention vaccine

Merck HIV vaccine fails, trials halted

Keith Alcorn 22 September 2007



PrEP Works if You Take It — Effectiveness and Adherence in Trials of Oral and Topical Tenofovir-Based Prevention



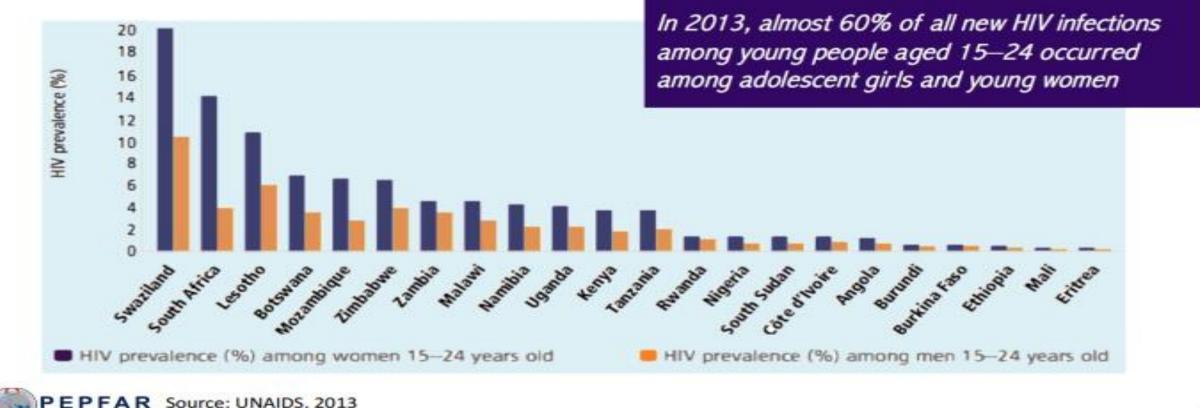
Percentage of participants' samples that had detectable drug levels



Young women have higher HIV rates than young men

Inside this youth bulge, young women are being infected at a disproportionately high rate. Adolescent girls and young women account for 75% of new infections in sub-Saharan Africa.

HIV Prevalence among Young Women & Young Men (15-24 years old) in Select African Countries, 2012



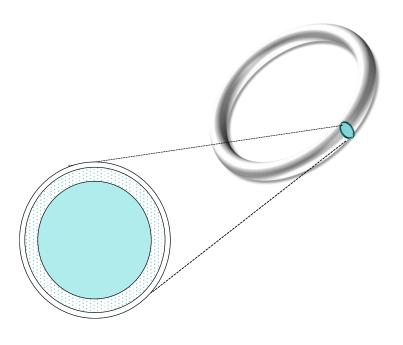
Partnership efforts to leverage MSD technology in HIV PrEP

Licenses in 2005 and 2008 for Novel HIV CCR5 and gp41 fusion inhibitors as microbicide candidates to the International Partnership for Mircrobicides

National Institute of Allergy and Infectious Diseases (NIAID). <u>Phase 1</u> <u>safety and pharmacokinetics study of MK-2048/vicriviroc (MK-4176)/MK-2048A intravaginal rings.</u> In: ClinicalTrials.gov. Bethesda (MD): National Library of Medicine (US). Registered on February 2, 2015. NLM Identifier: NCT02356302. Available at: https://www.clinicaltrials.gov/ct2/show/NCT02356302.

National Institute of Allergy and Infectious Diseases (NIAID). <u>Phase 1</u> <u>pharmacokinetic trial of two intravaginal rings (IVRs) containing</u> <u>different dose strengths of vicriviroc (MK-4176) and MK-2048.</u> In: ClinicalTrials.gov. Bethesda (MD): National Library of Medicine (US). Registered on April 14, 2015. NLM Identifier: NCT02419456







Phase II Trial of islatravir in Low Risk Individuals as monthly oral PrEP

NIH U.S. National Library of Medicine

ClinicalTrials.gov

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Safety and Pharmacokinetics of Oral Islatravir (MK-8591) Once Monthly in Participants at Low Risk of Human Immunodeficiency Virus 1 (HIV-1) Infection (MK-8591-016)

The safety and scientific validity of this study is the responsibility of the study sponsor and investigators. Listing a study does not mean it has been evaluated by the U.S. Federal Government. Know the risks and potential <u>benefits</u> of clinical studies and talk to your health care provider before participating. Read our <u>disclaimer</u> for details.

ClinicalTrials.gov Identifier: NCT04003103

Recruitment Status (): Recruiting First Posted (): July 1, 2019 Last Update Posted (): October 4, 2019

See Contacts and Locations

 Study Type 9:
 Interventional (Clinical Trial)

 Estimated Enrollment 9:
 250 participants

 Allocation:
 Randomized

 Allocation:
 Randomized

 Intervention Model:
 Parallel Assignment

 Masking:
 Double (Participant, Investigator)

 Primary Purpose:
 Prevention

 Official Title:
 A Phase 2a, Double-Blind, Placebo-Controlled Study to Evaluate the Safety, Tolerability, and Pharmacokinetics of Oral MK-8591 Once-Monthly in Participants at Low- Risk for HIV-1 Infection

 Actual Study Start Date 9:
 September 19, 2019

 Estimated Primary Completion Date 9:
 December 23, 2020

 Estimated Study Completion Date 9:
 April 5, 2021

First-in-human trial of MK-8591-eluting implants demonstrates concentrations suitable for HIV prophylaxis for at least one year

The New York Eimes

Someday, an Implant in the Arm Could Prevent H.I.V. Infection for One Year

By DONALD G. MCNEIL Jr. In what could eventually become a milestone for H.I.V. prevention, very preliminary tests of its new antiretroviral drug, islaan implant containing a new drug suggest that it may protect against infection for a full year. The new implant, by the drug company Merck, was tested in just a dozen subjects for 12 weeks. But experts were ouite excited at its potential to revolutionize the long battle against H.I.V. The research was described on Tuesday at an international AIDS conference in Mexico City. New H.I.V. prevention methods 6,000 young women under age 24 are desperately needed. About 75 million people have contracted the lethal virus since the AIDS epidemic began. Even now, about 1.7 million people are infected

are infected every week, and 80 percent of infected teenagers in Africa are girls. African girls are often victims of rape or pressured into sex with each year - despite decades of older men in return for food, promotion of condoms and absticlothes or cash. nence, and years of efforts to get Another study released Tuespeople to take a daily pill that preday at the same conference reinforced the extreme vulnerabil-

vents infection "If -- and I'm emphasizing if -- ity of young African women.

be removed if there are side e fects or H.I.V. infection." Merck's innovation is to deliver travir, with a proven technology long used for birth control: a matchstick-sized plastic rod inserted just under the skin of the upper arm that slowly releases tiny doses of the medication. Many people at risk of H.I.V. infection, particularly women in Africa, are desperate for prevention methods that are easier to use. and easier to conceal, than a bottle of pills According to Unaids, more than

birth-control implant, next to a penny for scale, is the same device that would slowly deliver a new antiretroviral drug, islatravir.

women in Africa often say they tion inhibitors, which block movecannot keep H.I.V. drugs at home ment of the enzyme responsible because they fear being accused for cloning the virus's DNA so that by family, neighbors and lovers of it can infect new cells. being immoral or of having H.I.V. Islatravir has "some remark-

strains with cross-resistance to en the implant and told to go out other H.I.V. drugs. and have sex or inject drugs. Ethi-Other drug companies have re- cally, they must be offered the best cently reported success with prevention methods available, inother long-acting forms of H.I.V. cluding oral PrEP condoms, clean prevention. For example, injec- syringes and intensive counseling tions of cabotegravir or rilpivirine about safe sex or safe drug use. deep into the buttocks have pro- That means many subjects ected study participants for a must be followed for years to see if the implant works better than month.

But monthly intramuscular in- other methods jections are inconvenient and Dr. Baynes, of Merck, declined sometimes painful. And implants to discuss how the next trial would can be removed. The half-life of in- be designed or to speculate or ectable cabotegravir, for exam- how long it would take. The comple, is about 40 days. If a user de- pany, he said, would consider test elops a "breakthrough" H.I.V in- ing in both the United States fection in spite of the injection, the where most H.I.V. transmission is ingering drug may drive the virus between gay men, and in Africa o mutate into a resistant form. where the virus is passed mostly Although scientists are excited between men and women. about the Merck implant's possi-He also declined to discuss the bilities, they warned that it still eventual cost, other than to say

needs to prove itself. "we're committed to responsible The drug has protected rats and pricing monkeys against multiple deliber- Price is a deeply contentious isate attempts to infect them, but sue in PrEP. High hopes for a human testing thus far has been quick end to the AIDS epidemic only for safety: to see whether a raised by Dr. Grant's 2010 study

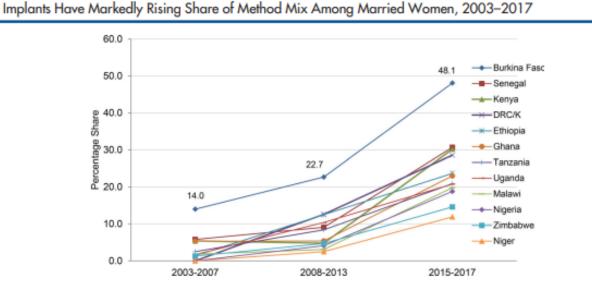
"If it pans out in a larger trial that it delivers a level of drug that's protective for a year, that would be a gamechanger." -Anthony Fauci, director, NIAID

First-in-human trial of MK-8591eluting implants demonstrates concentrations suitable for HIV prophylaxis for at least one year. Late-breaking Oral Presentation. IAC Tuesday, July 23, 16:30-18:00 CDT. Abstract TUAC0401LB. R. Matthews et al.

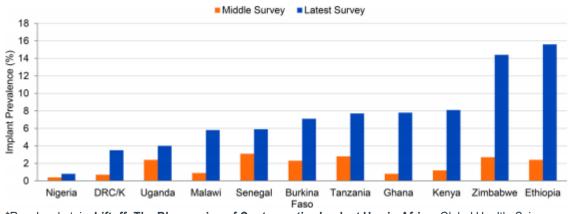
Global partnership efforts have led to a significant scale up in use of long acting contraceptives in the developing world

- At the 2012 London Summit on Family Planning, global leaders set an ambitious goal to ensure 120 million additional women and girls in the poorest countries would have access to modern contraception by 2020.
- As for 2018, nearly 46 million more girls and women are using contraception than in 2012
- Since the inception of the Implant Access Program in 2013, almost 53 million implants have been distributed in the world's poorest countries. Implant procurement in 2018 is double 2012 procurement.

Source: IMPLANT ACCESS PROGRAM: EXPANDING FAMILY PLANNING OPTIONS FOR WOMEN< November 2018, <u>http://www.familyplanning2020.org/sites/default/files/Our-Work/ppfp/2018%20IAP%202%20pager_VF.pdf</u>



Comparable Increases in Implant Use by Sexually Active Unmarried Women, 2008-14 to 2015-17



*Roy Jacobstein, Liftoff: The Blossoming of Contraceptive Implant Use in Africa. Global Health: Science and Practice March 2018, 6(1):17-39; https://doi.org/10.9745/GHSP-D-17-00396,

http://www.ghspjournal.org/content/ghsp/6/1/17.full.pdf

Challenges Ahead

- Regulatory Guidance for PrEP Development
- PrEP Program Implementation and Scale Up in Key Populations and Geographies
- Resourcing PrEP Scale Up







THANK YOU

