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# Researchers begin safety study of dapivirine ring and oral PrEP in breastfeeding women

***Similar study in pregnant women already underway***

**PITTSBURGH, Aug. 31, 2020** – The development of safe and effective HIV prevention methods for cisgender women has long been a global health priority, yet research in women during pregnancy and breastfeeding, when they are most vulnerable to infection, has lagged years behind.

Women need safe and effective methods for HIV prevention they can use at all times of their lives, say researchers from the National Institutes of Health-funded Microbicide Trials Network (MTN), who have just launched a new study called B-PROTECTED, or MTN-043. B-PROTECTED will enroll women who are breastfeeding, as well as their babies, at trial sites in Malawi, South Africa, Uganda and Zimbabwe.

In these and other sub-Saharan African countries, women are estimated to be up to four times more likely to acquire HIV when breastfeeding – more than at any other time in their lives, including during pregnancy. And if they get HIV while breastfeeding, chances are higher they will transmit the virus to their babies, as well.

The first sites to begin the B-PROTECTED study are the Wits Reproductive Health and HIV Institute (Wits RHI) Shandukani Research Centre in Johannesburg, South Africa, and the Makerere University-Johns Hopkins University (MU-JHU) Research Collaboration in Kampala, Uganda. A similar study involving pregnant women, called DELIVER (MTN-042), is also ongoing at these two sites; both studies will be conducted at the Malawi and Zimbabwe sites as well.

Both B-PROTECTED and DELIVER are open-label Phase IIIb studies designed to evaluate the safety of two HIV prevention methods – a daily antiretroviral (ARV) pill called Truvada®, an approach known as oral PrEP (short for pre-exposure prophylaxis) that is already approved in many countries, and the monthly dapivirine vaginal ring, a new HIV prevention method, which in late July received a positive opinion by the European Medicines Agency (EMA), a significant step toward its potential approval in African countries. The EMA's review of the ring was conducted in cooperation with the World Health Organization (WHO) through the Article 58 procedure.

If approved by national regulatory authorities, the monthly dapivirine ring would be the first biomedical prevention method designed specifically for cisgender women and the first long-acting method. Importantly, the ring would represent another option for women who are unable or prefer not to use daily oral PrEP.

DELIVER and B-PROTECTED aim to collect the kind of information needed for regulatory authorities and national programs to consider making the dapivirine ring available to pregnant and breastfeeding women. The results of these studies will also enable health care providers, and women themselves, to make informed choices about whether to use the ring or oral PrEP during pregnancy and breastfeeding.

Both methods have been shown to be well tolerated and to reduce the risk of HIV in previous trials involving nonpregnant and non-breastfeeding women.

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Most of the information about the safety of Truvada (which contains emtricitabine and tenofovir disoproxil fumarate), during pregnancy and breastfeeding is from women living with HIV who used it in combination with other drugs as treatment. It's based primarily on this safety data that the WHO recommends Truvada as daily oral PrEP during pregnancy and breastfeeding, while also acknowledging the need for safety data specifically in HIV-negative women. Thus far, a growing body of evidence suggests that PrEP use does not pose significant risk to the mother, her pregnancy or baby. Less is known about the use of the dapivirine ring during pregnancy and breastfeeding. B-PROTECTED is the first study of the ring in women who are actively breastfeeding. Likewise, DELIVER is the first study of the ring in pregnant women.

The dapivirine ring, which was developed by the nonprofit International Partnership for Microbicides (IPM), slowly releases the ARV dapivirine into the vagina – the potential site of HIV infection – during the month it is worn. Women can insert and replace the ring themselves.

B-PROTECTED will enroll up to 200 HIV-negative breastfeeding mothers and their 6- to 12-week-old babies. Participants will be randomly assigned to use either the monthly dapivirine ring or Truvada as daily oral PrEP, with more participants assigned to use the dapivirine ring than oral Truvada. Women will use their assigned product for three months and be followed by the study team for an additional two weeks. Researchers will assess how much drug from Truvada and the dapivirine ring passes into breast milk and how much passes to the baby after breastfeeding, and will measure the effects, if any, this may have on the health and safety of both mother and child.

In an earlier study called MTN-029/IPM 039, MTN researchers found dapivirine was absorbed at very low levels in breast milk and noted no safety concerns. MTN-029/IPM 039 enrolled 16 women in the United States who were no longer nursing their babies but still producing milk and who used the dapivirine ring for 14 consecutive days. The study was designed so that babies wouldn't be exposed to drug, but based on levels measured in maternal breast milk, researchers estimated an infant's daily exposure to drug would have been very low.

B-PROTECTED will be important for confirming these results in women who are actively breastfeeding and using the ring, as well as provide additional insight about the safety of Truvada as daily oral PrEP so that decisions about the use of these products while breastfeeding can be made based on evidence rather than guesswork.

"Quite simply, we want what's best for both mothers and their babies. We want babies to be able to receive the nutritional benefits that only breastmilk can provide and we want moms to remain HIV-free during the time they are breastfeeding," said Maxie Owor, MBChB, MMed (Paed), MPH, who is protocol chair of the B-PROTECTED study and based at the MU-JHU site.

Protocol co-chairs are Jennifer Balkus, Ph.D., MPH, from the University of Washington School of Public Health, and Lisa Noguchi, Ph.D., CNM, from Johns Hopkins Bloomberg School of Public Health, who also led the MTN-029/IPM 039 study.

"We aren't adequately addressing women's needs for HIV prevention unless we provide tools that can safely reduce their susceptibility while they are pregnant and breastfeeding, which for many women, adds up to be several years of their lives," commented Sharon L. Hillier, Ph.D., professor and vice chair of the department of obstetrics, gynecology and reproductive sciences at the University of Pittsburgh School of Medicine and MTN principal investigator.

"The MTN identified this as an imperative in our scientific agenda more than 14 years ago, when we were first funded as an HIV/AIDS clinical trials network. It's only fitting that the B-PROTECTED study be the final study we initiate as a network."

In addition to the two sites that have just started the study, B-PROTECTED will also be conducted at the College of Medicine-Johns Hopkins University Research Project in Blantyre, Malawi; and the University of Zimbabwe College of Health Sciences Clinical Trials Research Centre, Zengeza. B-PROTECTED is anticipated to be completed and report results in 2021.

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In parallel, and through a collaborative procedure coordinated by the WHO, IPM will seek regulatory approval of the dapivirine ring in Kenya, Malawi, Rwanda, South Africa, Tanzania, Uganda and Zimbabwe, where the public health need is great and previous studies of the dapivirine ring took place. The first of these approvals could be as early as mid-2021. IPM will seek approval from the U.S. Food and Drug Administration (FDA) as well. Also, in parallel, the WHO will review evidence on the ring as part of its treatment and prevention guidelines process and conduct an abbreviated review for the ring's prequalification, a quality assurance designation that facilitates access to medicines that meet global standards for quality, safety and efficacy.

Until data from the B-PROTECTED and DELIVER studies is available, national programs and health care providers are unlikely to recommend the ring's use by women who are pregnant or breastfeeding.

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*More information about B-PROTECTED can be found at https://mtnstopshiv.org/news/studies/mtn043 and https://mtnstopshiv.org/research/studies/mtn-043 or click here to watch a short video about both it and the DELIVER study. For more information about the dapivirine ring go to www.ipmglobal.org.*

*About the Microbicide Trials Network*

*The Microbicide Trials Network (MTN) is an HIV/AIDS clinical trials network established in 2006 by the National Institute of Allergy and Infectious Diseases with co-funding from the Eunice Kennedy Shriver National Institute of Child Health and Human Development and the National Institute of Mental Health, all components of the U.S. National Institutes of Health. Based at Magee-Womens Research Institute and the University of Pittsburgh, the MTN brings together international investigators and community and industry partners whose work is focused on the rigorous evaluation of promising microbicides – products applied inside the vagina or rectum that are intended to prevent the sexual transmission of HIV – from the earliest phases of clinical study to large-scale trials that support potential licensure of these products for widespread use. More information about the MTN is available at www.mtnstopshiv.org/.*

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