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MTN begins first trial of new dapivirine ring with both anti-HIV drug and contraceptive

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Researchers hoping for a single product that women could use to protect against both HIV and unintended pregnancy took an important step toward realizing their goal with the start of the first trial of a vaginal ring containing the antiretroviral (ARV) drug dapivirine and a hormonal contraceptive.

A vaginal ring containing dapivirine alone that women use for a month at a time has already been found to be safe and to help prevent HIV in two large trials called ASPIRE and The Ring Study. The dual-purpose ring now being tested in a Phase I trial by the National Institutes of Health-funded Microbicide Trials Network (MTN) contains levonorgestrel, a synthetic progestin used in many contraceptives, along with dapivirine, in quantities large enough to feasibly provide protection from HIV and unintended pregnancy for up to three months.

"Many of the women who have participated in our studies have told us that they want a single product that can provide both contraception and HIV prevention," said MTN Principal Investigator Sharon Hillier, Ph.D. "We are excited about the next-generation microbicide products that we hope will address that unmet need." Dr. Hillier is professor and vice chair, and director of reproductive infectious disease research, department of obstetrics, gynecology and reproductive sciences, at the University of Pittsburgh School of Medicine.

The study, called MTN-030/IPM 041, is being conducted at Magee-Womens Hospital of UPMC in Pittsburgh and the University of

Alabama at Birmingham (UAB), in close collaboration with the nonprofit International Partnership for Microbicides (IPM). IPM developed the monthly dapivirine ring and the three-month dual-purpose ring, as well as the three-month dapivirine-only ring that the MTN will be evaluating in a separate trial later this year.

First developed for contraceptive use, vaginal rings are flexible products that are worn inside the vagina, where they release medication slowly over time.

Investigators will enroll 24 women in MTN-030/IPM 041. Half will receive a ring containing 200 mg of dapivirine alone, and half will receive the dual-purpose ring containing 200 mg of dapivirine and 320 mg of levonorgestrel. Participants will be asked to wear their assigned ring for 14 days, during which time investigators will closely monitor safety and measure how dapivirine and levonorgestrel are each taken up by the body in the presence of the other. Results are expected by mid-2018.

"What we learn from this small but very important study will set the course for the future of the dual-purpose dapivirine vaginal ring," said Sharon L. Achilles, M.D., Ph.D., who is MTN-030/IPM 041 protocol chair and also a lead investigator at the Magee-Womens Hospital clinical research site.

"If all goes well, we would then proceed to studies involving more women who would use the ring longer, for up to three months, as it was intended. This study is a critical first step on a pathway that we hope will ultimately enable us to provide women with an easy-to-use product that can provide safe and effective, long-acting protection against both HIV and unintended pregnancy," added Dr. Achilles, who is also an assistant professor of obstetrics, gynecology and reproductive sciences at the University of Pittsburgh School of Medicine and director of the Magee-

Womens Research Institute Center for Family Planning Research.

Last year, research teams from the MTN and IPM reported results of two Phase III efficacy trials of the monthly 25 mg dapivirine vaginal ring - the first trials showing that a vaginal ring could deliver an ARV to prevent HIV infection. Across both studies, the overall risk of HIV infection was reduced by about 30 percent. Higher levels of protection were seen in women who used the ring most regularly, a later exploratory analysis found. The two trials - ASPIRE, conducted by MTN, and The Ring Study, led by IPM - together involved 4,588 women in four African countries where HIV rates for women continue to be among the highest globally, with heterosexual intercourse being the primary driver of HIV transmission.

Based on these results - and those of several smaller supporting studies, including other MTN-led studies—IPM intends to seek licensure of the monthly dapivirine ring. If approved, the monthly dapivirine ring would be the first biomedical HIV prevention product developed specifically for women.

Meanwhile, two open-label studies involving former Phase III trial participants - HOPE for former ASPIRE participants, and DREAM for former participants of The Ring Study - are collecting additional safety, adherence and efficacy data on the monthly dapivirine ring that will help inform its implementation, should it receive regulatory approval. MTN will also be conducting the REACH study, or MTN-034/IPM 045, evaluating safety and adherence of the monthly vaginal ring and daily use of Truvada as oral pre-exposure prophylaxis (PrEP) among adolescent girls and young women, and is also planning studies in pregnant and breastfeeding women.

Researchers recognize that a ring that only needs to be replaced every three months may be easier for women to use than a monthly ring. And

depending on individual and life circumstances, some women may find a product that can also double as their contraceptive method especially appealing.

Both types of products could have important public health impact in regions like sub-Saharan Africa, where HIV is not the only risk women face. With little to no access to contraceptive and reproductive health services, women here and elsewhere in the developing world experience high rates of complications during pregnancy and childbirth, often resulting in maternal and newborn death.

A second Phase I study, called MTN-036/IPM 047, plans to evaluate the safety of a 100 mg dapivirine ring and a 200 mg ring when used for 90 days compared to monthly use of the 25 mg dapivirine ring. Researchers will also look at levels of drug achieved within the body with each ring dosage. MTN-036/IPM 047, which is expected to start in the coming months, will be conducted at UAB and the Bridge HIV Clinical Research Site at the San Francisco Department of Public Health, where the study's protocol chair, Albert Liu, M.D., M.P.H., is director of clinical research.

Provided by Microbicide Trials Network