

Open-label study of a vaginal ring for HIV prevention suggests women want and will use it

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Results of an open-label study of vaginal ring intended to be used for a month at a time found the majority of women wanted the ring being offered, with measures of adherence also indicating that women are willing to use it to protect themselves against HIV. Researchers from the National Institutes of Health-funded Microbicide Trials Network (MTN) who conducted the study, known as HOPE, reported their findings today at the 10th IAS Conference on HIV Science (IAS 2019) in Mexico City.

The ring, which [women](#) can insert and replace themselves, slowly releases the antiretroviral (ARV) drug dapivirine into the vagina during the month it is used. The nonprofit International Partnership for Microbicides (IPM) developed the dapivirine ring and is seeking its regulatory approval.

The HOPE study (HIV Open-label Prevention Extension, or MTN-025) was designed to provide former participants of the ASPIRE (MTN-020) Phase III trial the opportunity to use to the dapivirine ring for one year while researchers collected additional information about its safety and how women would use the ring knowing that it was shown to reduce the risk of HIV in both ASPIRE and The Ring Study (IPM 027), a second Phase III trial that was led by IPM.

HOPE, which was conducted between July 2016 and October 2018, enrolled 1,456 women at 14 trial sites in Malawi, South Africa, Uganda and Zimbabwe. To be eligible, women needed to be HIV-negative, not be pregnant or breastfeeding and agree to use contraception during the study.

Importantly, women who enrolled in HOPE could at any time choose not to use or to accept the ring being offered.

"We wanted women to know that the decision was theirs to make, and theirs alone," explained Jared Baeten, MD, Ph.D., professor of global health, medicine and epidemiology at the University of Washington in Seattle, who reported the final results of HOPE at IAS.

"As it turns out, most participants wanted the dapivirine ring—they accepted the ring being offered. And women in HOPE also appeared to use the ring more consistently than they did in ASPIRE," said Dr. Baeten, who is also co-principal investigator of the MTN and led the HOPE study with Thesla Palanee-Phillips, MMed Sci, Ph.D., MSc., of the Wits Reproductive Health and HIV Institute, Johannesburg, South Africa, and Nyaradzo Mgodzi, MBChB, MMed, of the University of Zimbabwe College of Health Sciences in Harare.

At the start of HOPE, the majority of participants, or 92 percent, accepted the ring. And, overall, interest in the ring was high throughout the one-year study. At three months, 87 percent of participants accepted the ring being offered to them. Thereafter, when women started coming to the clinic quarterly as opposed to monthly, interest declined only slightly, with 83 percent of women wanting the ring at month six and 79 percent of women accepting the rings being offered at month nine. (At these quarterly visits, women were given the option of receiving three rings—one for each of the next three months.)

To calculate women's use of the ring, or adherence, researchers measured the amount of drug remaining in rings participants returned at each clinic visit. In HOPE, 90 percent of returned rings indicated use compared to 77 percent in ASPIRE. Residual drug levels cannot determine how long the ring was actually used—for the full month, for example, or just a few days—and therefore are not

an exact indication of adherence.

As in ASPIRE, there were no safety concerns with use of the ring in HOPE, and compared to ASPIRE, women's HIV risk appeared to be lower.

HIV incidence was 2.7 percent in HOPE, meaning that for every 100 women followed during the one-year study there were 2.7 women who became newly infected. In addition to being offered the ring in HOPE, all women received HIV prevention counseling and services during participation. Of the 1,456 participants, 35 acquired HIV. Using a method of statistical modeling that draws from the placebo group in ASPIRE, the researchers estimated the HIV incidence would have been 4.4 percent had women not been able to take part in HOPE and be offered the ring, suggesting a 39 percent reduction in HIV risk.

Final results of a second open-label study called DREAM (IPM 032) for former Ring Study participants, which were reported last month at the South African AIDS Conference, also found higher uptake of the ring compared to the original Phase III study, and using a similar modeling technique, suggest women's HIV risk was reduced by 63 percent. Unlike in HOPE, DREAM only enrolled women who agreed to use the ring during the study.

Both research teams caution that without a true placebo group in either study, these results cannot be viewed with the same degree of confidence as those from the earlier Phase III trials in which women were randomized to use either the active ring or a placebo ring. Overall, however, the researchers were encouraged that, together, the HOPE and DREAM open-label studies suggest HIV incidence was reduced by about half with use of the dapivirine ring.

In the ASPIRE and The Ring Study Phase III trials, the results of which were reported at Conference on Retroviruses and Opportunistic Infections (CROI) in 2016 and published in the *New England Journal of Medicine*, the ring was found to be well tolerated and reduced women's risk of acquiring HIV by about 30 percent overall (by 27 percent in ASPIRE and by 31 percent in The Ring Study).

Higher levels of protection were seen in women who used the ring most regularly.

The dapivirine ring is currently under regulatory review by the European Medicines Agency (EMA) through the Article 58 procedure, which allows the EMA, in cooperation with the World Health Organization (WHO), to provide a scientific opinion on the ring's use in low- and middle-income countries. IPM also plans to submit applications to the South African Health Products Regulatory Authority (SAHPRA) and the US Food and Drug Administration (FDA) later this year.

The monthly dapivirine ring could potentially represent a second biomedical option, in addition to oral pre-exposure prophylaxis (PrEP), for women wanting to protect themselves against HIV. Oral PrEP, which involves taking a daily ARV pill called Truvada® every day, is now approved in many countries, including in Africa, and recommended by the WHO for anyone at substantial HIV risk. Oral PrEP is highly effective, but only with consistent use, and daily pill-taking can be challenging for some people or not desired. Likewise, using a monthly vaginal ring may not be for everyone either.

"Having both PrEP and the dapivirine ring would be a significant milestone for HIV prevention, because the more options the better. No one method is going to be right for all women, and no method will be nor can be effective if it's not used or not available in the first place," commented Dr. Baeten.

Globally, more than half of all people currently living with HIV are women, and in sub-Saharan Africa, women account for nearly 60 percent of adults with HIV, with unprotected vaginal sex the primary driver of the epidemic.

Rates of infection are especially high among young women. Indeed, in parts of Africa, it's estimated that 1,000 girls ages 15-24 are infected every day. And when women are pregnant or breastfeeding, their risk of acquiring HIV is two to four times greater than when they are not.

The MTN is conducting studies to address the needs of these populations of women to inform

potential approval of the dapivirine ring for girls under age 18 and for women during pregnancy and breastfeeding in the future.

REACH (MTN-034) is an ongoing study evaluating both the ring and oral PrEP in girls ages 16-21 at sites in Kenya, South Africa, Uganda and Zimbabwe. Likewise, the DELIVER (MTN-042) and B-PROTECTED (MTN-042) studies are designed to assess the safety of the dapivirine [ring](#) and oral PrEP in pregnant and breastfeeding women. DELIVER and B-PROTECTED are expected to begin later this year at sites in Malawi, South Africa, Uganda and Zimbabwe.

Provided by Microbicide Trials Network

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