



**CONTACTS:** **Lisa Rossi**  
+1-412-641-8940  
+1-412-916-3315 (mobile)  
rossil@upmc.edu

**Clare Collins**  
+1-412-641-7299  
+1-412-770-8643 (mobile)  
collcx@upmc.edu

---

**FOR IMMEDIATE RELEASE**

**Researchers present additional evidence on the safety of the dapivirine vaginal ring for HIV prevention in women**

*Secondary analyses suggest using the ring does not alter vaginal microbiome in adolescent girls, women who are lactating or postmenopausal women, or lead to cervical cancer*

**MADRID, 23 October, 2018** – New findings reported by researchers from National Institutes of Health-funded [Microbicide Trials Network](#) (MTN) at the HIV Research for Prevention conference ([HIVR4P 2018](#)) shed additional light on the safety of the monthly dapivirine vaginal ring, an HIV prevention method designed specifically for women that is being considered for regulatory approval.

Use of the ring was associated with minimal changes in vaginal microbiota among adolescents, lactating women and postmenopausal women, said researchers who conducted a secondary analysis based on three Phase I trials. Vaginal microbiota are the bacteria living inside the vagina that serve as a natural defense against infections. A disruption in the type and number of certain bacteria can lead to infections, such as bacterial vaginosis (BV) or yeast vaginitis.

“While some very minor changes were observed during ring use, such changes would not be expected to lead to increases in BV or yeast vaginitis,” said Sharon L. Hillier, Ph.D., who, in addition to being principal investigator of the MTN, directs MTN’s microbiology laboratory at the University of Pittsburgh and Magee-Womens Research Institute.

Meanwhile, an analysis of Pap smear results for some 2,400 participants from the [ASPIRE](#) Phase III trial of the dapivirine ring found no evidence to suggest using the dapivirine ring increases the risk of developing changes in cells that can lead to cervical cancer. These findings should help allay concerns that use of the dapivirine ring could result in cervical cancer, a worry expressed by some of the women in ASPIRE.

“This information should help address any concerns about the dapivirine ring and cervical cancer, and also help communities better understand how the ring could be an important HIV prevention method for women,” stated Krishnaveni Reddy, M.Med.Sci., programme manager at the Wits Reproductive Health and HIV Institute (Wits RHI) in Johannesburg, South Africa, and formerly the study coordinator for the ASPIRE trial at Wits RHI, one of 15 clinical research sites where ASPIRE took place.

The vaginal ring, which slowly releases an antiretroviral (ARV) drug called dapivirine during the month that it is worn, was found to be well tolerated and to reduce the risk of HIV in two large clinical trials that together enrolled more than 4,500 women ages 18-45 in four African countries: ASPIRE, conducted by the MTN, and The Ring Study, conducted by the International Partnership for Microbicides (IPM), the nonprofit organization that developed the dapivirine ring. IPM is seeking regulatory approval of the dapivirine ring for women ages 18-45.

“Findings from these two secondary analyses, as well as others, are contributing to the evidence base about the safety of the dapivirine ring,” added Dr. Hillier.

In all, 20 oral and poster presentations will be given by MTN investigators at HIVR4P 2018, which runs Oct.22-25. Additional [presentations](#) include two plenary talks and a number of satellite sessions and conference symposia. The presentations being given by Dr. Hillier and Ms. Reddy, which are posters, are further described below.

### **Microbiome largely unchanged in different populations of women with dapivirine ring**

If approved, the dapivirine ring would not initially be indicated for adolescents under age 18, women who are pregnant or breastfeeding, or postmenopausal women, because those populations were not included in the Phase III trials. Regulatory authorities would need information about the safety of the ring in these populations before considering whether to expand approval to include these groups.

An important measure of safety, especially for a vaginal product, is whether its use affects the composition of bacteria that normally live inside the vagina. For instance, a reduction in the number of “good” bacteria called lactobacilli and an overgrowth of other bacteria can lead to infections with abnormal vaginal discharge, odor or itching.

In the ASPIRE Phase III trial, researchers did not observe an increase in vaginal infections in women using the dapivirine ring compared to women using a placebo ring. To determine what effect, if any, the ring had in adolescent girls, women who were breastfeeding and postmenopausal women, Dr. Hillier and her team conducted a secondary analysis that involved laboratory tests of vaginal swabs collected from participants across three Phase I studies conducted at U.S. MTN-affiliated sites: [MTN-023/IPM 030](#), a study of 96 adolescent girls ages 15-17 who used either the dapivirine ring or a placebo ring for six months; [MTN-024/IPM 031](#), in which 96 post-menopausal women used the dapivirine ring or a placebo ring for three months; and [MTN-029/IPM 039](#), a study of 16 lactating women, all of whom used the dapivirine ring for two weeks.

Because vaginal swabs were collected both before and after ring use, the researchers were able to determine any changes in the prevalence and concentration of vaginal microbiota between the placebo and dapivirine arms, and between the three study cohorts. The dapivirine ring was associated with minimal changes in all three populations.

“Prevention products should work for women across the life span. These data suggest that from adolescent girls to women who have gone through menopause, the ring can be safe to use,” said Dr. Hillier.

### **Putting rumors to rest: Analysis of ASPIRE data finds no link between dapivirine ring use and risk of developing cervical cancer**

Some of the women who participated in the ASPIRE study said they had not used the ring because they were concerned about cervical cancer, perhaps in part due to the ring being so unfamiliar. While no data has suggested such a risk exists, researchers sought to answer the question by looking at results of a test called a Pap smear, which involves taking a sample of cells from the cervix and checking for abnormalities that may be indicative of cervical cancer.

ASPIRE enrolled 2,629 women at 15 research sites in Malawi, South Africa, Uganda and Zimbabwe. Pap smear results were available for 2,394 women both before beginning use of their assigned ring (placebo or active product) and at the end of the study, after using the ring for about two years.

Pap smear results were nearly identical between the dapivirine and placebo vaginal ring groups both before and after ring use. Among women assigned to use the dapivirine ring, 91.6 percent had a negative test result (indicating no cancer risk) before starting the study, and 90.6 percent were negative after. Similarly, 92.6 percent of women in the placebo group tested negative at the start, with 91.5 percent having a negative test result after they stopped using the ring.

“Our findings suggest that use of the dapivirine vaginal ring over a two-year period is not associated with the development of abnormalities in cervical cells that could lead to cancer,” concludes Ms. Reddy.

The two posters, *Impact of the 25 mg Dapivirine and Placebo Vaginal Rings on the Vaginal Microbiota of Adolescents, Lactating and Post-menopausal Women* (P17.02) and *Dapivirine Vaginal Ring Use and Cervical Cytology Abnormalities: Data From the Placebo-controlled MTN-020/ASPIRE Trial* (P07.10) will be displayed and the authors available during the HIVR4P Poster Session on Wednesday, 24 October, from 17.30-19.30. Posters will be available on the HIVR4P website after the meeting. Oral sessions will be webcast and also be available for playback on the [HIVR4P website](#)

MTN-030/IPM 041 and the MTN are supported by the U.S. National Institutes of Health grants UM1AI068633, UM1AI068615, UM1AI106707.

### **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 <http://www.mtnstopshiv.org>.

### **About dapivirine**

Dapivirine, also known as TMC-120, belongs to a class of ARVs called non-nucleoside reverse transcriptase inhibitors that bind to and disable HIV's reverse transcriptase enzyme, a key protein needed for HIV replication. IPM holds an exclusive worldwide license for dapivirine from Janssen Sciences Ireland UC, one of the Janssen Pharmaceutical Companies of Johnson & Johnson (Janssen), which is designed to ensure that women in low-resource settings have affordable access to any dapivirine-based microbicide. For more information about the dapivirine ring, go to [www.ipmglobal.org](http://www.ipmglobal.org).

23-October-2018