90-day dapivirine ring for women's HIV prevention passes its first test in Phase I study

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If approved, the monthly dapivirine vaginal ring would be the first biomedical HIV prevention method designed specifically for cisgender

women, as well as the first long-acting method. Looking to the future, researchers from the National Institutes of Health-funded Microbicide Trials Network are hopeful that a vaginal ring that could be used for longer than a month at a time might also be made available someday.

Indeed, a 90-day dapivirine ring has passed its first test, with results of a Phase I clinical trial reported today at a virtual meeting of the Conference on Retroviruses and Opportunistic Infections (CROI) supporting its further development.

The study, known as MTN-036/IPM 047, evaluated two formulations of a ring designed to slowly release the antiretroviral drug dapivirine in the vagina over the course of 90 days, one containing 100 mg of dapivirine and the other containing 200 mg. Both formulations were well-tolerated and delivered target levels of drug throughout the three months of use, results that would suggest they may have the potential to provide long-acting and sustained HIV protection.

The nonprofit International Partnership for Microbicides (IPM) is developing a three-month ring, building on its monthly dapivirine ring, which last year received a positive opinion from the European Medicines Agency for its use among cisgender women ages 18 and older in developing countries, and soon after, was added to the World Health Organization (WHO) list of pre-qualified medicines. In January of this year, WHO recommended the ring as an additional HIV prevention choice for women at substantial risk of HIV. IPM is seeking approval of the monthly dapivirine ring in eastern and southern Africa initially, with the first of these decisions anticipated possibly by mid-year. IPM is also seeking regulatory approval from the US Food and Drug Administration.

"Regulatory approval of the monthly ring would be an incredible milestone for women, who have been the face of the HIV epidemic in much of the world and need and deserve to have a range of safe and

effective methods. Hopefully, an extended duration dapivirine ring that women replace every three months can be yet another option available to women in the not-too-distant future," commented Albert Liu, MD, MPH, clinical research director at the San Francisco Department of Public Health (SFDPH), who as protocol chair of the MTN-036/IPM 047 study, presented its results at CROI.

MTN-036/IPM 047 was designed to assess the safety and pharmacokinetics (how the body takes up the active drug) of the 100 mg and 200 mg 90-day rings, compared to the monthly dapivirine ring, which contains 25 mg of active drug.

The study enrolled 49 healthy HIV-negative women and individuals assigned female sex at birth at two MTN-affiliated clinical research sites in the United States: the University of Alabama at Birmingham, and Bridge HIV, affiliated with both the SFDPH and the University of California, San Francisco.

Participants were randomly assigned to one of three groups: one group that used the 100 mg dapivirine ring continuously for 13 weeks; a second group that used the 200 mg ring continuously for 13 weeks; and a third group that used the monthly ring, replacing it every four weeks.

All three rings were well tolerated by study participants with no safety concerns. Compared to the monthly ring, the two 90-day rings achieved higher dapivirine concentrations in blood plasma and vaginal fluid, with levels that were 1.3 to 1.9 times higher in plasma and 1.5 to 2.9 times higher in vaginal fluid. Similarly, cervical tissue concentrations were higher in the two three-month rings compared to the monthly ring.

These results, together with those of a bioavailability study IPM is planning, will be considered in its decision about which of the two formulations to move forward for further development.

"We are thrilled to be taking the three-month dapivirine ring to the next stage of development," said Bríd Devlin, executive vice president of product development for IPM. "Offering women a range of prevention methods is critical to meeting their diverse sexual and reproductive health needs, including longer-acting choices they can use on their own terms."

In addition to a 90-day dapivirine ring for HIV prevention, IPM is also developing a 90-day ring for both HIV prevention and contraception. In two Phase I studies conducted by the MTN, a dual-purpose ring containing 200 mg dapivirine and 350 mg of the contraceptive hormone levonorgestrel was found to be well tolerated. Results of the most recent study, MTN-044/IPM 053/CCN019, which were reported at the HIV Research for Prevention (HIVR4P) Virtual Conference earlier this year, also found the ring delivered sustained levels of both dapivirine and levonorgestrel continuously for 90 days.

Globally, more than half of all people currently living with HIV are cisgender women, and in sub-Saharan Africa, women account for nearly 60 percent of new infections among adults and adolescents ages 15 and older, with unprotected vaginal sex the primary driver of the epidemic.

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More information: www.mtnstopshiv.org/research/s … udies/mtn-036ipm-047

Provided by Microbicide Trials Network