Dapivirine ring did not confer drug resistance among women who acquired HIV in ASPIRE

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Among women who acquired HIV during ASPIRE, researchers found no differences in the frequency and patterns of HIV drug resistance between those assigned to use the ring containing an anti-retroviral (ARV) drug called dapivirine and those assigned to use a placebo ring with no active drug, say researchers who reported their findings at the biennial HIV Research for Prevention conference (HIVR4P 2016) taking place at the Sheraton Grand Hotel in Chicago.

Drug resistance is common with HIV, essentially because the virus is prone to making mistakes when it multiplies. Some of these mistakes, called mutations, can make HIV resistant to one or more ARV drug. If not recognized and properly managed, drug resistance can compromise the effectiveness of mainstay drugs used in the treatment of HIV.

ASPIRE- A Study to Prevent Infection with a Ring for Extended Use, or MTN-020, was a Phase III trial that found the dapivirine vaginal ring was both safe and helped protect against HIV. The trial, which was led by the National Institutes of Health-funded Microbicide Trials Network (MTN), enrolled women ages 18-45 at 15 trial sites in Malawi, Uganda, South Africa and Zimbabwe. The dapivirine ring, which is intended to be used for a month at a time, was developed by the nonprofit International Partnership for Microbicides (IPM). IPM also conducted The Ring Study, a sister Phase III study of the monthly ring with similar results.

While dapivirine, a type of ARV called a non-nucleoside reverse transcriptase inhibitor (NNRTI), is not used to treat HIV, other NNRTIs are. As such, women who acquired HIV during ASPIRE immediately stopped using their assigned ring to avoid the possibility that the virus could become resistant to dapivirine or other NNRTIs.

Of 2,629 women who participated in ASPIRE, 168 acquired HIV. The current analysis included 164 women—96 in the placebo ring group and 68 in dapivirine ring group. Using small samples of blood, the researchers conducted special tests that identify changes, or mutations, in the genetic makeup of HIV that are known to cause resistance to certain drugs. NNRTI drug resistance was detected in 10 of 96 women in the placebo group (10.4 percent prevalence) and in eight of 68 in the dapivirine ring group (11.8 percent prevalence), a difference that was not statistically significant. These mutations were not specific to dapivirine, suggesting that women were infected with virus already resistant to NNRTIs.

"We are encouraged that the dapivirine ring itself seems to have posed little risk for development of HIV drug resistance in ASPIRE. With the dapivirine ring now being used in the HOPE and DREAM open-label extension trials, it will be important to continue monitoring for and collecting more data to better understand the prevalence and potential risks for drug resistance," said Urvi Parikh, Ph.D., associate director of the MTN Laboratory Center Virology Core at the University of Pittsburgh.

As the follow-on study to ASPIRE, HOPE (HIV Open-label Prevention Extension), or MTN-025, former ASPIRE participants will have the opportunity to use the dapivirine ring in the context of knowing that it is safe and can help prevent HIV. In ASPIRE, HIV risk was reduced by 27 percent overall (there were 27 percent fewer women who acquired HIV in the group assigned to use the dapivirine ring than in the group

assigned to use a placebo ring containing no active drug); additional analyses have since found the level of HIV protection is at least 56 percent and may be as high as 75 percent or more when the ring is used most consistently.

HOPE will also gather additional information on the ring's safety and how women use the ring. Acknowledging that the ring may not be for everyone, HOPE also looks to better understand why it may work well as an HIV prevention strategy for some women but not for others. IPM is conducting a similar open-label extension study called DREAM that is open to former participants of The Ring Study.

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.

Other presentations by MTN researchers at HIV R4P include abstracts reporting additional results from ASPIRE, as well as VOICE and MTN-017, the first extended safety study of a rectal microbicide for HIV prevention from anal sex. Of the 22 presentations related to MTN studies, seven are oral abstracts.

MTN Principal Investigator Sharon L. Hillier, Ph.D., will also be giving an invited plenary talk, titled "Rings and Things," in the Wednesday (Oct. 19) plenary session, Which Way is Forward: Emerging Challenges and Opportunities. Dr. Hillier is professor and vice chair for faculty affairs, and director of reproductive infectious disease research in the department of obstetrics, gynecology and reproductive sciences at the University of Pittsburgh School of Medicine and the affiliated Magee-Womens Research Institute.