FACT SHEET
Ongoing, Planned and Completed Trials of the Microbicide Trials Network

Fast Facts

• The Microbicide Trials Network (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. More than 25 clinical research sites on four continents partner with the MTN in the conduct of its clinical trials.

• MTN’s unique research portfolio integrates both biomedical and behavioral science in the design and implementation of studies that, whether Phase I safety studies or large-scale Phase III effectiveness trials, are meant to support potential licensure of products for different high-risk populations.

• MTN’s first flagship trial, VOICE, found none of the daily products tested (oral Truvada, oral tenofovir and tenofovir vaginal gel) was effective. In fact, the study’s results, first reported in 2013, found that most women did not use their assigned products, making clear the need for approaches that fit better into the context of their lives. VOICE has also been a catalyst for the research community to reevaluate methods for monitoring and enhancing product adherence in clinical trials, including in helping current and prospective participants and local communities better understand the importance of correct and consistent product use and the impact that non-adherence can have on the findings of a research study.

• In ASPIRE, MTN has played a pivotal role in demonstrating that the dapivirine vaginal ring is safe and can help protect against HIV infection. ASPIRE and its sister study, The Ring Study, are the first efficacy trials with confirmatory results of an HIV prevention product developed specifically for women. The dapivirine ring is used for a month at a time. It was developed by the International Partnership for Microbicides (IPM), which also conducted The Ring Study. Findings from ASPIRE and The Ring Study, and from several smaller supporting studies, including those conducted by the MTN, could lead to the ring’s potential approval. In the meantime, former participants of each study are being offered the opportunity to use the ring in the context of open-label extension (OLE) trials – HOPE for former ASPIRE participants. MTN is also continuing to conduct a number of important studies of the ring, including in adolescent girls and young women, for example.

• The MTN has long recognized that women need products that will be safe and effective to use in all stages of life, including during pregnancy and breastfeeding, when the risk of acquiring HIV from an infected partner may be particularly high. Included in its scientific portfolio is a comprehensive research program purposefully designed to take incremental steps in determining whether HIV prevention products are safe and effective in protecting women against HIV infection during all stages of pregnancy and motherhood.

• Although the field has historically been more focused on products for preventing HIV through vaginal sex, the MTN has advanced a scientific agenda that recognizes the need for products to prevent HIV transmission through anal intercourse. The MTN continues to lead pioneering studies of HIV prevention products for both men and women who engage in anal sex, and in early 2016, reported results or MTN-017, from the first Phase II trial of a rectal microbicide.

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Ongoing and Planned Trials

**MTN-015** – MTN-015 is a long-term, observational study that aims to track the nature of HIV progression and treatment response among women who acquired HIV while taking part in an MTN “parent study” testing different antiretroviral (ARV)-based products for the prevention of HIV. MTN-015 will help to understand what impact the use of these products may have on the natural history and clinical course of HIV and on the prevalence and patterns of HIV drug resistance over time.

**MTN-016 – EMBRACE** – Evaluation of Maternal and Baby Outcome Registry After Chemoprophylactic Exposure – A study that seeks to learn whether HIV prevention products containing ARVs can affect a woman’s pregnancy outcome or her baby’s general growth and development. The study involves the creation of a database of health information collected from women who unintentionally became pregnant while participating in an MTN trial, or who participated in an MTN pregnancy or breastfeeding safety study. Health information about their babies is also included.

**MTN-025 – HOPE** – HIV Open Label Prevention Extension – An open-label follow-on trial to ASPIRE in which former ASPIRE participants are offered the opportunity to use the dapivirine ring (there is no placebo) in the context of a study. HOPE will build on the results of ASPIRE by gathering additional information on the ring’s safety, how women use the ring knowing that it can help reduce their risk of HIV and the relationship between adherence and HIV protection. The study also seeks to understand why the ring may work well as an HIV prevention strategy for some women but not for others. For this reason, former participants may enroll in HOPE even if they do not wish to use the ring. HOPE began in July 2016 and is expected to be completed late 2017.

**MTN-026/IPM 038** – A Phase I study that will evaluate whether a gel containing dapivirine is safe for use in the rectum. The study, which will include approximately 27 HIV-uninfected men and women at sites in the United States and Thailand, will help determine whether further testing on the safety and acceptability of dapivirine gel as a potential rectal microbicide can be conducted in a larger population.

**MTN-029/IPM 039** – The first study of its kind involving the dapivirine vaginal ring, MTN-029/IPM 039 will determine whether drug released from the dapivirine ring into the vagina gets absorbed by breastmilk. Approximately 16 women who are no longer breastfeeding but are still producing breast milk will be enrolled and use the ring for 14 consecutive days. Its results may support future studies involving both breastfeeding mothers and their infants. The study, which began in March 2016, is being conducted at two U.S.-based clinical research sites.

**MTN-030/IPM 041** – A Phase I trial of a vaginal ring containing the ARV drug dapivirine and the contraceptive hormone levonorgestrel that will assess the ring’s safety as well as absorption patterns of dapivirine and different dosages of levonorgestrel in vaginal tissue and in blood. MTN-030/IPM 041, which will be conducted at two U.S. sites, is an important first step toward developing a product for women that could both protect against HIV and prevent unplanned pregnancy.

**MTN-032** – A qualitative study that looks to better understand women’s use of the dapivirine ring in both ASPIRE and HOPE and if and how adherence patterns differ between ASPIRE, a placebo-controlled trial, and the HOPE open-label extension trial in which all women are offered the dapivirine ring, yet may choose not to accept it. MTN-032 will be conducted in two parts. Phase I, which began in June 2016, will involve up to 224 former ASPIRE participants who had been assigned to use the dapivirine ring who will take part in either a focus group or in-depth interview. Among those Phase I participants who opt to enroll in HOPE, approximately 84 will take part in a single in-depth interview in Phase 2. Researchers will be looking to understand the reasons women with varying levels of adherence in ASPIRE decide to enroll into HOPE, whether they choose to accept the ring and if and how knowing the ring’s efficacy has any bearing on both their intended and actual use. MTN-032 is being conducted at six of the 15 clinical research sites for ASPIRE and HOPE.

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MTN-033/IPM 044 – A Phase I study that will look at the safety and distribution of dapivirine gel when administered rectally with the use of an applicator compared to digital and phallic administration. The study, which will include 16 men who have sex with men (MSM) and transgender women, will help determine whether a rectal microbicide administered like a lubricant (without an applicator) can deliver enough drug in the tissue to feasibly provide HIV protection.

MTN-034/IPM 045 – A Phase IIa trial that seeks to understand the HIV prevention needs and preferences of adolescent girls and young women, who are among those at highest risk of HIV in sub-Saharan Africa. Specifically, MTN-034/IPM 045 will evaluate how adolescent girls and young women use the monthly dapivirine vaginal ring and Truvada® as daily PrEP, and their preferences for either or both approaches after using each for six months. The study will also collect much needed information on the safety of these approaches in young women and assess whether biological or physiological factors affect how the active drug in each of these products is taken up in the body or may contribute to HIV susceptibility. The study, which is expected to launch early 2017, will enroll approximately 300 girls and young women ages 16-21 at five trial sites in Kenya, South Africa and Zimbabwe.

Completed Trials

MTN-001 – A Phase II trial that looked at how the ARV tenofovir is absorbed in the body as either an oral tablet or a vaginal gel, as well as women’s preferences or ability to adhere to daily regimens of each approach. The study involved 144 women in the U.S., and Uganda and South Africa, who used each product daily for six weeks, as well as the two together. The final results of drug absorption and distribution studies, published in January 2013, found the gel was associated with vaginal tissue drug levels more than 130-times higher than the oral tablet; the tablet was associated with a 56-times higher concentration of active drug in blood compared to the gel. Although self-reported adherence was very high (94 percent) and most women said they liked both products, drug serum concentrations indicated only 64 percent of the women took the tablets consistently.

MTN-002 – The first study of a candidate topical microbicide ever to be conducted in pregnant women, MTN-002 sought to understand whether microbicides being developed for women to protect themselves against HIV are safe if used during pregnancy. The Phase I study involved giving a single dose of tenofovir gel to 16 healthy, HIV-uninfected women hours before they gave birth by scheduled Cesarean section. Results, reported in May 2010, found only small amounts of drug were absorbed into the mother’s bloodstream, amniotic fluid and umbilical cord (fetal) blood; and no serious side effects in either the mothers or their newborns.

MTN-003 –VOICE – Vaginal and Oral Interventions to Control the Epidemic – tested the safety and effectiveness of two different HIV prevention approaches among 5,029 women in Uganda, South Africa and Zimbabwe: daily use of an antiretroviral (ARV) tablet (tenofovir or Truvada) or daily use of a vaginal gel (tenofovir gel). The study was conducted from September 2009 to August 2012. Results, first reported in March 2013, found all three products were safe but not one was effective; most participants did not use them daily as recommended. Young, unmarried women were least likely to use study products and the most likely to acquire HIV, indicating the urgent need for safe, effective and practical HIV prevention methods women will actually use. For many women, drug was not detected in any blood sample taken at any time during the study, suggesting they may have never used the products at all. However, among women in the tenofovir gel group whose blood tests indicated use of the gel, HIV risk appeared to be reduced significantly, additional analysis showed.

MTN-003B (VOICE B) – Also known as the Bone Mineral Density Sub-study, VOICE B was an observational study in a subset of participants in VOICE designed to explore the potential effects, if any, that daily use of oral ARVs may have on bone health in HIV-negative women, and in particular, pre-menopausal women in Africa. VOICE B involved 518 women from Uganda and Zimbabwe who were assigned to one of the oral tablet regimens (oral tenofovir, oral Truvada or oral placebo) in VOICE. VOICE B found small reversible decreases in bone mineral density among young women with higher adherence to the oral tablet tenofovir, findings that are consistent with previous studies and were reversed when women in VOICE stopped using the product.

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MTN-003C (VOICE C) – Also known as the Community and Adherence Sub-study, VOICE C was designed to identify community-based factors and beliefs that may have influenced women’s ability and willingness to follow the daily regimens tested in VOICE. It was conducted in parallel with VOICE at a single site and involved 102 women enrolled in VOICE, as well as 26 male partners, 17 members of the site’s Community Advisory Board (CAB) and 23 community stakeholders, for a total of 164 participants. Its results suggest women didn’t use the products because they worried about their side-effects and the stigma associated with products meant for those infected with HIV; were ambivalent about being in a trial in which they didn’t know whether they’d been assigned to use an active product or placebo; and felt pressure from partners, family and friends.

MTN-003D (VOICE D) – A behavioral sub-study of VOICE that aimed to understand women’s actual and reported use of study products and sexual behavior during their participation in VOICE. Stage 1 involved 88 women who took part in individual in-depth interviews after exiting VOICE and before the trial’s results were publicly reported. Stage 2 was implemented in response to VOICE results and involved 127 former participants who took part in in-depth interviews and/or focus group discussions after learning the results of blood tests indicating their actual patterns of product use during the trial. The researchers hoped that sharing individual test results would elicit candid discussion about the challenges women experienced in using the products. The most common themes that emerged were fears about the products and their side effects, which were primarily fueled by other participants, relatives and community members’ negative attitudes about the products. Other findings indicated there was widespread misunderstanding and misinterpretation of questions participants were asked about the practice of anal sex.

MTN-004 – A Phase I study that tested the safety and acceptability of VivaGel® (SPL7013 Gel) in HIV-negative women ages 18 to 24. The study, a collaboration with the NIH’s Adolescent Trials Network (ATN) for HIV/AIDS Interventions, was conducted at two U.S. sites and one in Puerto Rico. Results, reported in May 2010, found VivaGel generally well-tolerated but less acceptable to use than the two placebo gels studied.

MTN-005 – An expanded safety and acceptability study of a non-medicated vaginal ring made of a silicone elastomer that enrolled 195 sexually active, HIV-negative women. The study was conducted at three sites – one in India and two in the United States – in collaboration with the Population Council. Data analysis is currently underway.

MTN-006 (RMP-02/MTN-006) – A Phase I study involving 18 HIV-negative men and women that was designed to determine whether the vaginal formulation of tenofovir gel is safe to use in the rectum, and through novel laboratory studies, if the gel prevents HIV infection in rectal tissue sampled from study participants. Results, reported in February 2011, found HIV infection was significantly inhibited in rectal tissue sampled from participants who used tenofovir gel daily for one week. Because some participants experienced gastrointestinal side effects, researchers subsequently reformulated the gel to include less glycerin. The study was conducted in collaboration with the Division of AIDS Integrated Pre-Clinical/Clinical Program for HIV Topical Microbicides of the National Institute of Allergy and Infectious Diseases.

MTN-007 – A Phase I follow-up study to RMP-02/MTN-006 that found rectal use of a reduced glycerin formulation of tenofovir gel safe and acceptable among the 60 men and women who took part in the study at three U.S. sites. Based on results, which were first reported February 2012, researchers proceeded with a Phase II trial of reduced glycerin tenofovir gel, MTN-017.

MTN-008 – An expanded Phase I safety and drug absorption study of tenofovir gel used daily for seven consecutive days in women in their third trimester of pregnancy, and women who were breastfeeding. The study enrolled 90 pregnant women – 45 women at 37 weeks gestation and 45 women at 34 weeks gestation; and 16 women who were breastfeeding. MTN-008 was a follow-up study to MTN-002 and conducted at two U.S. sites. Results, presented in August 2013 and 2014, indicated that daily use of tenofovir gel in the third trimester of pregnancy was safe and well-tolerated, tenofovir did not accumulate in breast milk, and absorption of the drug in breastfeeding infants was low.

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MTN-009 – Also called the HIV Drug Resistance Study, MTN-009 assessed the prevalence of HIV drug resistance in KwaZulu-Natal, South Africa. Results, published in April 2013, found the prevalence of HIV drug resistance was 7.4 percent, with the majority of women with resistance having virus with the K103N mutation that confers resistance to most drugs of the type called non-nucleoside reverse transcriptase inhibitors (NNRTIs). Nevirapine, for example, an NNRTI commonly used to prevent the transmission of HIV from mother to child, would not be effective in someone with the K103N mutation.

MTN-011 – A Phase I study that aimed to determine the effect vaginal sex may have on drug absorption and drug activity of tenofovir gel. The study, which was conducted at two sites in the U.S., enrolled 24 couples. Study results, presented in October 2014, showed that drug levels were highest when tenofovir gel was used one hour before and one hour after sex, suggesting that the timing of gel use relative to sex impacts the drug’s absorption and activity.

MTN-012/IPM 010 – A Phase I study that assessed the safety and tolerance of a vaginal microbicide containing the ARV drug dapivirine when applied topically to the penis of sexually abstinent men. Results, which were reported April 2012, found the gel safe and well tolerated. The study was conducted in collaboration with IPM.

MTN-013/IPM 026 – A Phase I safety and drug absorption study testing 28-day use of a vaginal ring containing either dapivirine, maraviroc or the two ARVs combined that was conducted at three U.S. sites in collaboration with IPM. The study was the first clinical trial of a vaginal ring containing maraviroc, and the first to test a vaginal ring with two active drugs. Results, reported in March 2014, found the ring was safe in women and evidence of dapivirine in cervical tissue and blood. In addition, laboratory tests of tissues samples showed that dapivirine was able to block HIV infection, though levels of maraviroc were not sufficient to have a similar effect.

MTN-014 – A Phase I study that examined drug absorption patterns in both rectal and vaginal tissue when a reduced glycerin formulation of tenofovir gel was applied either vaginally or rectally. The study enrolled 14 women at a U.S.-based clinical research site. Results, reported in July 2015, demonstrated that when tenofovir gel was applied into the vagina, a low amount of active drug was distributed to the rectum and, similarly, when the gel was applied into the rectum, a low amount of active drug was distributed to the vagina.

MTN-017 – A Phase II trial designed to evaluate the rectal safety, drug absorption and acceptability of a reduced glycerin formulation of tenofovir gel, as well as oral Truvada, at sites in Peru, South Africa, Thailand and the U.S., including Puerto Rico. The study enrolled 195 men who have sex with men (MSM) and transgender women. Results, which were reported February 2016, found the gel was safe to use, with participants preferring to use the gel around the time of sex compared to daily use.

MTN-020 – ASPIRE – A Study to Prevent Infection with a Ring for Extended Use – was a Phase III study to determine whether a vaginal ring containing the ARV drug dapivirine is a safe and effective method for protecting against the sexual transmission of HIV when used by women for a month at a time. ASPIRE enrolled 2,629 sexually active HIV-negative women ages 18-45 and was conducted between August 2012 and June 2015 at 15 clinical research sites in Malawi, Uganda, South Africa and Zimbabwe. Results, reported in February 2016, found 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 placebo ring group. There was a 37 percent reduction in HIV infections in a second analysis planned early into the study that excluded data from two sites with less than ideal retention and adherence. HIV risk was cut by more than half (56 percent) in women older than 21, who also appeared to use the ring most consistently. Additional analyses suggest even higher levels of protection can be achieved with regular and consistent use. The ring was developed by International Partnership for Microbicides (IPM), which conducted another Phase III trial, The Ring Study, in parallel with ASPIRE.
MTN-023/IPM 30 – A Phase I safety study of the dapivirine vaginal ring in adolescent girls that was conducted at six U.S. research sites between August 2013 and July 2016 in collaboration with the National Institutes of Health-funded Adolescent Medicine Trials Network (ATN) for HIV/AIDS interventions. The study was designed to collect data that regulatory bodies would require when considering whether to approve the dapivirine ring for HIV prevention. As such, MTN-023/IPM 030 is part of a package of studies, with ASPIRE and The Ring Study as the centerpiece, that IPM, as the ring’s developer and regulatory sponsor, plans to submit for regulatory review. Results from MTN-023/IPM 30 are expected late 2016 or early 2017.

MTN-024/IPM 31 – A Phase I safety study of the dapivirine ring in post-menopausal women conducted at three sites in the U.S. that found the ring was safe and well-tolerated. As with MTN-023/IPM 30, the study was designed to collect data that regulatory bodies would require when considering whether to approve the dapivirine ring for HIV prevention. As such, MTN-024/IPM 031 is part of a package of studies, with ASPIRE and The Ring Study as the centerpiece, that IPM, as the ring’s developer and regulatory sponsor, plans to submit for regulatory review.

MTN-027 – Along with its companion study, MTN-028, MTN-027 is the first clinical trial to test a type of ARV called an integrase inhibitor as a potential microbicide. A Phase I trial, MTN-027 looked at the safety of three vaginal rings: one that contains the integrase inhibitor MK-2048; a second ring containing vicriviroc (MK-4176), which is a CCR5-receptor antagonist; and a third ring that contains both active drugs. The study, which has completed follow-up of 48 women at two U.S. sites, also assessed the absorption and distribution of the drug(s) contained in each ring. Results are anticipated in late 2016 or early 2017.

MTN-028 – A Phase I trial that evaluated two vaginal rings, each containing a different dose of the same two ARV drugs – a CCR5-receptor antagonist called vicriviroc (MK-4176) and an integrase inhibitor, MK-2048. While the safety and acceptability of these agents alone and in combination are being evaluated in MTN-027, MTN-028, which also completed follow-up of participants, seeks to understand the optimal doses of MK-4176 and MK-2048 needed to achieve concentrations of drug in tissue that could feasibly provide HIV protection. Both studies are the first clinical trials to test an integrase inhibitor as a potential microbicide. Results are anticipated in late 2016 or early 2017.

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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 www.mtnstopshiv.org.

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