NIH launches large study to compare treatments for pregnant women with HIV

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The National Institutes of Health has launched a large international study to compare the safety and efficacy of three antiretroviral treatment regimens for pregnant women living with HIV and the safety of these regimens for their infants. The study will evaluate the current preferred first-line regimen for pregnant women recommended by the World Health Organization (WHO) and two regimens containing newer antiretroviral drugs that are becoming more widely used. It will provide data on the use of these newer drugs during pregnancy, helping to ensure that women living with HIV and their infants receive the best available treatments.

Each year worldwide, an estimated 1.5 million women living with HIV give birth. Previous research has clearly demonstrated that antiretroviral therapy to suppress HIV prevents perinatal HIV transmission and benefits the health of both mother and child. In the new study, investigators will compare the virologic efficacy of the three regimens by measuring the mother's viral load (amount of HIV in the blood) at delivery. The study also will compare how the regimens affect rates of adverse pregnancy outcomes, such as preterm delivery and low infant birth weight; maternal adverse events; and infant adverse events.

"Women should have access to the best available HIV medications throughout their lives," said Anthony S. Fauci, M.D., director of NIH's National Institute of Allergy and Infectious Diseases (NIAID). "Our priority is to evaluate newer, improved antiretroviral drugs during pregnancy to

identify the optimal regimens for women living with HIV and their infants."

The first participants in the new clinical trial have begun receiving treatment at research sites in Zimbabwe. Clinical trial sites in the United States and Zimbabwe are now open for enrollment, with additional sites in Botswana, Brazil, Haiti, India, Malawi, South Africa, Tanzania, Thailand, Uganda, the United States and Zimbabwe expected to open in the coming months. The trial is supported by NIAID, the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD) and the National Institute of Mental Health (NIMH), all part of NIH. It is being conducted by theInternational Maternal Pediatric Adolescent AIDS Clinical Trials (IMPAACT) network.

Currently, WHO recommends a regimen of three antiretroviral drugs—efavirenz (EFV), lamivudine (3TC) or emtricitabine (FTC), and tenofovir disoproxil fumarate (TDF)—for pregnant women living with HIV in resource-limited settings. However, this regimen is not well-tolerated by or otherwise appropriate for all women. EFV has been linked to neuropsychiatric symptoms, including suicidal thoughts, as well as liver problems. TDF can cause kidney problems and loss of bone mineral density in adults, and some evidence suggests that prenatal exposure to TDF could cause bone loss in infants.

The new study will compare maternal EFV/FTC/TDF with regimens containing a newer drug, dolutegravir (DTG), and either tenofovir alafenamide (TAF), an alternative formulation of tenofovir, or TDF. The study, known as IMPAACT 2010 or VESTED (Virologic Efficacy and Safety of Antiretroviral Therapy Combinations with TAF/TDF, EFV and DTG), is co-chaired by Shahin Lockman, M.D., M.Sc., of Brigham and Women's Hospital in the United States, and Lameck Chinula, M.B.B.S., M.Med., of the University of North Carolina Project at Kamuzu Central Hospital in Malawi.

DTG currently is included in two of the preferred first-line regimens recommended for adults living with HIV in the United States, and recently was included in WHO guidelines as an alternative first-line agent in non-pregnant adults. Advantages of DTG include once-daily dosing, a good safety profile, a high barrier to development of drug resistance and a relatively low production cost. Research so far indicates that TAF is as effective as TDF but appears to cause fewer kidney and bone side effects. Only a few studies have assessed the use of DTG in pregnancy, and minimal data are available on the safety and efficacy of TAF in pregnant women.

“Therapies for pregnant women and new mothers should be based on the best available evidence, always keeping in mind the health of the woman, her developing fetus and her newborn,” said Nahida Chakhtoura, M.D., of the Maternal and Pediatric Infectious Disease Branch at NICHD. “The results of this study will help inform optimal treatment of pregnant women living with HIV in both resource-limited and well-resourced settings.”

IMPAACT 2010, a Phase 3 study, aims to enroll 639 women who are 14 to 28 weeks into their pregnancies, are living with HIV and are not currently on antiretroviral treatment. The women will be randomly assigned to treatment with EFV/FTC/TDF, DTG/FTC/TAF or DTG/FTC/TDF. Their infants also will be enrolled in the study and will receive local standard-of-care interventions for HIV prophylaxis after birth. Mothers will be counseled on infant feeding options consistent with local standards of care, which may include breastfeeding or formula feeding.

The investigators will monitor both mother and infant for 50 weeks after delivery. Study staff will provide women with counseling on antiretroviral medication adherence, which is essential to keep HIV suppressed. The mothers’ viral loads will be closely monitored, and infants also will be tested for HIV. If an infant becomes infected with HIV during the study,

investigators will provide referrals to local sources of HIV care and treatment. Throughout the study, investigators will closely monitor the health of mother and infant, including assessing the mother’s liver and kidney function and screening for anxiety and depression. Investigators also will conduct bone density scans of a subset of infants at 26 weeks of age and their mothers at 50 weeks postpartum. The study is expected to last for approximately three years.

“Limited pregnancy data for newer, better antiretroviral drugs—such as DTG and TAF—can mean that pregnant women may not receive the most effective and safest medications, and can delay the general adoption of better regimens in low-resource settings with high HIV prevalence,” said Dr. Lockman. “We hope that the VESTED trial will provide urgently needed information regarding the safety and efficacy of these newer drugs in pregnant women and their babies, so that optimal antiretroviral regimens can be offered to pregnant women and recommended for first-line treatment of adults living with HIV throughout the world.”

Source:

https://www.niaid.nih.gov/news-events/nih-begins-large-hiv-treatment-study-pregnant-women