Medicines Control Authority of Zimbabwe

Clinical Trials Registry

PUBLIC TITLE/ACRONYM	O-PrEP
Scientific Title	Optimizing PrEP regimens for pregnant women in sub-Saharan Africa

Primary Sponsor Details

Sponsors *	University of North Carolina

Secondary Sponsor Details

Contact for Public Queries

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Countries of Recruitment *

Zimbabwe

Source of Funds	United States National Institutes of Health (NIH) through the University of North Carolina at Chapel Hill
Health Condition(s) or Problem(s) Studied *	The study seeks to identify the optimum for of FTC/TDF for daily oral PrEP during pregnancy in cis-gender pregnant women eligible for PrEP as per national guidelines and their infants. The study will also evaluate the extended maternal and infant safety of an increased FTC/TDF dose for daily oral PrEP during pregnancy.
Medicine Name *	: Emtricitabine/Tenofovir Disoproxil Fumarate (Truvada®) tablets
Quantity of medicine required *	720 bottles of 30s

7.0 PRINCIPAL INCLUSION CRITERIA *

Inclusion criteria

Maternal participants

- Maternal participants aged 16 years or older
- PrEP-eligible by local guidelines
- Pregnant with a viable singleton pregnancy of between 14 and 23 completed weeks of gestation (from 14 weeks + 0 days to 23 weeks + 6 days) by ultrasonography at study entry
- HIV-negative based on the study-specific screening algorithm
- Hepatitis B surface antigen (HBsAg)-negative
- Weight >35kg
- Provided informed consent and expressed willingness to participate in study activities with their infants, including daily administration of oral PrEP under direct observation.

Infant participants

- Infant participants enter the study with mother as unborn infants. There are no specific eligibility criteria for infant participation otherwise. If an infant is deemed too ill to undergo study procedures, procedures necessary for clinical management may be prioritised.

7.1 PRINCIPAL EXCLUSION CRITERIA *

Exclusion criteria

- Grade 2 or greater laboratory parameters for alanine transaminase (ALT) or aspartate aminotransferase (AST), haemoglobin (HB), and absolute neutrophil count (ANC).
- Estimated creatinine clearance (CrCl) 90mL/min or below, using the Cockcroft-Gault formula.
- Known history or evidence of current significant disease process, including haematological conditions, renal disease, unexplained bone fractures, environmental enteric dysfunction, or allergies/sensitivities to FTC/TDF.
- Other current significant or uncontrolled disease process (active or chronic) substance use, or social circumstances that, in the judgement of the site investigator, would make participation in the study inappropriate or unsafe.
- Foetuses with known or suspected major foetal anomaly, either from screening ultrasound or via medical record
- Intention to leave the study site's catchment area before scheduled study exit.
- Current use of prohibited medications listed in the protocol Section 5.8
- Concurrent use of other biomedical HIV prevention interventions (vaginal ring, injectable PrEP, any investigational prevention product).

7.2 PRIMARY END POINTS *

The key safety endpoints are

- maternal renal function, measured via CrCl;
- maternal grade >2 adverse events, including renal events.
- adverse pregnancy outcome composite that includes fetal death (spontaneous abortion and stillbirth), preterm birth, and small for gestational age;
- infant grade >3 adverse events and major congenital anomalies reported between birth and study exit. Gestational age will be determined by best obstetric estimate, based on obstetric ultrasound prior to study entry. We will use the INTERGROWTH-21st standards for weight-for-gestational age at birth.

The area under the dose-concentration curve (AUC) of tenofovir diphosphate (TFV-DP) in peripheral blood mononuclear cells (PBMCs) serves as the primary PK endpoint.

9.0 DESIGN OF THE TRIAL

Type of trial *	Opened

If controlled

Randomised	Yes
Single Blind	No
Double Blind	No

Parallel group	Yes
Cross over	No
Other	Yes
If yes to other, specify	3 parallel arms for Stage 1: Arm 1: Arm 1A standard FTC/TDF dose (200mg/300mg) in pregnancy and postpartum Arm 2: Arm 1B 150% standard FTC/TDF dose (300mg/450mg) in pregnancy and postpartum Arm 3: Arm 1C 200% standard FTC/TDF dose (200mg/300mg) in pregnan
If controlled, specify the comparator	No placebo. Different doses of Truvada will be compared.
Other medicinal product(s)	
Placebo	Yes
Other	
If yes to other, specify	
Other	Yes

Expected Number of participants in Zimbabwe *	332
Total enrolment in each site: (if competitive enrolment, state minimum and maximum number per site.) *	54 mother-infant pairs (18 per arm to give at least 12 evaluable women per arm) for stage 1 and 56 mother-infant pairs per study arm for stage 2. (potential need to replace ppts if more than 6 in any Stage 1 arm do not meet criteria to be included in the PK analysis)
Total participants worldwide *	332

Time period for the trial *	5 YEARS