Medicines Control Authority of Zimbabwe

Clinical Trials Registry

PUBLIC TITLE/ACRONYM	CT183/2019 MTN-042
Scientific Title	CT183/2019 MTN-042: A Phase 3b, Randomized, Open Label, Safety Trial of Dapivirine Vaginal Ring and Oral TRUVADA Use in Pregnancy

Primary Sponsor Details

Sponsors *	NIAID/DAIDS

Secondary Sponsor Details

Contact for Public Queries

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Countries of Recruitment *

South Africa

Malawi

Uganda

Zimbabwe

Source of Funds	NIAID/DAIDS
Health Condition(s) or Problem(s) Studied *	A Phase 3b study of the Dapivirine ring and PrEP in Pregnant women
Medicine Name *	Dapivirine Vaginal Ring 25mg

Quantity of medicine required * 700

7.0 PRINCIPAL INCLUSION CRITERIA *

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  - Age 18 through 40 years
  - Evidence of a viable, intrauterine, singleton pregnancy with sonographic confirmation, including for gestational age assessment.
  - At Enrollment, pregnancy within gestational age limits of the currently enrolling cohort
  - HIV-uninfected based on testing performed at Screening and Enrollment
  - Intending to continue her pregnancy until delivery.
  - Intending to deliver at a health center or hospital where adequate records may be obtained, as defined in site SOPs.
  - Willing to be randomized at time of enrollment to either of the two study arms, and to continue study product use until delivery.
  - Able and willing to comply with all study requirements and complete all study procedures.

7.1 PRINCIPAL EXCLUSION CRITERIA *

Participants who meet any of the following criteria will be excluded from this study:

- Use oral PrEP outside the context of study participation.
- Relocate away from the study site.
- Travel away from the study site for a time period that would interfere with study participation.
- At screening or Enrollment, has a positive HIV test.
- At Screening or Enrollment, diagnosed with urinary tract infection (UTI), cervicitis, STI or reproductive tract infection (RTI) requiring treatment per WHO guidelines.
- At Enrollment, has a clinically apparent Grade 2 or higher pelvic exam finding.
- Cervical friability bleeding associated with speculum insertion
- Participant report, clinical evidence and/or antenatal/medical care record of any of the following:

1. Currently breastfeeding at Enrollment.
2. Known adverse reaction to any of the study products (ever).
3. Known adverse reaction to latex and polyurethane (ever).
4. Symptoms suggestive of acute HIV infection at Screening or Enrollment.
5. Non-therapeutic injection drug use in the 12 months prior to Enrollment.
6. Use of HIV post-exposure prophylaxis (PEP) and/or PrEP during the current pregnancy.
7. Paiticipation in any other research study involving drugs, medical devices, vaginal products, or vaccines during the current pregnancy.
8. At Screening or Enrollment, known to have any of the following during the current pregnancy:
   - Multiple gestation
   - Placenta previa
   - Cervical cerclage
   - Abnormal fetal anatomy (in the opinion of the IoR or designee)
   - Intrauterine growth restriction
   - Pre-existing or gestational diabetes
   - Hypertensive disorder of pregnancy
   - Severe malaria
   - Treatment for preterm labor
   - Abnormal quantity of amniotic fluid (oligohydramnios or polyhydramnios)
9. At Screening, known to have had any of the following in a previous pregnancy:
   - Intrauterine growth restriction
   - Gestational diabetes
   - Hypertensive disorder of pregnancy
   - Intrauterine fetal demise (estimated gestational age ≥20 weeks)
   - Delivery prior to 37 0/7 weeks

10. At Enrollment has any significant obstetrical complication or uncontrolled active or chronic cardiovascular, renal, liver, hematologic, neurologic, gastrointestinal, psychiatric, endocrine**,** respiratory, immunologic disorder or infectious disease that would make study participation unsafe.

- Has any of the following laboratory abnormalities:
  - Positive for hepatitis B surface antigen (HBsAg).
  - Aspartate aminotransferase (AST) or alanine transaminase (ALT) ≥: Grade 1.
  - Hemoglobin ≥ Grade 2.
  - Platelet count ≥ Grade I.
  - Creatinine ≥ Grade I.
  - Estimated creatinine clearance 2 ≥ Grade I (Cockcroft Gault formula).
  - Glycosuria ≥ Grade 2.
  - Proteinuria ≥ Grade 2.
- Has any condition that, in the opinion of the IoR/designee, would preclude informed consent, make study participation unsafe, complicate interpretation of study outcome data, or otherwise interfere with achieving the study objectives.

7.2 PRIMARY END POINTS *

Maternal Safety (Composite)

- All serious adverse events, including maternal deaths
- All grade 3 or higher AEs as defined by the Division of AIDS (DAIDS) Table for Grading the Severity of Adult and Pediatric Adversee Events, Corrected Version 2.1, July 2017 and/or Addendum 1 (Female Genital Grading Table for Use in Microbicide Studies [Dated November 2007]

Infant Safety (Composite)

- All serious adverse events, including infant deaths and congenital anomalies
- All Grade 3 or higher AEs as defined by the Division of AIDS (DAIDS) Table for Grading the Severity of Adult and Pediatric Adverse Events, Corrected Version 2.1, July 2017

Pregnancy Outcomes

- Frequency of the following pregnancy outcomes:
  - Full term live birth (≥37 weeks)
  - Premature live birth (< 37 weeks)
  - Pregnancy loss (≥20 weeks)
  - Pregnancy loss (<20 weeks)

9.0 DESIGN OF THE TRIAL

Type of trial *	Controlled

If controlled

Randomised	Yes
Single Blind	
Double Blind	
Parallel group	
Cross over	
Other	
If yes to other, specify	
If controlled, specify the comparator	
Other medicinal product(s)	
Placebo	
Other	
If yes to other, specify	
Other	

Expected Number of participants in Zimbabwe *	190
Total enrolment in each site: (if competitive enrolment, state minimum and maximum number per site.) *	
Total participants worldwide *	750

Time period for the trial *	Total study duration including infant follow-up for all cohorts will be approximately 49-61 months. Approximately 750 participants and their infants will be enrolled across four cohorts. The accrual period for Cohorts 1-3 will be approximately 4-5 months, while the accrual period for Cohort 4 will be approximately 7-9 months. Participant accrual will be paused at all sites once accrual goals are met for the currently enrolling Cohort. This will be done to allow all enrolled participants to give birth and, for Cohorts l-3, to conduct interim safety analyses to determine if accrual into the next Cohort can commence. The duration of these accrual pauses will vary depending on the Cohort and on the quantity and quality of data collected, and likely will resemble the following: approximately 3-4 months after Cohort l, approximately 4-6 months after Cohort 2, and approximately 6-8 months after Cohort 3. Therefore, it is expected that the Cohort l phase of the study will last approximately 7-9 months, Cohort 2 approximately 8- l l months, Cohort 3 approximately 10-13 months, and Cohort 4 approximately l 3-17 months, for a study duration of approximately 38-50 months. In addition, infants born to MTN-042 participants will be followed up for approximately one year, though this will not be part of the interim safety analyses after Cohorts l-3.