VOICE
Eligibility Criteria

MTN-003 Operational Walkthrough

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Johannesburg, South Africa

Screening and Enrollment Overview

- All participants enrolled in VOICE must meet the study eligibility criteria
- Screening procedures are performed to determine and document eligibility (and baseline medical condition)
- All screening and enrollment procedures must take place within a 56-day period
- At least two screening visits are required, more visits are allowed
- Protocol defines Screening Part 1 visit procedures, Screening Part 2 visit procedures, and screening procedures performed on the day of Enrollment

Inclusion Criteria

1) Age 18 through 40 years (inclusive) at screening, verified per site SOPs; within this range sites may restrict the upper age limit per site SOPs, to target women at high risk of HIV infection
2) Able and willing to provide written informed consent to be screened for and to take part in the study
3) Able and willing to provide adequate locator information, as defined in site SOPs

Inclusion Criteria

4) HIV-uninfected based on testing performed by study staff at screening and enrollment (per applicable algorithms in Appendices II and III)
   - Clarification: Follow the screening algorithm in Appendix II

5) Per participant report, sexually active, defined as having vaginal intercourse at least once in the 3 months prior to Screening Part 1

Inclusion Criteria

6) Per participant report, using an effective method of contraception at enrollment, and intending to use an effective method for the next 24 months; effective methods include hormonal methods; intrauterine contraceptive device; and sterilization (of participant or her sexual partner or partners as applicable and with verification as defined in site SOPs)
7) At screening and enrollment, agrees not to participate in other research studies involving drugs, medical devices, or vaginal products for the next 24 months

Exclusion Criteria

1) Participant reported any of the following:
   a) Known adverse reaction to any of the study products (ever)
   b) Known adverse reaction to latex (ever)
   c) Pathologic bone fracture not related to trauma (ever)
   d) Non-therapeutic injection drug use in the 12 months prior to Screening Part 1
   e) Post-exposure prophylaxis (PEP) for HIV infection within 6 months prior to enrollment

Exclusion Criteria

1) Participant reported any of the following:
   - f) Last pregnancy outcome 42 days or less prior to enrollment
   - g) Gynecologic or genital procedure (e.g., biopsy, tubal ligation, dilation and curettage, piercing) 42 days or less prior to enrollment
   - h) Participation in any other research study involving drugs, medical devices, or vaginal products 30 days or less prior to enrollment
   - i) Currently breastfeeding

Exclusion Criteria

1) Participant reported any of the following:

   j) Currently using spermicide; interferon or interleukin therapy; medication(s) with significant nephrotoxic potential, including but not limited to amphotericin B, aminoglycosides, cidovir, foscarnet and systemic chemotherapy; medication(s) that may inhibit or compete for elimination via active renal tubular secretion (including but not limited to probenecid)

Exclusion Criteria

1) Participant reported any of the following:
    k) As determined by the IoR/designee, any significant uncontrolled active or chronic cardiovascular, renal, liver, hematologic, neurologic, gastrointestinal, psychiatric, endocrine, respiratory, immunologic disorder or infectious disease, including active tuberculosis

Exclusion Criteria

2) Has any of the following lab abnormalities:
   a) AST or ALT greater than 1.5 x site lab ULN
   b) Calculated creatinine clearance less than 60 mL/min (Cockcroft-Gault formula)
   c) Serum creatinine greater than the site lab ULN
   d) Hemoglobin less than 10.0 g/dL
   e) Platelet count less than 100,000/mm^3
   f) Serum phosphate level below site lab LLN
   g) Positive Hepatitis B surface antigen (HBsAg) test result

Exclusion Criteria

2) Has any of the following lab abnormalities:

   h) Grade 2 or higher Pap result (at sites with capacity, where standard of care)

   Note: Women with a documented normal result within the 12 months prior to enrollment need not have Pap smear during the screening period. Women with abnormal Pap smears can be enrolled upon completion of the initial phase of evaluation if no current treatment is indicated (based on local standard of care for management of abnormal cervical cytology). Need for a repeat Pap within 6 months does not preclude enrollment prior to that result becoming available.

Exclusion Criteria

What are your expectations re: Pap smears? Will many women have a documented normal Pap within the 12 months prior to enrollment?

Exclusion Criteria

2) Has any of the following lab abnormalities:

i) Dipstick urinalysis results for protein

- Any result of 2+ or greater at a single visit
- At least two results of 1+ or greater at separate visits

j) Dipstick urinalysis results for glucose

- Any single result of 2+ or greater at a single visit
- At least two results of 1+ or greater at separate visits

Exclusion Criteria

2) Has any of the following lab abnormalities:

Note: Otherwise eligible participants with an exclusionary test result other than urine dipstick results may be re-tested during the screening process. If a participant is re-tested and a non-exclusionary result is documented within 56 days of providing informed consent for screening, the participant may be enrolled.

Exclusion Criteria

3) Is pregnant

Note: Self-reported pregnancy is adequate for exclusion from the study. A documented negative pregnancy test performed by study staff is required for inclusion.

Exclusion Criteria

4) Per participant report at Screening Part 1:
   a) Intends to become pregnant in the next 24 months
   b) Plans to relocate away from the study site in the next 24 months
   c) Plans to travel away from the study site for more than 8 consecutive weeks during the next 24 months

Exclusion Criteria

5) Diagnosed with urinary tract infection (UTI)

Note: Otherwise eligible participants diagnosed with UTI during screening will be offered treatment and may be enrolled after completing treatment and all symptoms have resolved. If treatment is completed and symptoms have resolved within 56 days of obtaining informed consent for screening, the participant may be enrolled.

Exclusion Criteria

6) Diagnosed with PID, an STI or RTI requiring treatment per current WHO guidelines

Note: Otherwise eligible participants diagnosed during screening with pelvic inflammatory disease or STI/RTI requiring treatment per WHO guidelines — other than asymptomatic BV and asymptomatic candidiasis — will be offered treatment and may be enrolled after completing treatment and all symptoms have resolved. If treatment is completed and symptoms have resolved within 56 days of obtaining informed consent for screening, the participant may be enrolled. Genital warts requiring treatment also must be treated prior to enrollment. Genital warts requiring therapy are defined as those that cause undue burden of discomfort to the participant, including bulky size, unacceptable appearance, or physical discomfort.

Exclusion Criteria

7) Has a clinically apparent Grade 2 or higher pelvic exam finding (observed by study staff)

Note: Cervical friability judged to be within the range of normal according to the clinical judgment of the IoR/designee is not exclusionary.

Note: Otherwise eligible participants with exclusionary pelvic exam findings may be enrolled/randomized after the findings have improved to a non-exclusionary severity grading or resolved. If improvement to a non-exclusionary grade or resolution is documented within 56 days of providing informed consent for screening, the participant may be enrolled.

Exclusion Criteria

8) Has any other 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

Co-Enrollment Guidelines

- Participants should not take part in other research studies involving drugs, medical devices, or vaginal products while taking part in VOICE.
- Participants will be discouraged from taking part in non-investigational studies, except:
  - Participants may take part in ancillary studies approved by the VOICE Protocol Chairs
  - Participants who become infected with HIV may take part in observational and/or interventional studies for HIV-infected persons