Medicines Control Authority of Zimbabwe

Clinical Trials Registry

PUBLIC TITLE/ACRONYM	IMPOWER 022
Scientific Title	A Phase 3, Randomized, Active-Controlled, Double-blind Clinical Study to Evaluate the Efficacy and Safety of Oral Islatravir Once-Monthly as Preexposure Prophylaxis in Cisgender Women at High Risk for HIV-1 Infection

Primary Sponsor Details

Sponsors *	Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc. (hereafter referred to as the Sponsor or MSD)

Secondary Sponsor Details

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Countries of Recruitment *

South Africa, United States of America, Zimbabwe, Eswatini, Zambia, Malawi, Uganda and Kenya

Source of Funds	
Health Condition(s) or Problem(s) Studied *	HIV Prevention Trial
Medicine Name *	Oral Islatravir
Quantity of medicine required *	The amount of medicine required will be determined by the number of participants enrolled.

7.0 PRINCIPAL INCLUSION CRITERIA *

A participant will be eligible for inclusion in the study if the participant:

Type of Participant and Disease Characteristics

1. Is confirmed HIV-uninfected based on negative HIV-1/HIV-2 test results before randomization.

Note: If a positive result is obtained for any HIV test prior to randomization, the participant is not eligible for the study. Additional testing to confirm suspected HIV infection during screening will be performed in accordance with local guidelines. If HIV infection is confirmed, participants will be referred for appropriate care, as necessary.

2. Has been sexually active with a male sexual partner in the 30 days prior to Screening.

3. Is at high risk for HIV-1 infection as defined by a risk score ≥5 using a VOICE risk score tool (ex-US sites) or meets the CDC criteria for PrEP eligibility (US sites).

Demographics

4. Was assigned female sex at birth, is cisgender, 16 years to 45 years of age, inclusive, at the time of providing informed consent/assent.

Female Participants

5. A female participant is eligible to participate if she is not pregnant or breastfeeding, and at least one of the following conditions applies:

• Is not a WOCBP

OR

• Is a WOCBP and using an acceptable contraceptive method, as described in Appendix 5 during the intervention period and for at least 42 days after the last dose (corresponding to the time needed to eliminate any study intervention [approximately 5 terminal halflives]).

• A WOCBP must have a negative highly sensitive pregnancy test ([urine or serum] as required by local regulations) within 24 hours before the first dose of study intervention.

• If a urine test cannot be confirmed as negative (eg, an ambiguous result), a serum pregnancy test is required. In such cases, the participant must be excluded from participation if the serum pregnancy result is positive.

• Additional requirements for pregnancy testing during and after study intervention are located in Appendix 2.

• The investigator is responsible for review of medical history, menstrual history, and recent sexual activity to decrease the risk for inclusion of a woman with an early undetected pregnancy.

• Contraceptive use by women should be consistent with local regulations regarding the methods of contraception for those participating in clinical studies.

Informed Consent

6. The participant (or legally acceptable representative) has provided documented informed consent/assent for the study. The participant may also provide consent/assent for future biomedical research. However, the participant may participate in the main study without participating in future biomedical research.

Additional Categories

7. Has no plans to relocate or travel away from the site for ≥4 consecutive weeks during study participation.

7.1 PRINCIPAL EXCLUSION CRITERIA *

The participant must be excluded from the study if the participant:

Medical Conditions

1. Has hypersensitivity or other contraindication to any of the components of the study interventions as determined by the investigator.
2. Has active HBV infection (defined as HBsAg-positive or HBV DNA positive)

3. Current or chronic history of liver disease (eg, nonalcoholic or alcoholic steatohepatitis) or known hepatic or biliary abnormalities (with the exception of Gilbert's syndrome, asymptomatic gallstones, or cholecystectomy), unless the participant has stable liver function tests and no significant hepatic synthetic dysfunction.
Note: Hepatic synthetic dysfunction is defined as a serum albumin <2.8 g/dL or an INR >1.7 in the absence of another explanation for the abnormal laboratory value.
4. Has a history of malignancy within 5 years of screening except for adequately-treated basal cell or squamous cell skin cancer, or in situ cervical cancer.
5. Has a history or current evidence of any condition (including active tuberculosis infection), therapy, laboratory abnormality or other circumstance (including drug or alcohol use or dependence) that might, in the opinion of the investigator, confound the results of the study or interfere with the participant's participation for the full duration of the study, such that it is not in the best interest of the participant to enroll.

Prior/Concomitant Therapy

6. Has taken cabotegravir at any time (past or current use)
7. Is currently receiving or is anticipated to require any prohibited therapies outlined in Section 6.5 from 30 days prior to Day 1 through the duration of the study.

Prior/Concurrent Clinical Study Experience

8. Is currently participating in or has participated in an interventional clinical study with an investigational compound or device, including HIV prevention compounds or devices within 30 days prior to Day 1 through the duration of the study.

Diagnostic Assessments

9. Has exclusionary laboratory values within 45 days prior to Day 1 as listed below.

Laboratory Assessment Exclusionary Values

Absolute neutrophil count ≤750 cells/mm^3

Alkaline Phosphatase >3 × ULN

AST >3 × ULN

ALT >3 × ULN

Bilirubin ≥2.5 × ULN

Calculated CrCl <60 mL/min[a] based on the Cockcroft-Gault

equation (Appendix 9).

Hemoglobin <10.0 g/dL

Platelet count <100,000/mm^3

ALT=alanine aminotransferase; AST=aspartate aminotransferase; CrCl=creatinine clearance; ULN=upper

limit of normal.

[a] Although not protocol exclusionary, sites should carefully consider the advisability of enrolling

participants with calculated CrCl between 60 to 70 mL/min, as limited changes in CrCl during study

conduct will lead to protocol-mandated product holds and may alter the risk-benefit considerations of study participation.

Other Exclusions

10. Is expecting to conceive or donate eggs at any time during the study.

7.2 PRIMARY END POINTS *

Primary Outcome Measures

1. The primary efficacy objective will be assessed based on the incidence rate per year of

confirmed incident HIV-1 infections.

1. Safety and tolerability will be assessed by clinical review of all relevant parameters including AEs and laboratory tests.

9.0 DESIGN OF THE TRIAL

Type of trial *	Controlled
If controlled	
Randomised	Yes
Single Blind	No
Double Blind	Yes
Parallel group	No
Cross over	No
Other	No
If yes to other, specify	
If controlled, specify the comparator	Emtricibine/Tenofovir Disoproxil-ratiopharm® 200mg/245mg film-coated tablets
Other medicinal product(s)	Yes
Placebo	Yes
Other	Yes
If yes to other, specify	Placebo Islatravir and Placebo Emtricibine/Tenofovir Disoproxil tablets
Other	No

Expected Number of participants in Zimbabwe *	150
Total enrolment in each site: (if competitive enrolment, state minimum and maximum number per site.) *	75 per site
Total participants worldwide *	4500

Time period for the trial *	The Sponsor estimates that the study will require approximately 3 years from the time the first participant (or their legally acceptable representative) provides documented informed consent/assent until the last participant's last study-related contact.