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Dapivirine Monthly Vaginal Ring

Based on public information

Developer(s)

International Partnership for Microbicides

Originator

https://www.ipmglobal.org/

United States

IPM's mission is to develop HIV prevention products and other sexual and reproductive health technologies for women, and to make them available and accessible where they are urgently needed.

Population Council

Originator

https://popcouncil.org/

Global

The Population Council is a leading research organization dedicated to building an equitable and sustainable world that enhances the health and well-being of current and future generations. We generate ideas, produce evidence, and design solutions to improve the lives of underserved populations around the world.

Janssen Pharmaceuticals

Sponsor(s)

USAID

https://www.usaid.gov/

Partnerships

Ajinomoto OmniChem (Aji Bio-Pharma Services)
https://ajibio-pharma.com/

Nusil Technologies
https://www.avantorsciences.com/pages/en/nusil

QPharma
https://www.qpharma.com/

Technology information

Type of technology

Intra-vaginal ring

Administration route

Topical (Vaginal)

Development state and regulatory approval

Active Pharmaceutical Ingredient (API)

Dapivirine (DPV)

Development Stage

Marketed

Regulatory Approval

Positive scientific opinion from the European Medicines Agency for use among women ages 18 and older in developing countries. in WHO guidelines

Description

Silicone matrix vaginal ring delivering dapivirine over one month.

Technology highlight

The ring is made of a flexible silicone polymer and contains the ARV dapivirine, an NNRTI, which is dispersed in the silicone matrix and slowly released over the course of a month. The ring delivers dapivirine directly at the site of potential HIV infection, with low systemic absorption. Women insert the flexible, long-acting ring themselves into the vagina and replace it every month.

Technology main components

Dapivirine 25 mg and silicone

Information on the raw materials sourcing, availability and anticipated price

9 to 13 USD/ring

Delivery device(s)

Silicone vaginal ring

APIs compatibility profile

API desired features

Small molecules

Dapivirine

Additional solubility data

Not provided

Additional stability data

Not provided

API loading: Maximum drug quantity to be loaded

< 10 wt%

API co-administration

1 single API : Still being investigated

LogP

Not provided
Dapivirine LogP = 5.6

Scale-up and manufacturing prospects

Scale-up prospects

current scale: ~9000 rings future scale (2022 and beyond): ~45000 rings

Tentative equipment list for manufacturing

injection molding machine mixer automated inspection machine automated packaging machine

Manufacturing

GMP ISO class 8 area

Specific analytical instrument required for characterization of formulation

HPLC tensile tester dissolution apparatus analytical balance

Clinical trials

ASPIRE (MTN-020)

Identifier

NCT01617096

Link

https://clinicaltrials.gov/study/NCT01617096

Phase

Phase III

Status

Completed

Sponsor

International Partnership for Microbicides, Inc.

More details

Phase 3 Safety and Effectiveness Trial of Dapivirine Vaginal Ring for Prevention of HIV-1 in Women This is a double-blind, randomised, placebo-controlled study to assess the safety and efficacy of a silicone elastomer vaginal matrix ring.

Purpose

Phase 3 Safety and Effectiveness Trial of Dapivirine Vaginal Ring for Prevention of HIV-1 in Women

Interventions

Intervention 1

Dapivirine Monthly Vaginal Ring

Intervention 2

Placebo Ring

Countries

Zimbabwe

South Africa

Uganda

Malawi

Sites / Institutions

Not provided

Trials dates

Anticipated Start Date

Not provided

Actual Start Date

2012-07-24

Anticipated Date of Last Follow-up

2022-12-19

Estimated Primary Completion Date

2012-06-12

Estimated Completion Date

2012-06-12

Actual Primary Completion Date

2022-12-21

Actual Completion Date

2015-12-01

Studied populations

Age Cohort

- Adults

Genders

- Female

Accepts pregnant individuals

No

Accepts lactating individuals

No

Accepts healthy individuals

Yes

Comments about the studied populations

Inclusion Criteria: * Age 18 through 45 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 * Able and willing to provide written informed consent to be screened for and to take part in the study * Able and willing to provide adequate locator information, as defined in site SOPs * HIV-uninfected based on testing performed by study staff at screening and enrollment (per applicable algorithm in Appendix II) * Per participant report, sexually active, defined as having vaginal intercourse at least once in the 3 months prior to screening * Using an effective method of contraception at enrollment, and intending to use an effective method for the duration of study participat

Health status

Negative to : HIV

Study type

Interventional (clinical trial)

Enrollment

2629

Allocation

Randomized

Intervention model

Parallel Assignment

Intervention model description

Not provided

Masking

Double-blind masking

Masking description

Not provided

Frequency of administration

Monthly

Studied LA-formulation(s)

Non-Implantable Device

Studied route(s) of administration

Topical (Vaginal)

Use case

PrEP

Key resources

Type	Title	Content	Link
Link	Experiences with simultaneous use of contraception and the vaginal ring for HIV prevention in sub-Saharan Africa		https://pubmed.ncbi.nlm.nih
Link	Patterns of Adherence to a Dapivirine Vaginal Ring for HIV-1 Prevention Among South African Women in a Phase III Randomized Controlled Trial		https://pubmed.ncbi.nlm.nih
Link	Acceptability of the Dapivirine Vaginal Ring for HIV-1 Prevention and Association with Adherence in a Phase III Trial		https://pubmed.ncbi.nlm.nih

Type	Title	Content	Link
Link	Clinical and Virologic Outcomes Following Initiation of Antiretroviral Therapy Among Seroconverters in the Microbicide Trials Network-020 Phase III Trial of the Dapivirine Vaginal Ring		https://pubmed.ncbi.nlm.nih
Link	Vaginal Ring Use in a Phase 3 Microbicide Trial: A Comparison of Objective Measures and Self-reports of Non-adherence in ASPIRE		https://pubmed.ncbi.nlm.nih

A Safety Study of Dapivirine Vaginal Ring in Africa

Identifier

NCT01071174

Link

https://clinicaltrials.gov/study/NCT01071174

Phase

Phase I/II

Status

Completed

Sponsor

International Partnership for Microbicides, Inc.

More details

This is a double-blind, randomized, placebo-controlled Phase I/II study to assess the safety of a silicone elastomer vaginal ring containing 25mg dapivirine.

Purpose

A Safety Study of Dapivirine Vaginal Ring in Africa

Interventions

Intervention 1
Dapivirine

Intervention 2
Placebo

Countries

Kenya
Malawi
South Africa
Tanzania, United Republic of

Sites / Institutions

Not provided

Trials dates

Anticipated Start Date

Not provided

Actual Start Date

2010-04-01

Anticipated Date of Last Follow-up

2011-08-01

Estimated Primary Completion Date

2010-02-19

Estimated Completion Date

2010-02-19

Actual Primary Completion Date

2011-08-02

Actual Completion Date

2011-07-01

Studied populations

Age Cohort

- Adults

Genders

- Female

Accepts pregnant individuals

No

Accepts lactating individuals

No

Accepts healthy individuals

Yes

Comments about the studied populations

Inclusion Criteria: * Women between 18 and 40 years of age inclusive who can provide informed consent * Available for all visits and consent to follow all procedures scheduled for the study * Healthy and self-reported sexually active * HIV-negative * On a stable form of contraception and willing to continue OR have undergone surgical sterilization at least 3 months prior to enrollment * In the absence of the use of exogenous hormone(s), have a self-reported regular menstrual cycle defined as having a minimum of 21 days and a maximum of 35 days between menses * Upon pelvic/speculum examination and colposcopy at the time of enrolment, the cervix and vagina appear normal as determined by the investigator * Asymptomatic for genital infections at the time of enrolment * Willing to refrain from

Health status

Not provided

Study type

Interventional (clinical trial)

Enrollment

280

Allocation

Randomized

Intervention model

Parallel Assignment

Intervention model description

Not provided

Masking

Triple-blind masking

Masking description

Not provided

Frequency of administration

Monthly

Studied LA-formulation(s)

Non-Implantable Device

Studied route(s) of administration

Topical (Vaginal)

Use case

PrEP

Key resources

Not provided

Pharmacokinetic Study of the Dapivirine Vaginal Ring in Lactating Women

Identifier

NCT02808949

Link

https://clinicaltrials.gov/study/NCT02808949

Phase

Phase I

Status

Completed

Sponsor

International Partnership for Microbicides, Inc.

More details

Phase 1 PK Study of the Dapivirine Vaginal Ring in Lactating Women.

Purpose

Pharmacokinetic Study of the Dapivirine Vaginal Ring in Lactating Women

Interventions

Intervention 1

Dapivirine

Countries

United States of America

Sites / Institutions

Not provided

Trials dates

Anticipated Start Date

Not provided

Actual Start Date

2015-02-01

Anticipated Date of Last Follow-up

2018-03-12

Estimated Primary Completion Date

2016-06-22

Estimated Completion Date

2016-06-22

Actual Primary Completion Date

2018-03-13

Actual Completion Date

2018-03-03

Studied populations

Age Cohort

- Adults

Genders

- Female

Accepts pregnant individuals

Yes

Accepts lactating individuals

No

Accepts healthy individuals

Yes

Comments about the studied populations

Inclusion Criteria: Women must meet all of the following criteria (by self-report, unless otherwise indicated) to be eligible for inclusion in the study: 1. Age 18 or older at screening as verified per site SOP 2. Per participant report, at least 6 weeks postpartum at Enrollment 3. Willing and able to provide written informed consent to be screened for and take part in the study 4. Willing and able to provide adequate locator information, as defined in site SOP 5. Willing and able to communicate in spoken and written English 6. HIV-1/2 uninfected at Screening and Enrollment, per applicable algorithm in Appendix II and willing to receive HIV test results Note: HIV-1/2 screening may be omitted at Enrollment if the time between Screening and Enrollment is \< 30 days 7. Prior to Enrollment,

Health status

Negative to : HIV

Study type

Interventional (clinical trial)

Enrollment

16

Allocation

Non-randomized

Intervention model

Single group assignment

Intervention model description

Not provided

Masking

Open label

Masking description

Not provided

Frequency of administration

Monthly

Studied LA-formulation(s)

Non-Implantable Device

Studied route(s) of administration

Topical (Vaginal)

Use case

PrEP

Key resources

Not provided

B-PROTECTED (MTN-043)

Identifier

NCT04140266

Link

https://clinicaltrials.gov/study/NCT04140266

Phase

Phase III

Status

Completed

Sponsor

National Institute of Allergy and Infectious Diseases (NIAID)

More details

The purpose of this study is to evaluate the safety and drug detection of the dapivirine monthly vaginal ring and oral Truvada in breastfeeding mother-infant pairs.

Purpose

Safety and Drug Detection Study of Dapivirine Vaginal Ring and Oral TRUVADA® in Breastfeeding Mother-Infant Pairs

Interventions

Intervention 1

Dapivirine (DPV) Monthly Vaginal Ring (VR)-004

Intervention 2

Oral TDF/FTC (Truvada tablet)

Countries

Malawi
South Africa
Uganda
Zimbabwe

Sites / Institutions

Not provided

Trials dates

Anticipated Start Date

Not provided

Actual Start Date

2020-09-24

Anticipated Date of Last Follow-up

2023-07-14

Estimated Primary Completion Date

2019-10-25

Estimated Completion Date

2019-10-25

Actual Primary Completion Date

2023-08-04

Actual Completion Date

2021-11-04

Studied populations

Age Cohort

Adults

- Older Adults

Genders

- Female
- Cisgender female

Accepts pregnant individuals

No

Accepts lactating individuals

Yes

Accepts healthy individuals

Yes

Comments about the studied populations

Inclusion Criteria: Inclusion Criteria - Mother Participant mothers must meet all the following criteria to be eligible for inclusion in the study: * Age 18 years or older at Screening, as verified per site Standard Operating Procedures (SOPs). * At Enrollment, between 6 to 12 weeks postpartum (verified by birth records and/or similar supportive documentation and defined as between 42 - 84 days after delivery, inclusive). * By participant report at Screening and Enrollment, currently exclusively breastfeeding one infant and willing and able to continue exclusively breastfeeding that infant for the duration of their participation in the study. * Note: Exclusive breastfeeding will be defined as infant nutrition solely from breast milk, as determined by 7-day recall breastfeeding histor

Health status

Negative to : HIV

Study type

Interventional (clinical trial)

Enrollment

394

Allocation

Randomized

Intervention model

Parallel Assignment

Intervention model description

Not provided

Masking

Open label

Masking description

Not provided

Frequency of administration

Monthly

Studied LA-formulation(s)

Non-Implantable Device

Studied route(s) of administration

Oral
Topical (Vaginal)

Use case

PrEP

Key resources

Not provided

DELIVER (MTN-042)

Identifier

NCT03965923

Link

https://clinicaltrials.gov/study/NCT03965923

Phase

Phase III

Status

Active, not recruiting

Sponsor

National Institute of Allergy and Infectious Diseases (NIAID)

More details

The purpose of this study is to evaluate the maternal and infant safety of the dapivirine (DPV) monthly vaginal ring (VR) and daily oral Truvada in HIV-uninfected pregnant women and their infants.

Purpose

Randomized, Open Label Safety Trial of Dapivirine Vaginal Ring and Oral TRUVADA® Use in Pregnancy

Interventions

Intervention 1

Dapivirine (DPV) Monthly Vaginal Ring (VR)

Intervention 2

oral TDF/FTC (Truvada Tablet)

Countries

Malawi
South Africa
Uganda
Zimbabwe

Sites / Institutions

Not provided

Trials dates

Anticipated Start Date

Not provided

Actual Start Date

2020-01-09

Anticipated Date of Last Follow-up

2023-02-01

Estimated Primary Completion Date

2019-05-29

Estimated Completion Date

2019-05-29

Actual Primary Completion Date

2023-02-02

Actual Completion Date

2024-06-30

Studied populations

Age Cohort

- Adults

Genders

- Female
- Cisgender female

Accepts pregnant individuals

Yes

Accepts lactating individuals

No

Accepts healthy individuals

Yes

Comments about the studied populations

Inclusion Criteria: * Age 18 through 40 years (inclusive) at Enrollment, verified per site standard operating procedures (SOPs). * At Enrollment, evidence of a viable, intrauterine, singleton pregnancy with sonographic confirmation, including for gestational age assessment. * Note: If adequate (per judgment of Investigator of Record \[IoR\]/designee) sonographic results are not available from medical records at Screening, an ultrasound must be performed and results be available for review at Enrollment for all Cohorts. The ultrasound should be performed no later than the 36th week of gestation for Cohort 1 or the 28th week of gestation for Cohort 2. * At Enrollment, pregnancy within gestational age limits of the currently enrolling cohort (per the study protocol). * HIV-uninfected base

Health status

Negative to : HIV

Study type

Interventional (clinical trial)

Enrollment

859

Allocation

Randomized

Intervention model

Sequential assignment

Intervention model description

Not provided

Masking

Open label

Masking description

Not provided

Frequency of administration

Monthly

Studied LA-formulation(s)

Non-Implantable Device

Studied route(s) of administration

Topical (Vaginal)

Use case

PrEP

Key resources

Not provided

HOPE (MTN-025)

Identifier

NCT02858037

Link

https://clinicaltrials.gov/study/NCT02858037

Phase

Phase III

Status

Completed

Sponsor

International Partnership for Microbicides, Inc.

More details

HIV Open-label Prevention Extension (HOPE) to Assess the Continued Safety of and Adherence to a Monthly Vaginal Ring Containing Dapivirine in Women

Purpose

Trial to Assess the Continued Safety of and Adherence to a Vaginal Ring Containing Dapivirine in Women

Interventions

Intervention 1

Dapivirine Vaginal Ring

Countries

Malawi

South Africa

Uganda

Zimbabwe

Sites / Institutions

Not provided

Trials dates

Anticipated Start Date

Not provided

Actual Start Date

2016-07-18

Anticipated Date of Last Follow-up

2022-10-24

Estimated Primary Completion Date

2016-08-08

Estimated Completion Date

2016-08-08

Actual Primary Completion Date

2022-10-25

Actual Completion Date

2018-10-10

Studied populations

Age Cohort

- Adults

Genders

Female

- Cisgender female

Accepts pregnant individuals

No

Accepts lactating individuals

No

Accepts healthy individuals

Yes

Comments about the studied populations

Inclusion Criteria: Women must meet all of the following criteria to be eligible for inclusion in the study 1. Previously enrolled in MTN-020 (ASPIRE) 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 4. HIV-uninfected based on testing performed by study staff at Screening and Enrollment 5. Using an effective method of contraception at Enrollment, and intending to use an effective method for the duration of study participation; effective methods include hormonal methods (except contraceptive ring); intrauterine contraceptive device (IUCD); and sterilization (of participant, as defined in site SOPs) 6. At Screening and Enrollment, agrees not to partic

Health status

Negative to : HIV
Other health status: Previously enrolled in ASPIRE (MTN-020) trial

Study type

Interventional (clinical trial)

Enrollment

1456

Allocation

Non-randomized

Intervention model

Single group assignment

Intervention model description

Participants will receive a silicone elastomer vaginal matrix ring containing 25 mg of dapivirine to be replaced each month for a total period of 12 months of use.

Masking

Open label

Masking description

Not provided

Frequency of administration

Monthly

Studied LA-formulation(s)

Non-Implantable Device

Studied route(s) of administration

Topical (Vaginal)

Use case

PrEP

Key resources

Not provided

Ring Study (IPM 027)

Identifier

NCT01539226

Link

https://clinicaltrials.gov/study/NCT01539226

Phase

Phase III

Status

Completed

Sponsor

International Partnership for Microbicides, Inc.

More details

The Ring study was a Phase 3, double-blind, randomised, placebo-controlled study to assess the safety and efficacy of a silicone elastomer monthly vaginal matrix ring.

Purpose

Safety and Efficacy Trial of a Dapivirine Vaginal Matrix Ring in Healthy HIV-Negative Women

Interventions

Intervention 1

Placebo Vaginal Ring

Intervention 2

Dapivirine Monthly Vaginal Ring, 25 mg

Countries

South Africa

Uganda

Sites / Institutions

Not provided

Trials dates

Anticipated Start Date

Not provided

Actual Start Date

2012-03-27

Anticipated Date of Last Follow-up

2022-09-26

Estimated Primary Completion Date

2012-02-27

Estimated Completion Date

2012-02-27

Actual Primary Completion Date

2022-10-19

Actual Completion Date

2016-12-13

Studied populations

Age Cohort

- Adults

Genders

- Female

Accepts pregnant individuals

No

Accepts lactating individuals

No

Accepts healthy individuals

Yes

Comments about the studied populations

Inclusion Criteria: * Women \> 18 and \< 45 years of age, at screening, who can provide informed consent; * Available for all visits and consent to follow all procedures scheduled for the trial; * Self-reported sexually active (defined as an average of at least one penetrative penile-vaginal coital act per month for the last 3 months prior to screening); * HIV-negative as determined by the HIV algorithm applied at screening and enrolment; * On a stable form of contraception as defined within section 5.4 and willing to continue on stable contraception for the duration of the clinical trial, unless post-menopausal or surgically sterilised; * Asymptomatic for genital infections at the time of enrolment (if a woman is diagnosed with any clinically significant curable STI, she must have initia

Health status

Negative to : HIV

Study type

Interventional (clinical trial)

Enrollment

1959

Allocation

Randomized

Intervention model

Parallel Assignment

Intervention model description

Not provided

Masking

Double-blind masking

Masking description

Not provided

Frequency of administration

Monthly

Studied LA-formulation(s)

Non-Implantable Device

Studied route(s) of administration

Topical (Vaginal)

Use case

PrEP

Key resources

Not provided

DREAM (IPM 032)

Identifier

NCT02862171

Link

https://clinicaltrials.gov/study/NCT02862171

Phase

Phase III

Status

Completed

Sponsor

International Partnership for Microbicides, Inc.

More details

A follow-on, open label trial to assess continued safety of and adherence to the Dapivirine(25mg) vaginal ring-004 in healthy, HIV-negative women

Purpose

To Assess Continued Safety of and Adherence to the Dapivirine (25 mg) Vaginal Ring-004 in Healthy, HIV-negative Women

Interventions

Intervention 1

Dapivirine Vaginal Ring-004

Countries

South Africa

Uganda

Sites / Institutions

Not provided

Trials dates

Anticipated Start Date

Not provided

Actual Start Date

2016-07-12

Anticipated Date of Last Follow-up

2022-10-24

Estimated Primary Completion Date

2016-08-10

Estimated Completion Date

2016-08-10

Actual Primary Completion Date

2022-10-25

Actual Completion Date

2019-01-11

Studied populations

Age Cohort

- Adults

Genders

- Female

Cisgender female

Accepts pregnant individuals

No

Accepts lactating individuals

No

Accepts healthy individuals

Yes

Comments about the studied populations

Inclusion Criteria: Women must meet all the following criteria to be eligible to enrol in the trial: 1. Previously enrolled in the IPM 027 trial 2. Available for all visits and consent to follow all procedures scheduled for the trial 3. Using an effective method of contraception at the Enrolment Visit, and intending to use an effective contraceptive method for the duration of trial participation, unless post-menopausal with no history of menses for one year prior to screening 4. HIV-negative as determined by the HIV algorithm applied at Screening/Pre- Enrolment 5. Willing to refrain from participation in another research trial using drugs, vaccines, medical devices and microbicides for the duration of the IPM 032 trial 6. Willing to provide adequate locator information for trial retentio

Health status

Negative to : HIV
Other health status: Previously enrolled in the IPM 027 trial

Study type

Interventional (clinical trial)

Enrollment

941

Allocation

Non-randomized

Intervention model

Single group assignment

Intervention model description

Not provided

Masking

Open label

Masking description

Not provided

Frequency of administration

Monthly

Studied LA-formulation(s)

Non-Implantable Device

Studied route(s) of administration

Topical (Vaginal)

Use case

PrEP

Key resources

Not provided

Excipients

Proprietary excipients used

silicone elastomer for extended use

Novel excipients or existing excipients at a concentration above Inactive Ingredients Database (IID) for the specified route of administration

excipient has been included in regulatory dossier for product

Residual solvents used

No residual solvent used

Additional features

Other features of the technology

- Drug-eluting
- Removable
- Molded
- Room temperature storage
- At least 1 year shelf life

Release properties

Releases dapivirine over a one-month period

Injectability

Not Applicable

Safety

There were no safety concerns with long-term use of the ring in Phase III clinical studies. Data from two open-label (Phase IIIB) studies show a similar favorable safety profile as do 12 smaller safety studies.

Stability

ICH Climate Zone IV (A/B)

Storage conditions and cold-chain related features

5 years shelf life This product does not require specific temperature storage conditions. Store in the original package to protect from light.

Potential application(s)

Therapeutic area(s)

HIV

Use case(s)

Pre-Exposure Prophylaxis (PrEP)

Use of technology

Ease of administration

- Administered by a community health worker
- Administered by a nurse
- Administered by a specialty health worker
- Self-administered

Frequency of administration

Monthly

User acceptance

Phase III and open label extension studies indicate a high user acceptance

Targeted user groups

Age Cohort

- Adolescents
- Adults

Genders

- Female

Pregnant individuals

Yes

Lactating individuals

Yes

Healthy individuals

Yes

Comment

Women at substantial risk of contracting HIV through receptive vaginal sex

Potential associated API(s)

Dapivirine (DPV)

Class(es)

microbicide

Development stage

Marketed

Clinical trial number(s)

Not provided

Foreseen/approved indication(s)

Prevention of HIV infection through vaginal sex

Foreseen user group

women older than 18 at substantial risk of contracting HIV through vaginal sex

Foreseen duration between application(s)

1 month

Applications to Stringent Regulatory Authorities (SRA) / regulatory approvals

Positive scientific opinion from the European Medicines Agency for use among women ages 18 and older in developing countries. in WHO guidelines

Patent info

Technology patent families

Not patent applicable for this technology

Dapivirine 25 mg (vaginal ring)

Patent informations

Patent description	Representative patent	Categories	Patent holder	Licence with MPP	Patent source
Dapivirine compounds and analogues (Markush structure) Expiry date: 2019-03-24 The invention is concerned with pyrimidine derivatives having HIV replication inhibiting properties. The invention further relates to methods for their preparation and pharmaceutical compositions comprising them. The invention also relates to the use of said compounds in the manufacture of a medicament useful for the treatment of subjects suffering from HIV (Human Immunodeficiency Virus) infection	WO9950250	Compound	JANSSEN PHARMACEUTICA NV	No	MPP Search

Patent status

Patent status/countries	Low, Low- middle and upper-middle	High income

Granted		United States of America
Filed		Hungary
Not in force	North Macedonia, Albania, Botswana, Gambia (the), Ghana, Kenya, Lesotho, Malawi, Sierra Leone, Sudan, Eswatini, Uganda, Zambia, Zimbabwe, Argentina, Brazil, China, Turkmenistan, Belarus, Tajikistan, Kazakhstan, Azerbaijan, Kyrgyzstan, Armenia, Moldova, Republic of, Indonesia, Benin, Cameroon, Burkina Faso, Chad, Guinea-Bissau, Mali, Senegal, Congo, Guinea, Gabon, Niger, Mauritania, Togo, Côte d'Ivoire, Central African Republic, Türkiye, Ukraine, South Africa, Mexico, Viet Nam, Philippines, World Intellectual Property Organization (WIPO), Malaysia	Belgium, Germany, France, Luxembourg, Netherlands, Switzerland, United Kingdom, Sweden, Italy, Austria, Liechtenstein, Greece, Spain, Denmark, Monaco, Portugal, Ireland, Finland, Cyprus, Romania, Latvia, Lithuania, Slovenia, Australia, Bulgaria, Canada, Czechia, Russian Federation, Estonia, Hong Kong, Croatia, Hungary, Israel, Japan, Korea, Republic of, Norway, New Zealand, Poland, Slovakia, Taiwan, Province of China, United States of America, Singapore, World Intellectual Property Organization (WIPO)

Patent informations

Patent description	Representative patent	Categories	Patent holder	Licence with MPP	Patent source
Dapivirine and analogues topical use for the prevention of HIV infection Expiry date: 2023-05-13 The invention concerns the microbicidal activity of certain pyrimidine or triazine containing non-nucleoside reverse transcriptase inhibitors. The compounds of the present invention inhibit the systemic infection of a human being with HIV, in particular, the present compounds prevent sexual HIV transmission in humans.	WO03094920	Composition,Use	TIBOTEC PHARM LTD	No	MPP Search

Patent status

Patent status/countries	Low, Low- middle and upper-middle	High income
Granted		Belgium, Germany, France, Luxembourg, Netherlands, Switzerland, Sweden, Italy, Liechtenstein, Greece, Denmark, Finland, Estonia, Hungary, Latvia, Israel, Korea, Republic of, Poland, United States of America, Singapore
Filed		Cyprus

Patent status/countries	Low, Low- middle and upper-middle	High income
Not in force	Türkiye, North Macedonia, Albania, Botswana, Gambia (the), Ghana, Kenya, Lesotho, Malawi, Mozambique, Sierra Leone, Sudan, Eswatini, Tanzania, United Republic of, Uganda, Zambia, Zimbabwe, Argentina, Brazil, China, Turkmenistan, Belarus, Tajikistan, Kazakhstan, Azerbaijan, Kyrgyzstan, Armenia, Moldova, Republic of, Mexico, South Africa, India, Indonesia, Philippines, Thailand, Viet Nam, Benin, Cameroon, Burkina Faso, Chad, Guinea-Bissau, Mali, Senegal, Congo, Guinea, Gabon, Niger, Equatorial Guinea, Mauritania, Togo, Côte d'Ivoire, Central African Republic, World Intellectual Property Organization (WIPO)	Germany, United Kingdom, Austria, Spain, Monaco, Portugal, Ireland, Bulgaria, Czechia, Slovakia, Romania, Lithuania, Slovenia, Australia, Canada, Russian Federation, Hong Kong, Croatia, Japan, Norway, New Zealand, United States of America, World Intellectual Property Organization (WIPO)

Supporting material

Publications

**Evaluating the potential impact and cost-effectiveness of dapivirine vaginal ring pre-exposure prophylaxis for HIV prevention.
 Reidy M, Gardiner E, Pretorius C, Glaubius R, Torjesen K, Kripke K. PLoS One. 2019;14(6):e0218710. Published 2019 Jun 26. doi:10.1371/journal.pone.0218710
 **

Background

Expanded HIV prevention options are needed to increase uptake of HIV prevention among women, especially in generalized epidemics. As the dapivirine vaginal ring moves forward through regulatory review and open-label extension studies, the potential public health impact and cost-effectiveness of this new prevention method are not fully known. We used mathematical modeling to explore the impact and cost-effectiveness of the ring in different implementation scenarios alongside scale-up of other HIV prevention interventions. Given the knowledge gaps about key factors influencing the ring's implementation, including potential uptake and delivery costs, we engaged in a stakeholder consultation process to elicit plausible parameter ranges and explored scenarios to identify the possible range of impact, cost, and cost-effectiveness.

Methods and findings

We used the Goals model to simulate scenarios of oral and ring pre-exposure prophylaxis (PrEP) implementation among female sex workers and among other women ≤21 years or >21 years with multiple male partners, in Kenya, South Africa, Uganda, and Zimbabwe. In these scenarios, we varied antiretroviral therapy (ART) coverage, dapivirine ring coverage and ring effectiveness (encompassing efficacy and adherence) by risk group. Following discussions with stakeholders, the maximum level of PrEP coverage (oral and/or ring) considered in each country was equal to modern contraception use minus condom use in the two age groups.

We assessed results for 18 years, from 2018 to 2035. In South Africa, for example, the HIV infections averted by PrEP (ring plus oral PrEP) ranged from 310,000 under the highest-impact scenario (including ART held constant at 2017 levels, high ring coverage, and 85% ring effectiveness) to 55,000 under the lowest-impact scenario (including ART reaching the UNAIDS 90-90-90 targets by 2020, low ring coverage, and 30% ring effectiveness). This represented a range of 6.4% to 2.2% of new HIV infections averted. Given our assumptions, the addition of the ring results in 11% to 132% more impact than oral PrEP alone. The cost per HIV infection averted for the ring ranged from US$13,000 to US$121,000.

Conclusions

This analysis offers a wide range of scenarios given the considerable uncertainty over ring uptake, consistency of use, and effectiveness, as well as HIV testing, prevention, and treatment use over the next two decades. This could help inform donors and implementers as they decide where to allocate resources in order to maximize the impact of the dapivirine ring in light of funding and implementation constraints. Better understanding of the cost and potential uptake of the intervention would improve our ability to estimate its cost-effectiveness and assess where it can have the most impact.

Safety , adherence , and HIV-1 seroconversion among women using the dapivirine vaginal ring (DREAM): an open-label , extension study.
 Nel A, Niekerk N Van, Baelen B Van, et al. Lancet HIV. 2021;8:77-86. doi:10.1016/S2352-3018(20)30300-3

Background

The Ring Study, a phase 3 trial in 1959 sexually active women (randomised 2:1), showed a favourable safety profile and a 31% HIV-1 infection risk reduction for a vaginal ring containing 25 mg of dapivirine, compared with a placebo ring. We report

here the DREAM study, which aimed to evaluate safety, adherence, and HIV-1 incidence in those using the dapivirine vaginal ring (DVR) in open-label use.

Methods

The DREAM study is an open-label extension of The Ring Study, done at five research centres in South Africa and one research centre in Uganda. Former participants from The Ring Study, who remained HIV-negative and who did not discontinue the study due to an adverse event or safety concern that was considered to be related to the investigational product, were eligible. Women who were pregnant, planning to become pregnant, or breastfeeding at screening for DREAM were excluded. All participants received the DVR for insertion at the enrolment visit. Participants attended a 1-month follow-up visit and could either proceed with visits once every 3 months or attend monthly visits up to month 3 and then continue with visits once every 3 months. At each visit, HIV testing and safety evaluations were done, and residual dapivirine measured in used rings (approximately 4 mg is released from the DVR over 28 days of consistent use). HIV-1 incidence was compared descriptively with the simulated incidence rate obtained from bootstrap sampling of participants in the placebo group of The Ring Study, matched for research centre, age, and presence of sexually transmitted infections at enrolment. This study is registered with ClinicalTrials.gov, NCT02862171.

Findings

Between July 12, 2016, and Jan 11, 2019, 1034 former participants from The Ring Study were screened, 941 were enrolled and 848 completed the trial. 616 (65·5%) of 941 participants reported treatment-emergent adverse events. Of these, six (0·6%) had events considered to be treatment-related. No treatment-related serious adverse events were reported. Measurements of monthly ring residual amounts in participants enrolled in both trials showed consistently lower mean values in DREAM than in The Ring Study. Arithmetic mean ring residual amounts of participants in The Ring Study DVR group who enrolled in DREAM were 0·25 mg lower (95% CI 0·03–0·47; p=0·027) than the mean ring residual amounts of these participants in The Ring Study. 18 (1·9%) HIV-1 infections were confirmed during DVR use, resulting in an incidence of 1·8 (95% CI 1·1–2·6) per 100 person-years, 62% lower than the simulated placebo rate.

Interpretation

Although efficacy estimation is limited by the absence of a placebo group, the observed low HIV-1 incidence and improved adherence observed in DREAM support the hypothesis that increased efficacy due to improved adherence occurs when women know the demonstrated safety and efficacy of the DVR. The feasibility of a visit schedule of once every 3 months was shown, indicating that the DVR can be used in a real-world situation in usual clinical practice.

Additional documents

- Ring resources
- IPM Ring Backgrounder

Useful links

- Presentation of dapivirine monthly ring
- MTN-034 (REACH) Phase 2a
- MTN-042 (Deliver) Phase 3b
- MTN-043 (B-Protected) Phase 3b
- Experiences with simultaneous use of contraception and the vaginal ring for HIV prevention in sub-Saharan Africa
- Patterns of Adherence to a Dapivirine Vaginal Ring for HIV-1 Prevention Among South African Women in a Phase III Randomized Controlled Trial
- Acceptability of the Dapivirine Vaginal Ring for HIV-1 Prevention and Association with Adherence in a Phase III Trial
- Clinical and Virologic Outcomes Following Initiation of Antiretroviral Therapy Among Seroconverters in the Microbicide Trials Network-020 Phase III Trial of the Dapivirine Vaginal Ring
- Vaginal Ring Use in a Phase 3 Microbicide Trial: A Comparison of Objective Measures and Self-reports of Non-adherence in ASPIRE

Access principles

Collaborate for development

Consider on a case by case basis, collaborating on developing long acting products with potential significant public health impact, especially for low- and middle-income countries (LMICs), utilising the referred to long-acting technology

Not provided

Share technical information for match-making assessment

Provide necessary technical information to a potential partner, under confidentiality agreement, to enable preliminary assessment of whether specific medicines of public health importance in LMICs might be compatible with the referred to long-acting technology to achieve a public health benefit

Not provided

Work with MPP to expand access in LMICs

In the event that a product using the referred to long-acting technology is successfully developed, the technology IP holder(s) will work with the Medicines Patent Pool towards putting in place the most appropriate strategy for timely and affordable access in low and middle-income countries, including through licensing

Not provided

Comment & Information

Illustrations

Dapivirine Vaginal Ring (DapiRing) - (1)

Dapivirine Vaginal Ring (DapiRing) - (2)