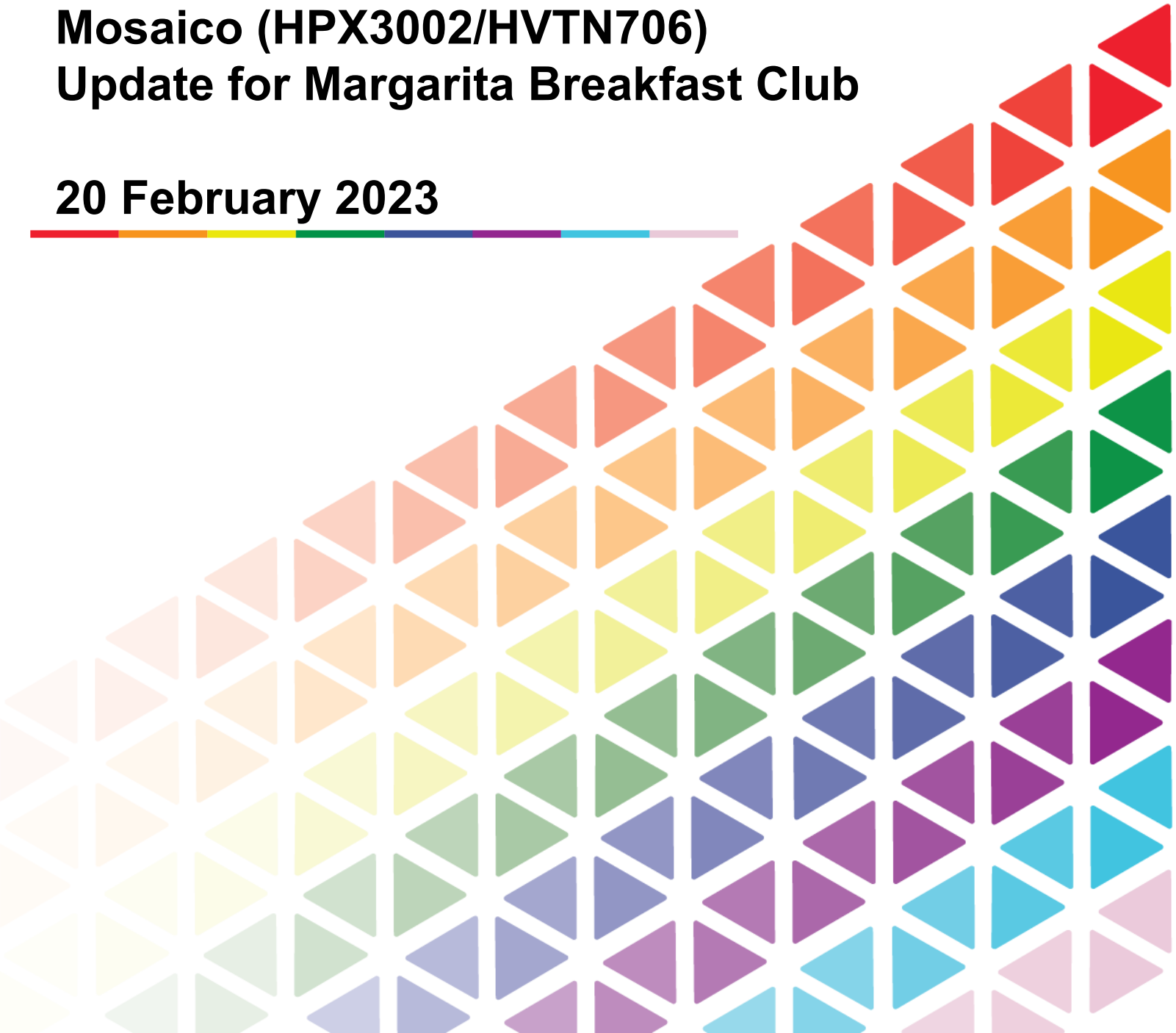
Mosaico (HPX3002/HVTN706)
Update for Margarita Breakfast Club

20 February 2023

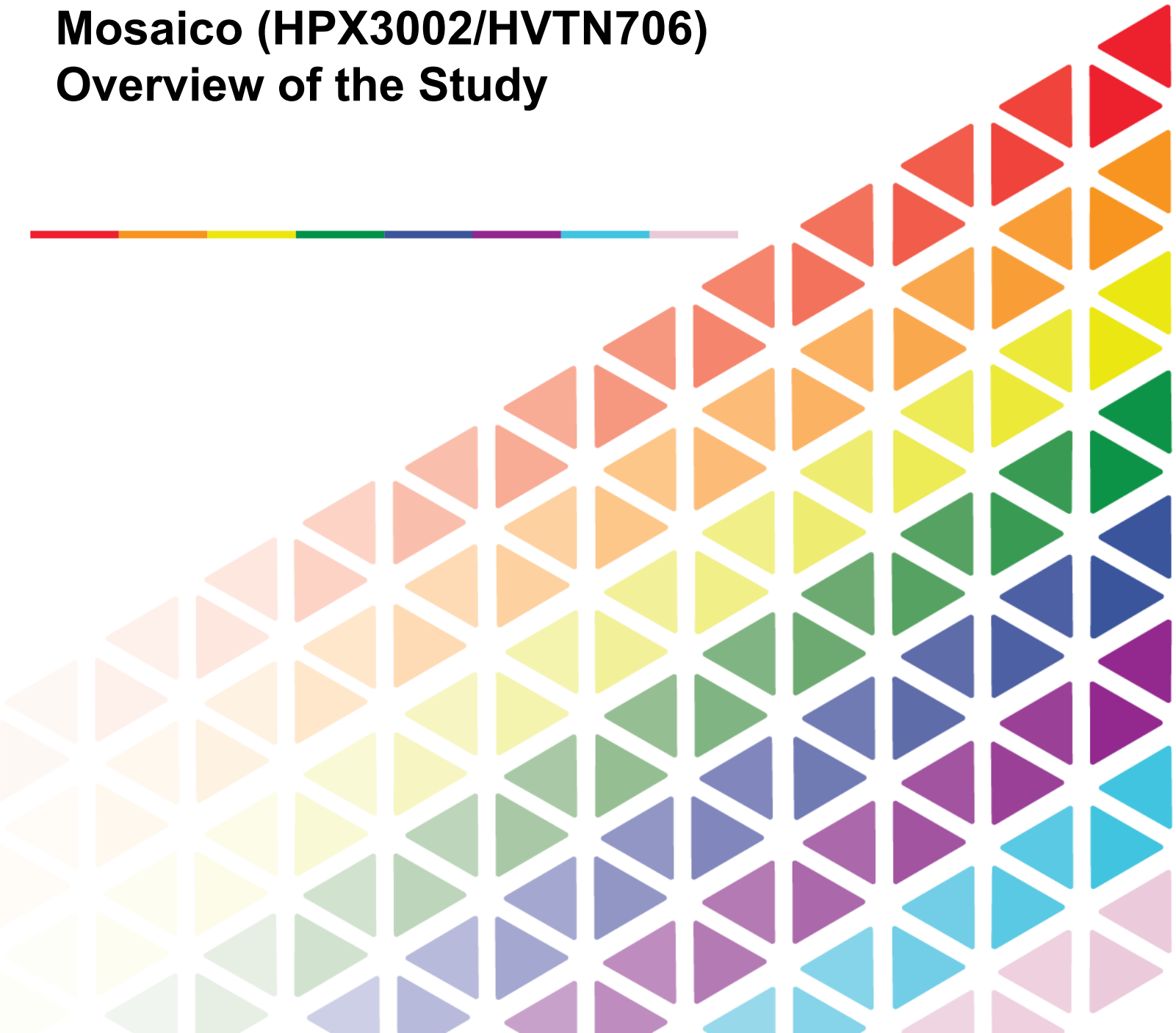


HPX3002 / HVTN 706

Outline

- Overview of the study
- PrEP considerations
- Study outcomes

Mosaico (HPX3002/HVTN706)
Overview of the Study

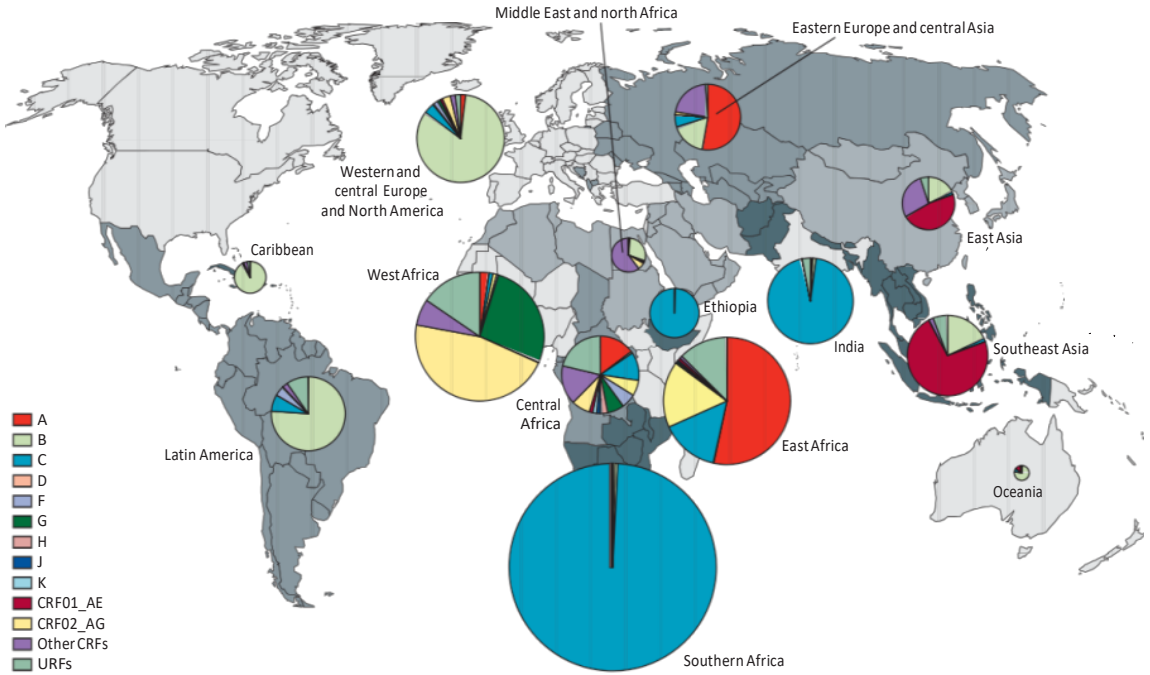


HPX3002 / HVTN 706

Goal: develop a prophylactic HIV vaccine that could protect against the globally relevant strains of HIV-1

Mosaic design

For coverage of globally circulating HIV strains



Heterologous vaccine regimen using **Ad26** vectors expressing **mosaic** Gag, Pol and Env antigens, and soluble trimeric **gp140** envelope proteins :

Ad26.Mos4.HIV

For the induction of potent cellular and humoral HIV-specific immunity

Trimeric envelope proteins

For the enhancement of HIV-specific immunity

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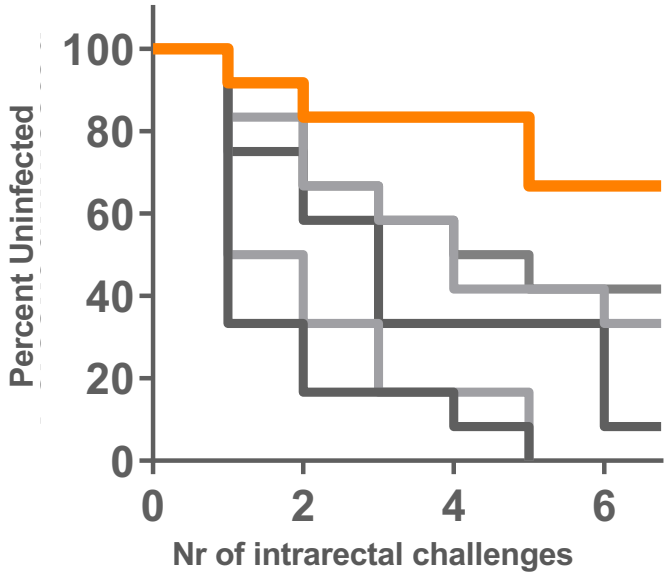
Janssen Infectious Diseases & Vaccines
PHARMACEUTICAL COMPANIES OF Johnson & Johnson

Ad26/Ad26+gp140 vaccine regimen selected based on: superior efficacy in Non-Human Primates (study 13-19)



Regimen wk 0, 12	wk 24, 48	Risk reduction *Per exposure*	Full protection *6 challenges*
Ad26	Ad26+gp140	94%	67%
Ad26	MVA+gp140	87%	42%
Ad26	gp140	84%	33%
Ad26	MVA	71%	8%
Ad26	Ad26	35%	0%
Sham		0%	0%

- HIV Env binding **antibodies** together with Env specific **T cells** correlated with protection
- **Functional antibodies** as assessed by **ADCP** were found to correlate with protection

Barouch, Tomaka, Wegmann, et al., The Lancet, 2018

Janssen Infectious Diseases & Vaccines
PHARMACEUTICAL COMPANIES OF Johnson & Johnson

Final vaccine regimen for Mosaico Phase 3 study
4 vaccinations over a year

Vaccinations at month 0 and 3

Ad26.Mos4.HIV

Ad26 vectors with Mosaic *gag-pol* or *env* inserts

- Ad26.Mos1.Gag-Pol
- Ad26.Mos2.Gag-Pol
- Ad26.Mos1.Env
- Ad26.Mos2S.Env

Vaccinations at month 6 and 12

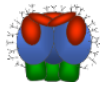
Ad26.Mos4.HIV

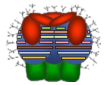
Ad26 vectors with Mosaic *gag-pol* or *env* inserts

- Ad26.Mos1.Gag-Pol
- Ad26.Mos2.Gag-Pol
- Ad26.Mos1.Env
- Ad26.Mos2S.Env

Gp140 Clade + Mosaic

Soluble gp140 env proteins with Aluminum Phosphate


Clade C


Mosaic

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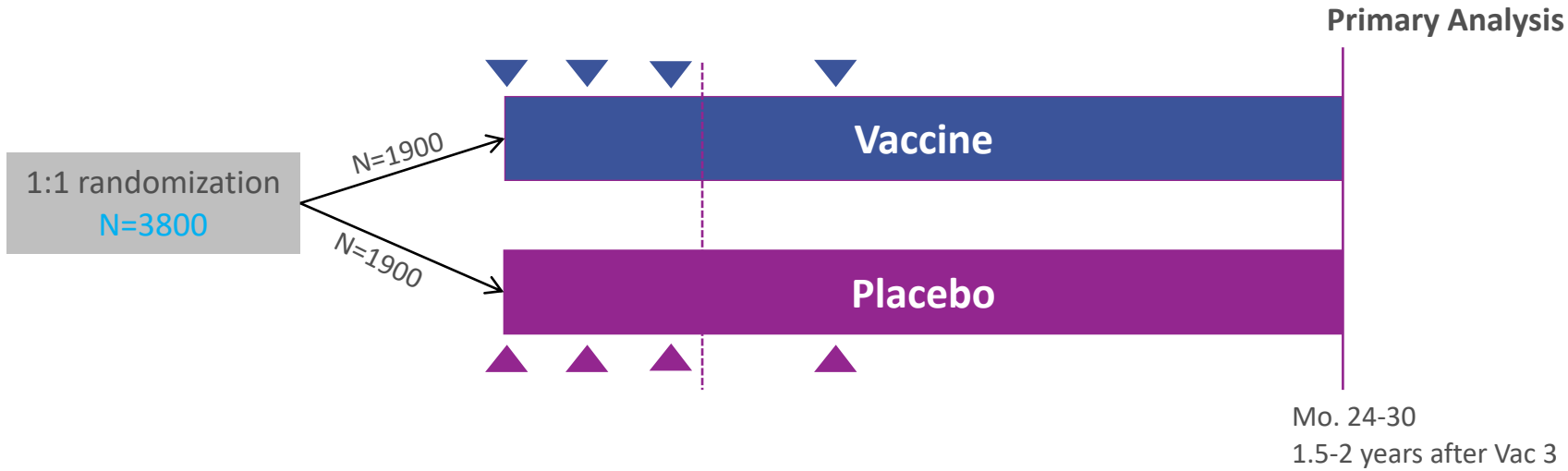
Overview Phase 3 Mosaico Study

- 3,800 participants; randomized in a 1:1 ratio to the study vaccine or placebo (randomization stratified by site)



Follow-up:
- At least 24 months after the 3rd vaccination in participants who remain HIV-1 negative
- 6 months after diagnosis of HIV-1 infection in participants who become HIV-1 infected

N	Month 0	Month 3	Month 6	Month 12
1900	Ad26.Mos4.HIV#	Ad26.Mos4.HIV#	Ad26.Mos4.HIV# + Mosaic & Clade C gp140*	Ad26.Mos4.HIV# + Mosaic & Clade C gp140*
1900	Placebo	Placebo	Placebo + Placebo	Placebo + Placebo

Ad26.Mos4.HIV=$5x10^{10}$ vp *Clade C + Mosaic gp140= 125 + 125 micrograms of glycoprotein

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Global Site Distribution

Americas

Europe

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Study progress

- The study started in November 2019
- Recruitment was paused from 17 March 2020 until 1 June 2020 due to the COVID-19 pandemic
  - At start of pause, 29 participants were enrolled
- Enrollment was completed in September 2021
- Last participant completing the vaccine regimen occurred in October 2022

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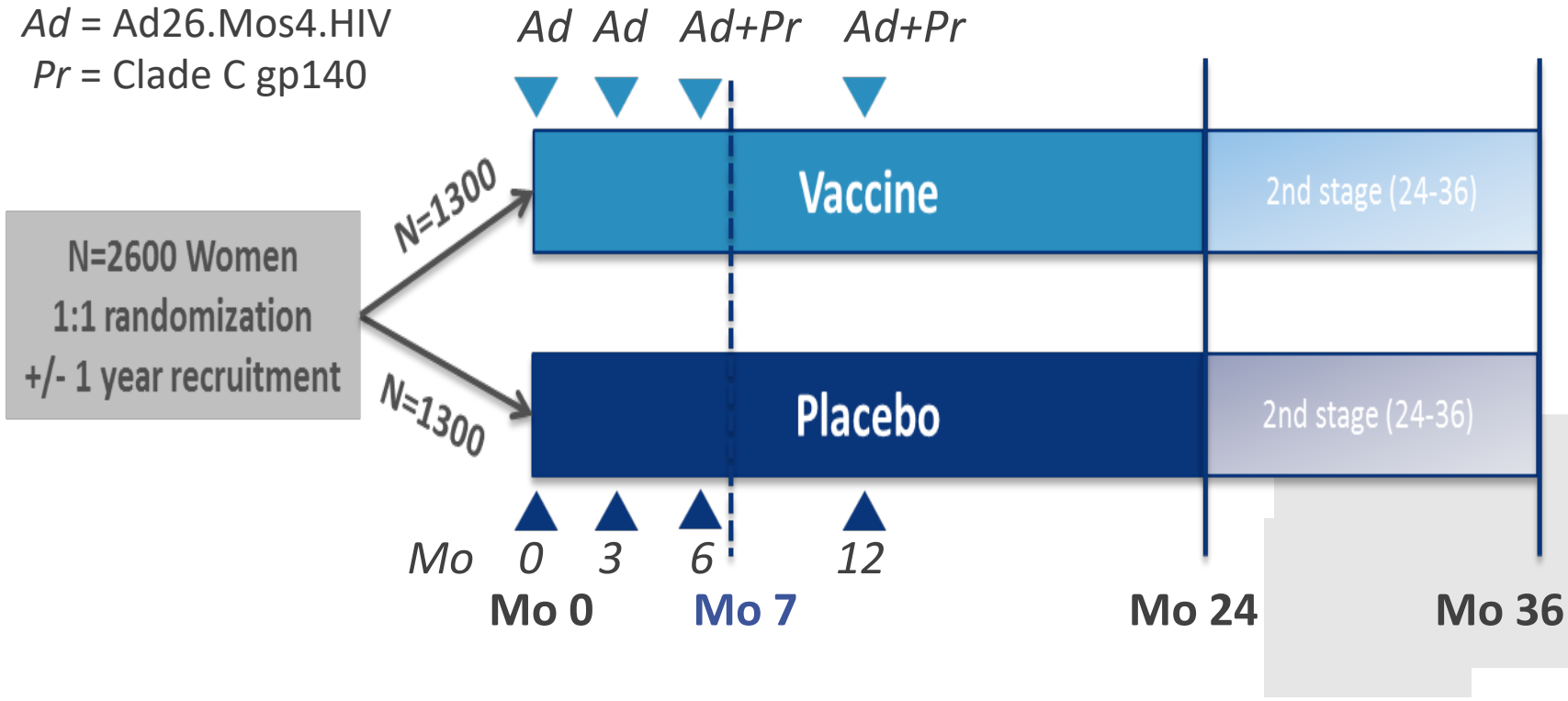
Reminder

Phase 2b Imbokodo Trial (HVTN705/HPX2008)

- **Study population**: HIV-uninfected women in southern Africa aged 18-35 years at risk for HIV infection
- **Primary objectives**: (1) to assess vaccine efficacy (VE) to prevent HIV-1 infection between months 7 and 24, and (2) to evaluate vaccine safety and tolerability.



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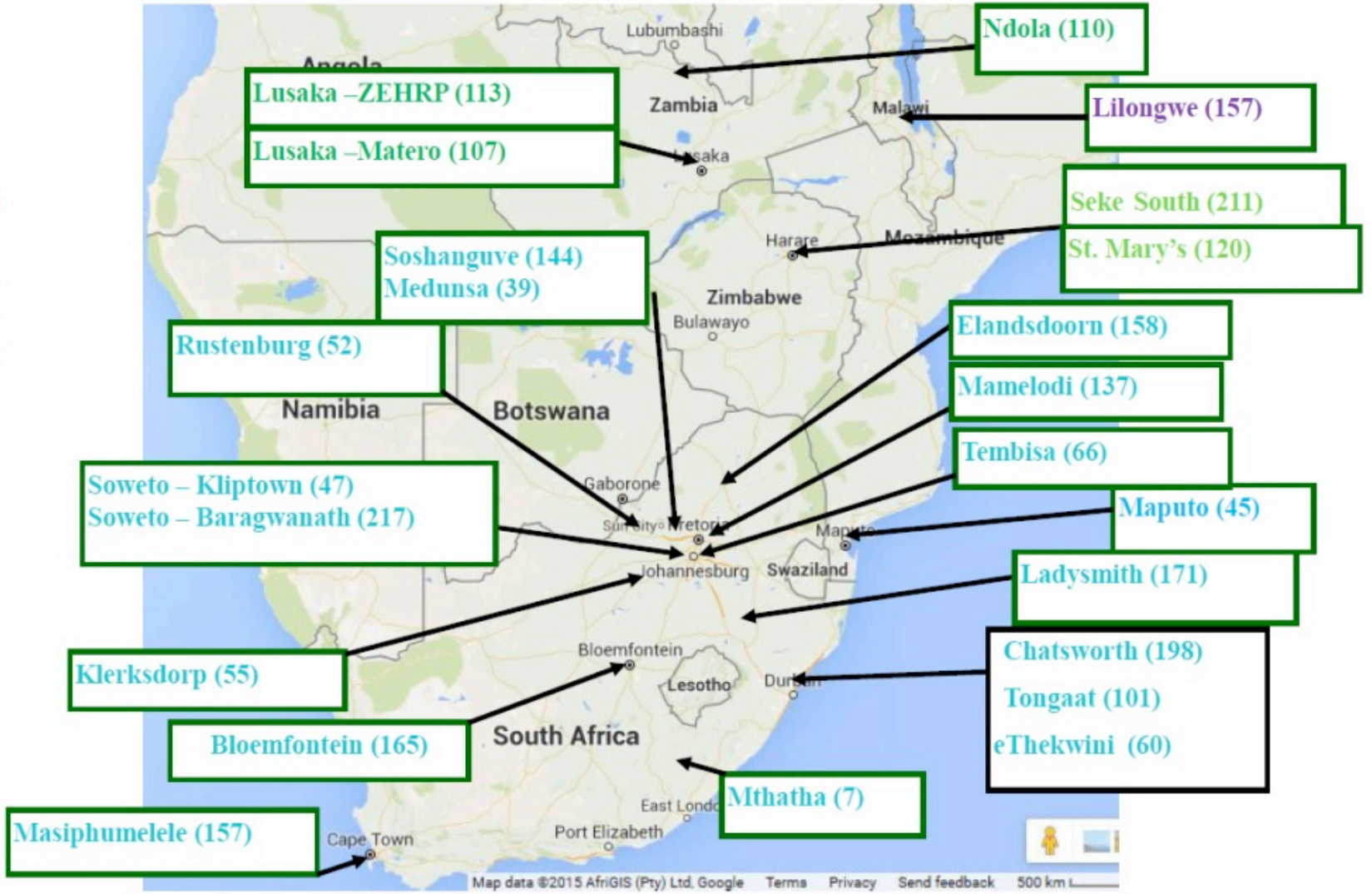
Reminder

Imbokodo study sites

- **Enrollment**: 2,637 women enrolled in 23 sites across 5 countries
- **Time period:** 2017 to 2021



HIV VACCINE TRIALS NETWORK

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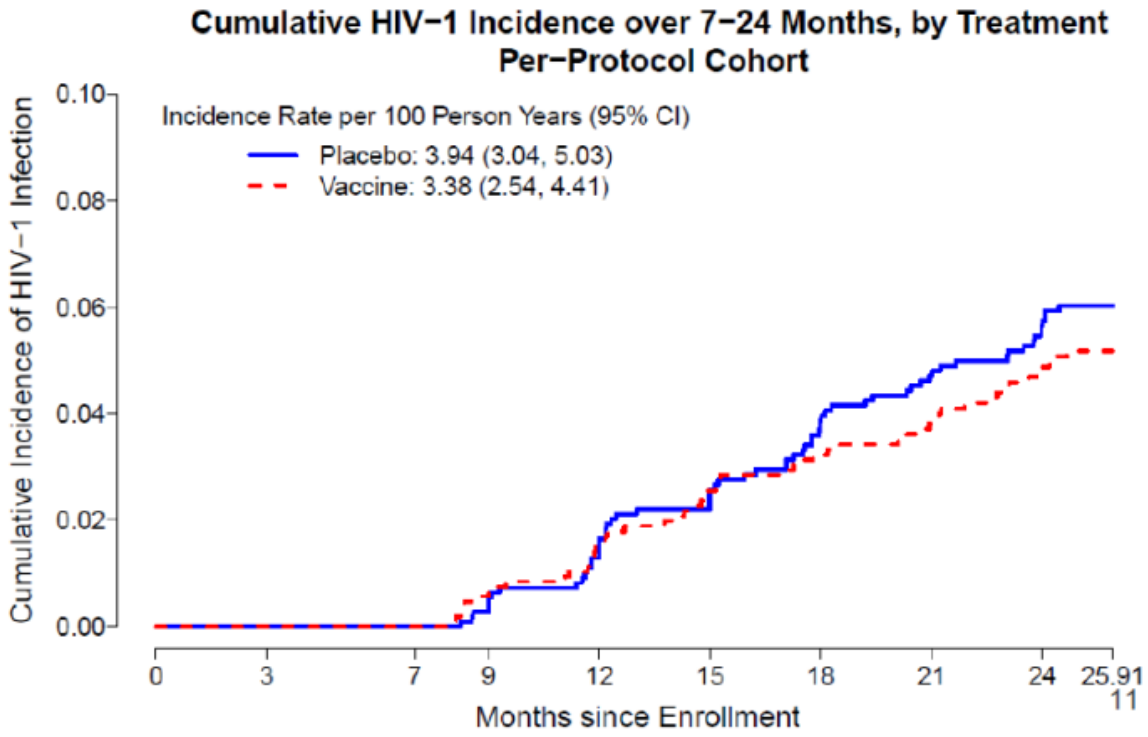
Reminder

Imbokodo: Low VE not significantly different from zero

	Endpoints M7 to M24	Incidence rate per 100 PYRs M7 to M24 (95% CI)
Placebo	65	3.94 (3.04, 5.03)
Vaccine	54	3.38 (2.54, 4.41)

VE (mo. 7 to 24):

14% (95% CI: -22%, 40%), P=0.40



HIV VACCINE TRIALS NETWORK

Key differences

	Phase 2b	Phase 3
Vaccine regimen/composition	Tetravalent Ad26.Mos4.HIV **+ Clade C gp140**	Tetravalent Ad26.Mos4.HIV **+ bivalent gp140 (Clade C + Mosaic)**
Countries	**Southern Africa** (South Africa, Zimbabwe, Zambia, Malawi, Mozambique)	**Americas and Europe** (USA, Mexico, Peru, Brazil, Argentina, Spain, Italy, Poland)
Population	**Women (18–35 years)**	**MSM + TGI* (18–60 years)**
HIV subtype	**Clade C**	**Mainly clade B**
Other prevention	**Observed** limited PrEP use	**Expected** increased PrEP use *(note: limited used to date)*
Incidence	+/- 4%	Dependent on PrEP use (**2%?**)
Transmission	**Intravaginal** (mainly)	**Intrarectal** (mainly)

IMBOKODO HPX2008/HVTN705: NCT03060629

MOSAICO HPX3002/HVTN706: NCT03964415

Data on file

*MSM: Men who have sex with men; TGI: Transgender individuals

Note: NHP model based on intrarectal challenges; challenge virus with HIV Clade B envelope

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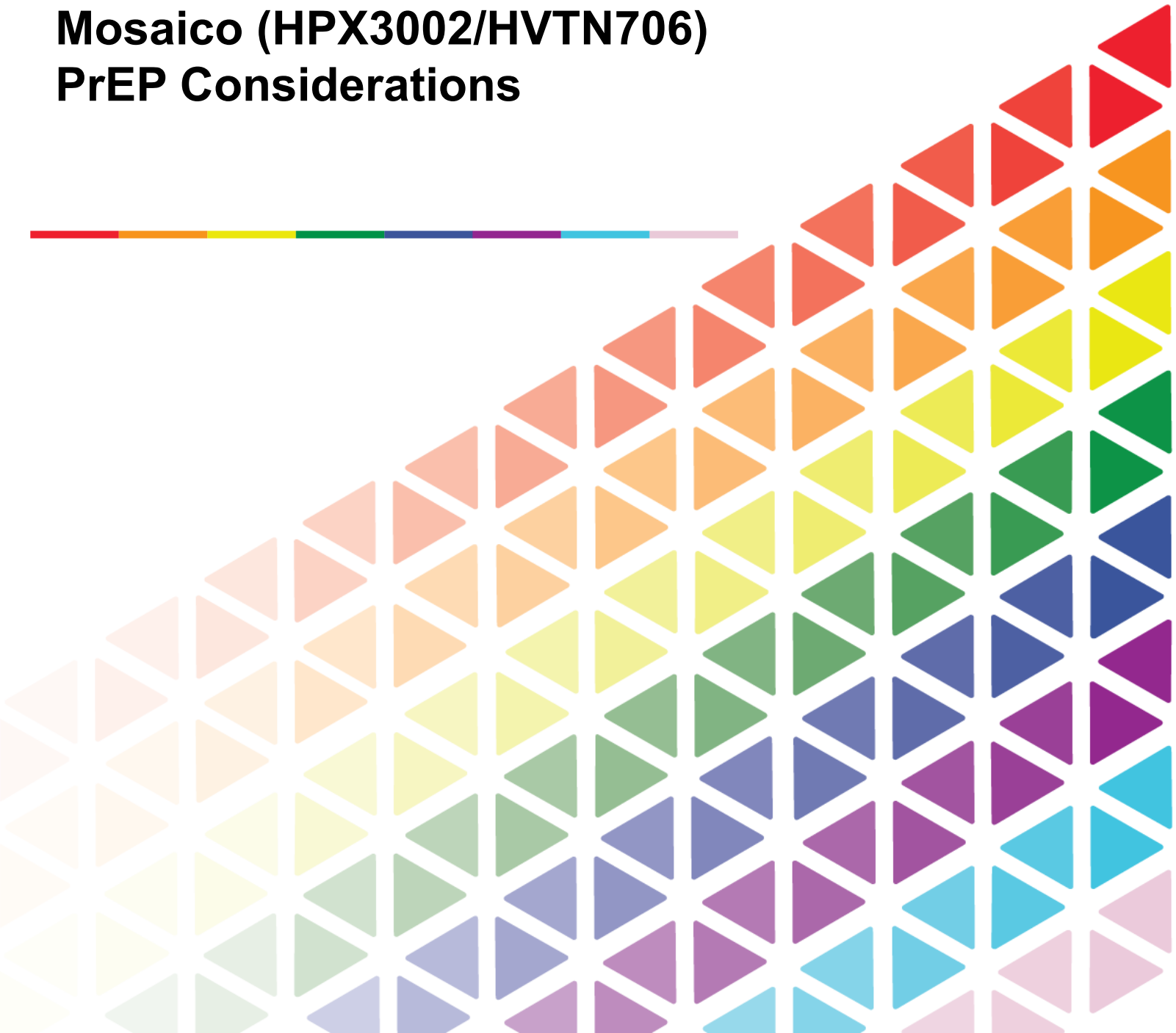
Mosaico (HPX3002/HVTN706)
PrEP Considerations



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HPX3002 / HVTN 706

Oral PrEP is safe and highly effective against sexual exposures for MSM and TGW: known for a decade

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 DECEMBER 30, 2010 VOL. 363 NO. 27

Preexposure Chemoprophylaxis for HIV Prevention in Men Who Have Sex with Men

Robert M. Grant, M.D., M.P.H., Javier R. Lama, M.D., M.P.H., Peter L. Anderson, Pharm.D., Vanessa McMahan, B.S., Albert Y. Liu, M.D., M.P.H., Lorena Vargas, Pedro Goicochea, M.Sc., Martín Casapía, M.D., M.P.H., Juan Vicente Guanira-Carranza, M.D., M.P.H., Maria E. Ramirez-Cardich, M.D., Orlando Montoya-Herrera, M.Sc., Telmo Fernández, M.D., Valdilea G. Veloso, M.D., Ph.D., Susan P. Buchbinder, M.D., Suwat Chariyalertsak, M.D., Dr.P.H.,

GUIDANCE ON PRE-EXPOSURE ORAL PROPHYLAXIS (PrEP) FOR SERODISCORDANT COUPLES, MEN AND TRANSGENDER WOMEN WHO HAVE SEX WITH MEN AT HIGH RISK OF HIV:

Recommendations for use in the context of demonstration projects

July 2012

World Health Organization

CDC Interim Guidance on HIV Pre-Exposure Prophylaxis for Men Who Have Sex with Men

Below is CDC interim guidance for health-care providers electing to provide pre-exposure prophylaxis (PrEP) for the prevention of HIV infection in adult men who have sex with men and who are at high risk for sexual acquisition of HIV.

Before initiating PrEP

Determine eligibility

- Document negative HIV antibody test(s) immediately before starting PrEP medication.

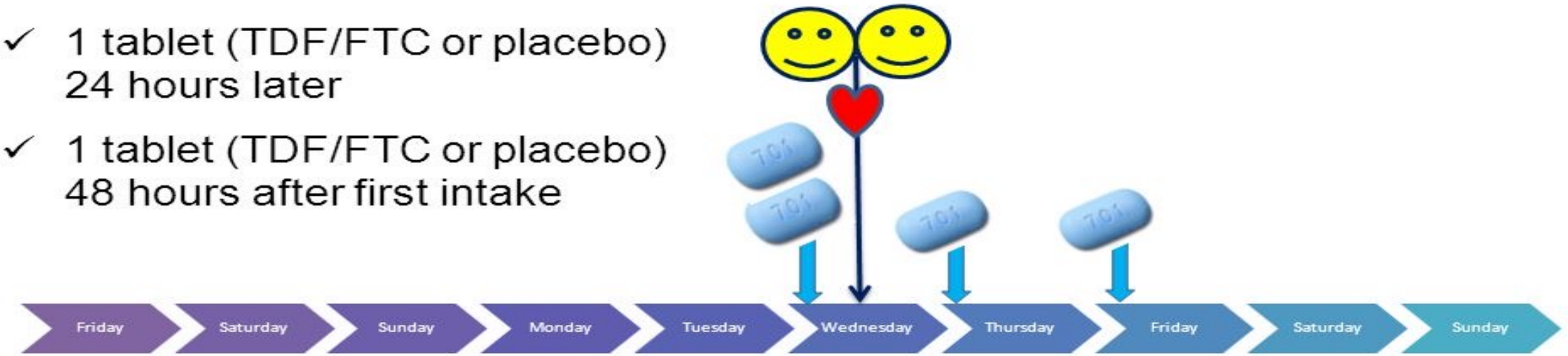
Follow-up while PrEP medication is being taken

- Every 2–3 months, perform an HIV antibody test; document negative result.
- Evaluate and support PrEP medication adherence at each follow-up visit, more often if inconsistent adherence is identified.

MOSAICO

Ipergay : Event-Driven iPrEP

- ✓ 2 tablets (TDF/FTC or placebo)
  2-24 hours before sex
- ✓ 1 tablet (TDF/FTC or placebo)
  24 hours later
- ✓ 1 tablet (TDF/FTC or placebo)
  48 hours after first intake



“2-1-1 or on-demand PrEP”

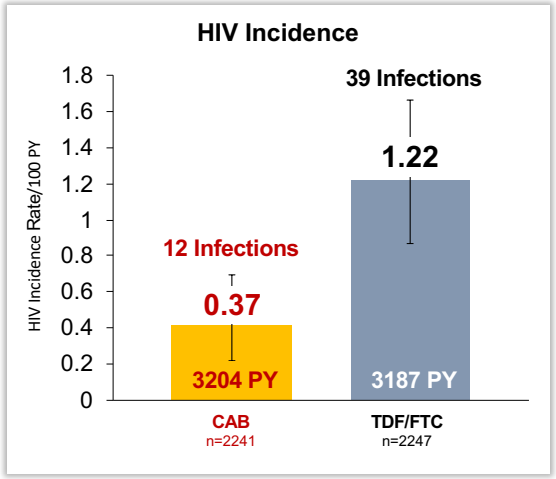
97% relative reduction vs. Placebo

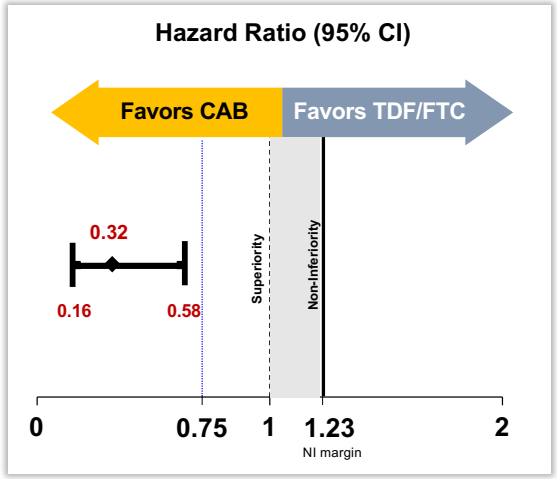
HIV Incidence: CAB vs. TDF/FTC

HPTN 083

an HIV prevention clinical trial

Efficacy: 68%

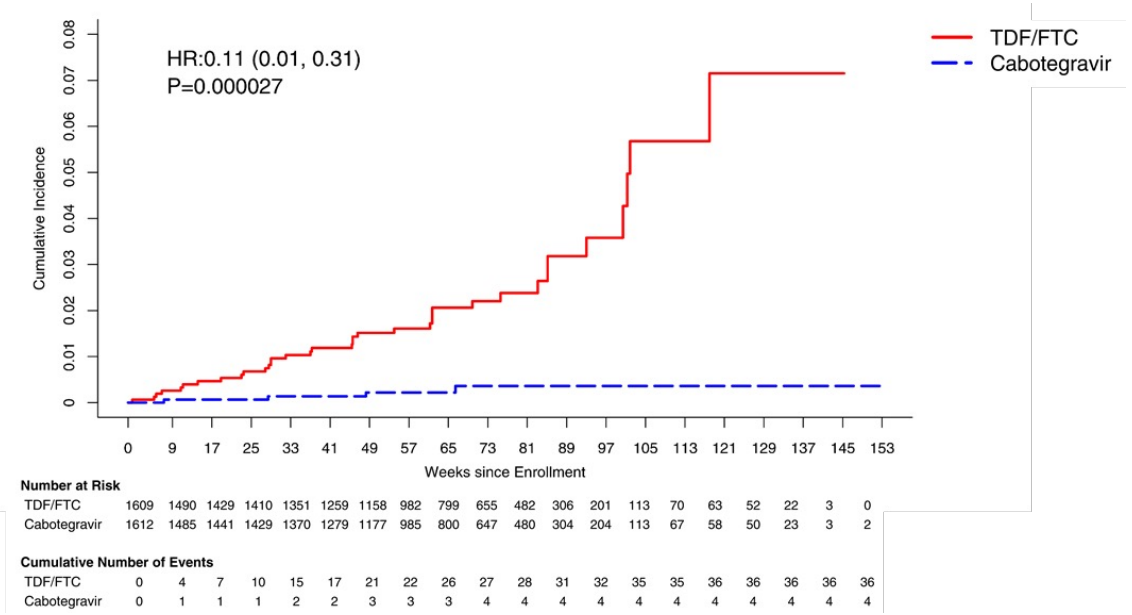




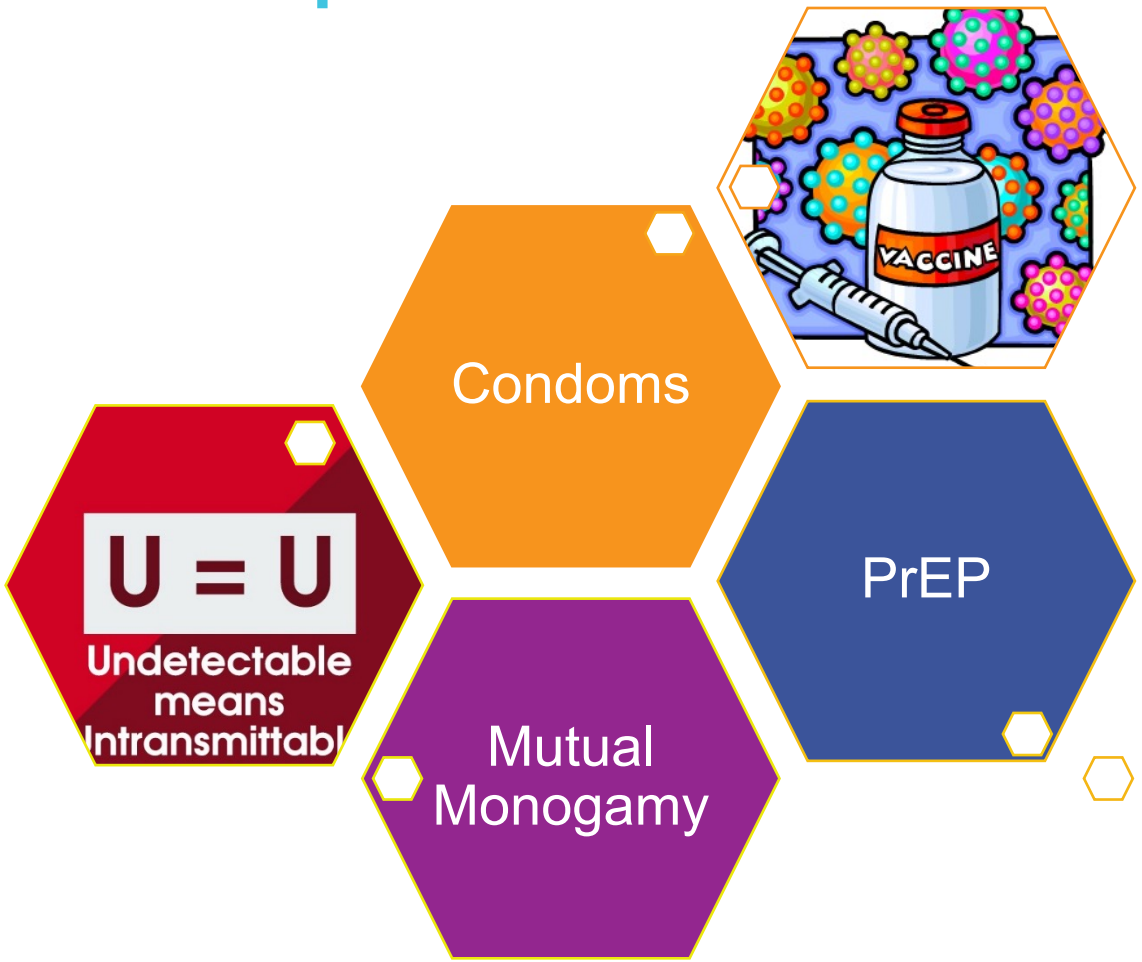
HPTN 084

Long-acting Injectable For the Epidemic

Efficacy: 89%



Trying to fill the mosaic of highly effective prevention options



Mechanics of PrEP in Mosaico

- Because we were enrolling participants at risk of HIV acquisition and PrEP is highly effective, participants currently on PrEP were not eligible to enroll
- Wanted to ensure that an authentic choice was being made about participation in the trial, so:
  - Participants in screening were counseled about PrEP and, if interested, linked to low/no-cost PrEP services during the pre-screening process. Linkage to PrEP services occurred instead of trial participation
- After enrollment, participants received HIV risk reduction counseling, including about PrEP, at each study visit. If participants desired PrEP at any time during the trial, they were linked to low or no-cost PrEP services or provided PrEP at the trial site and remained in the trial
- All sites, prior to study activation, had approved PrEP component plans for both the screening and post-enrollment periods

P(r)EP Use

	N (%)
Total Enrolled	3887
PreP use	
Has ever taken PreP	346/3668 (9.4%)
Month 1 – 3 in study	64/3650 (1.8%)
Month 4 – 6 in study	94/3546 (2.7%)
Month 7 – 9 in study	182/3408 (5.3%)
Month 9 – 12 in study	231/3364 (6.9%)
Month 12 - 15 in study	294/3163 (9.3%)
Month 15 - 18 in study	216/2238 (9.7%)
Month 18 - 21 in study	118/1135 (10.4%)
Month 21 – 24 in study	44/434 (10.1%)
Month 24 – 27 in study	11/77 (14.3%)
Month 27 – 30 in study	2/20 (10.0%)

PrEP

- Data source: Questionnaire

PEP

- Data source: Concomitant Medication
- 342/3887 (8.8%) of the participants had at least one PEP course

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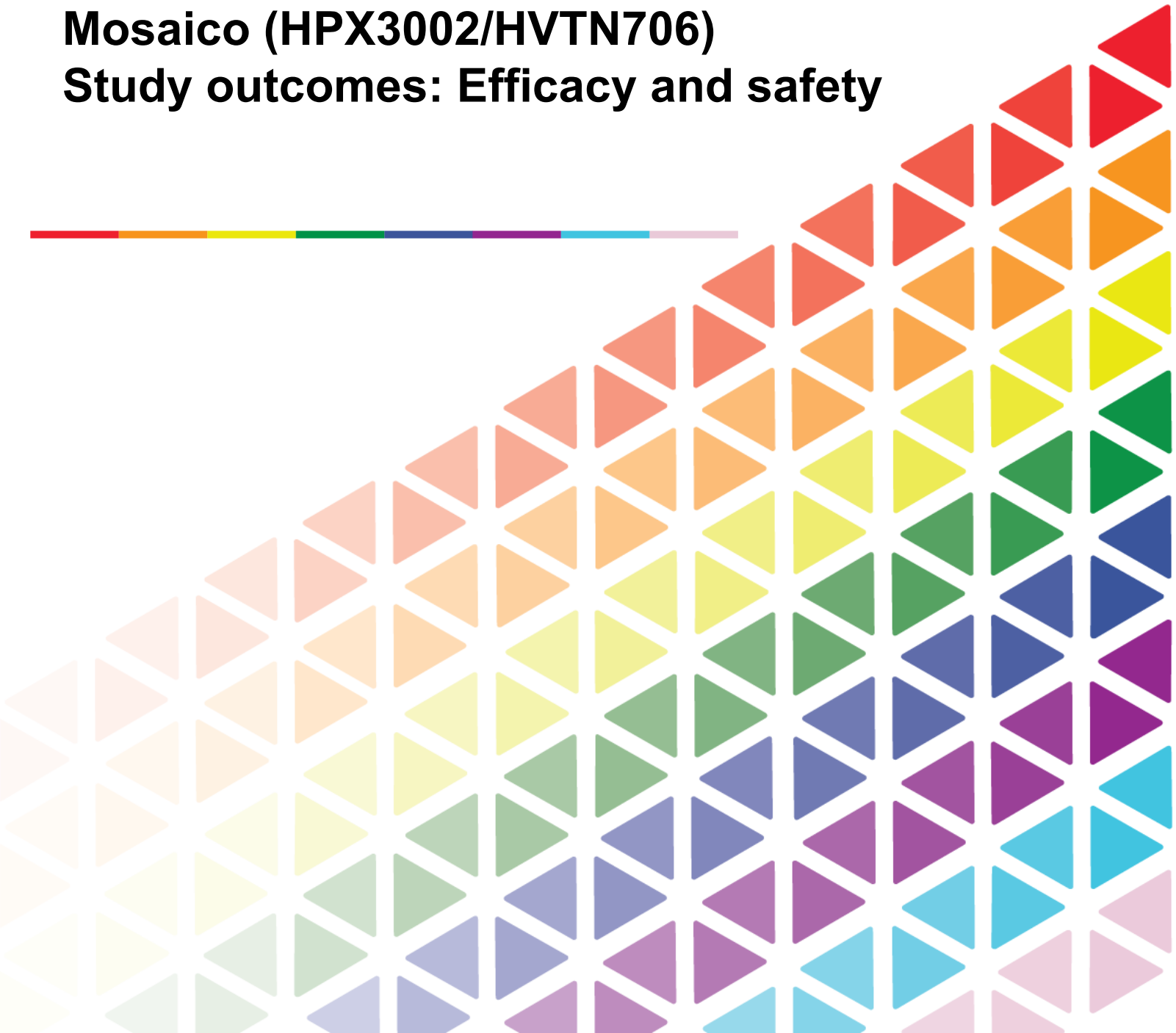
Mosaico (HPX3002/HVTN706)
Study outcomes: Efficacy and safety



Baseline Characteristics of Mosaico

- Most of the participants had a male gender identity at screening
  - 8.5% were transgender or non-binary individuals
- The study population was young with a mean age of 28 years of age
- 87% were Hispanic or Latino and 8% were Black or African American
  - In the US 28% were Hispanic or Latino and 19% were Black or African American

Country	N Enrolled (%)
Argentina	402 (10.3%)
Brazil	852 (21.9%)
Italy	91 (2.3%)
Mexico	347 (8.9%)
Peru	1615 (41.5%)
Poland	116 (3.0%)
Puerto Rico	10 (0.3%)
Spain	262 (6.7%)
USA	192 (4.9%)

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Monitoring for Non-Efficacy

- There was an independent Data and Safety Monitoring Board (DSMB) that reviewed the data twice a year (and in real-time, as needed) to monitor safety of the vaccine, and to determine if there was efficacy (or if there was not efficacy – “non-efficacy”) during the trial.
- Vaccine efficacy was evaluated when there was sufficient follow-up time to determine whether or not the vaccine provided efficacy.
- Pre-determined “stopping rules” were created for the DSMB to determine if the vaccine was not effective “non-efficacy”, that it should be recommended that the trial be stopped.
- Stopping criteria: the lower 95% confidence bound lies below 0% AND the upper 95% confidence bound lies below 50%. That would indicate that the vaccine did not provide at least 50% protection.
- Criteria should be met for both the overall study population, as well as those who got their first 3 doses of vaccine on time and remained HIV negative for at least one month after the 3rd dose (to give the vaccine time to work)

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Stopping the trial

- On January 12, 2023, the DSMB met and the stopping rules for non-efficacy were met. They recommended stopping the trial.
- The Governing Council (comprised of leadership at Janssen, the HIV Vaccine Trials Network, and the US National Institutes of Health) spoke with the DSMB, and also concluded that the trial should be stopped.
- The site investigators were informed that the trial was to be stopped.
- A press release was issued on January 18, 2023, trial participants were notified, and informed about whether they got the vaccine or the placebo

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Safety summary

- **No safety issues with the vaccine regimen were identified**
  - 78% of participants in the vaccine group experienced local reactogenicity events; most were mild or moderate in severity
  - 79% of participants in the vaccine group experienced systemic reactogenicity events; most were mild or moderate in severity
- Unsolicited adverse events were observed in 37% of the participants in the vaccine and placebo arms.
- Serious adverse events were observed in around 4% of the participants in the vaccine (3.8%) and placebo (3.4%) arms.
- No cases of thrombosis with concurrent thrombocytopenia were observed (this had been seen very rarely with Adenoviral vector COVID-19 vaccines).

Conclusions: The safety profile of the study vaccine is favorable, reactogenicity is mostly mild or moderate and short-lived.

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HIV Vaccines
2015 - 2023

- In 2015, the HVTN set out a strategy to execute a series of efficacy trials to define:
  1) Whether non-neutralizing antibodies could be elicited at high enough titer to be useful
     - Ad26 / gp140 & ALVAC + gp120 trials
  2) Determine if we could prevent HIV acquisition with a broadly neutralizing antibody as a model for both passive prophylaxis and bnAb inducing vaccines
     - AMP trials
- We now know the answers to the questions:
  1) No
  2) Yes

Special Session: Tuesday, Feb 21, 5:40-6pm

- Results from the Mosaico Trial
  - Includes PrEP use as measured in dried blood spots
  - Kaplan-Meier curves showing infections in the vaccine vs. placebo arms
  - Infection rates by age and by geographic region

- Future Directions for HIV vaccines (by Larry Corey)

Acknowledgements

- Mosaico participants
- Clinical Research Sites and their communities
- Advocacy groups
- Study team
- Study partners

Back-up slides:
Community Involvement in Mosaico

Community Consultative Process – Protocol Development

- March 1, 2019 (Seattle)- Community Review of Protocol and Informed Consent Form (ICF)
  - 11 US and Latin American representatives- HVTN site community educators and CAB members
    - Decided on language for ICF and harmonized ICF with protocol

- April 19, 2019 (Atlanta)- Community and Ethical Review
  - 42 global community and ethicists representatives, site investigators, and academic partners
  - Included study background and overview
  - Outcomes/feedback included:
    - Positive feedback on study design considerations
    - Communities need education about biomedical HIV prevention research and technologies, including clinical trial design and history
    - “Intended use” language regarding PrEP interest - not recommended, instead consider offering PrEP to everyone, and those who do not wish to accept it can enter the study
    - Site PrEP/prevention plans need clear language, should include local considerations, and should be informed by community stakeholders

Community Consultative Process – Protocol Development/Implementation

- April 25-26, 2019 (Philadelphia area)- Protocol Team Review
  - 20+ protocol team members, including US and Latin American community representatives
    - Further aligned protocol and ICF, and finalized ICF

- Ongoing: CRS investigators engaging their local communities to provide an overview of the study, inquire about acceptability of study in local context, and build community support for implementation

Community Consultative Process – Conference Events

- Early 2019 discussions began with the Black AIDS Institute (BAI) and Treatment Action Group (TAG) on cooperative stakeholder engagement activities which would center the MOSAICO study.
- Implemented a survey to guide activities and messages – to hear and learn perspectives on the safest, most ethical, and most effective ways to study new biomedical HIV prevention interventions in planned and ongoing efficacy trials. Potential new biomedical HIV prevention interventions include HIV vaccines, antibody or immune-based approaches, and new forms of antiviral pre-exposure prophylaxis (PrEP).
- Both organizations have participated in monthly planning and evaluation calls to explore engagement of community advocates in U.S. noting social media channels, and other networks sharing information about HIV education, prevention, and treatment.
- BAI and TAG partnership will continue into 2020 (and beyond), and include dissemination of survey findings and other collaborative activities to disseminate study messages developed by protocol team and clinical research sites

Community Consultative Process – Conference Events

- July 22, 2019 (Mexico City)- *HIV Vaccines R&D: a Vision for 2020 and Beyond*
  - Sponsored by IAS Global HIV Vaccine Enterprise in collaboration with HVTN and AVAC
  - 60 advocates, clinical trial researchers, funders, regulators from countries involved in HIV vaccine research

Objectives:

- To identify stakeholder perspectives on the current state of HIV vaccine R&D and the ongoing need for vaccine research and development in the larger context of HIV prevention.
- To identify next steps and priorities for incorporating stakeholder perspectives into the research and prevention agenda by decision-makers.

Webinar w/ Black AIDS Institute and Treatment Action Group

May 9, 2019 Interactive Webinar

- Discussed the history of research around biomedical interventions and how it pertains to Black communities.
- Discussed the current conversations and understanding around the design of clinical trials to evaluate biomedical interventions, with a focus on vaccines.
- Discuss the importance of community input in vaccine trials and best practices for becoming involved with trials and research.