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Insights in HIV Vaccine Research

Looking Back on the Mosaico Study

HIVR4P 2024

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Outline

- Background of the HIV prevention field
- Study design
- P(r)EP Use
- Results
- Conclusions

Control of the HIV epidemic Remains an Unmet Need Worldwide

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39 million people
worldwide actually
living with HIV

1.5 million children
actually **living with HIV**

630,000 deaths
of AIDS-related diseases

1.7 million of new HIV infections
5,000 per day

29.8 million people
living with HIV
receiving antiretroviral therapy

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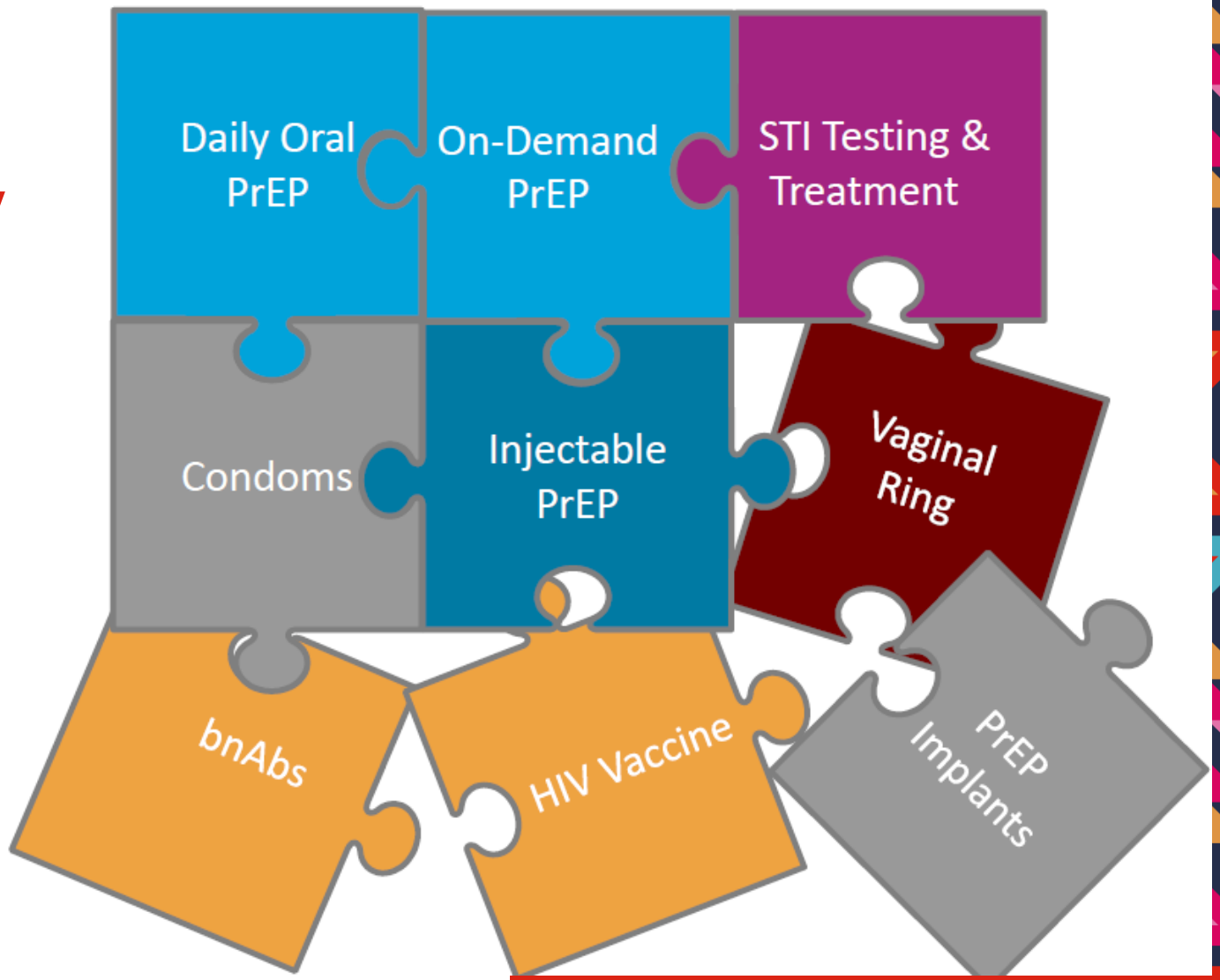
Completing the HIV Prevention Mosaic



Scott Lancet HIV 2019;
Haynes Curr Opinion in Imm 2015;
Landovitz Curr Opinion HIV 2016;
Green AIBE 2017

Mosaico: Prophylactic HIV Vaccine That Protects Against Globally Relevant Strains of HIV-1

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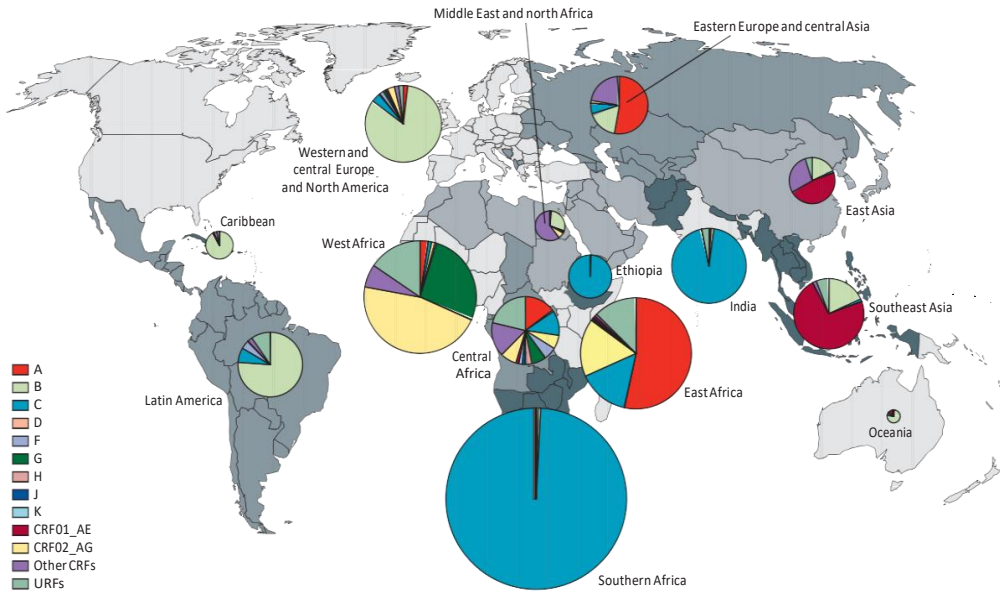
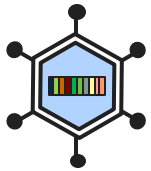
Mosaic design

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

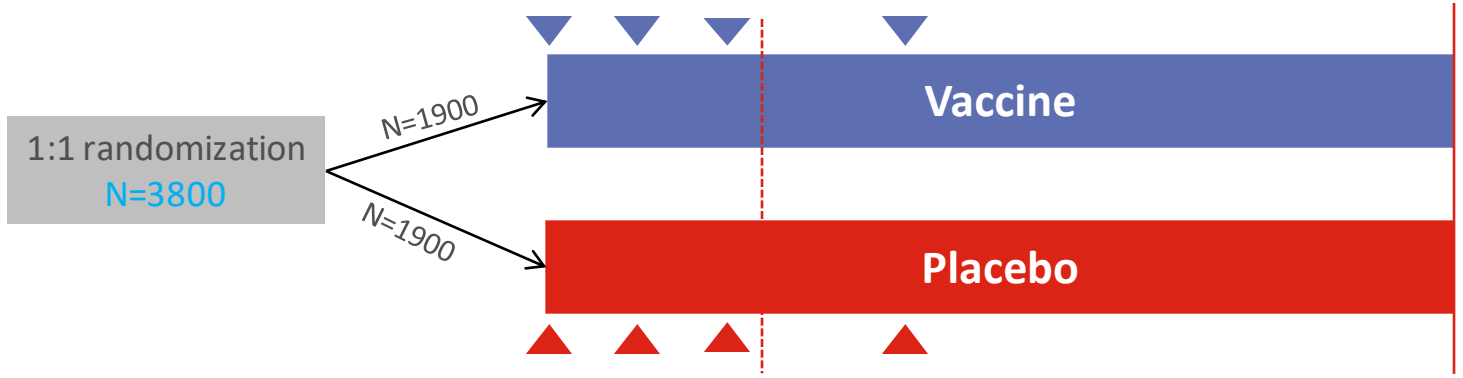
Trimeric envelope proteins

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

For the enhancement of HIV-specific immunity

Study Design

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

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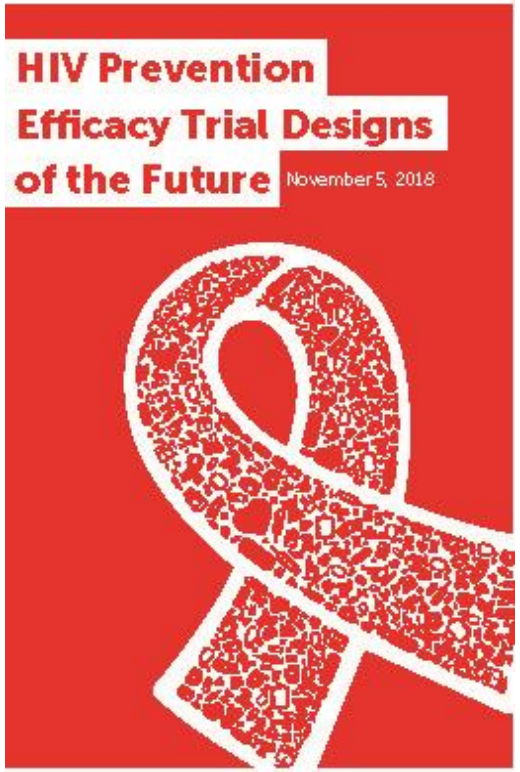
Symposium: November 5, 2018



Contributors: Clinical Trialists, Statisticians, Advocates, Ethicists, US FDA and NIH, BMGF

Consensus:

- Identifying participants who “opt-out” of PrEP is ethical and acceptable
- Requires complete transparency and ongoing participant education about effectiveness and availability of PrEP

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Additional Input into PrEP Planning

- Community consultations with community groups were carry out started since the beginning of the study
- Consultation held in April 2019 that included community activists, ethicists, faith leaders
- All of these consultations formed the basis for developing the PrEP access plans for Mosaico
- The Mosaico protocol team was committed to ensure that all study participants receive access to the highest standard of prevention after enrollment according to local and national guidelines, including counseling, condoms, lubricant, STI diagnosis and treatment, and **complete education and access to PrEP** while remaining in the trial

Mechanics of PrEP in Mosaico

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- We engaged community organizations, activists, ethicists, and clinical trialists to determine how PrEP would be incorporated into the trial.
- All potential participants were counseled about PrEP and if interested, linked to PrEP services during the pre-screening process.* Linkage to PrEP services occurred instead of trial participation

*Participants desiring PrEP but needing support were able to receive free PrEP and PrEP monitoring

- Because Mosaico was enrolling participants at risk of HIV acquisition and oral PrEP and CAB-LA are highly effective, participants currently on oral PrEP or previously/currently on CAB-LA were not eligible to enroll
- After enrollment, participants continued to receive risk reduction counseling, including PrEP. If participants changed their mind and desired PrEP at any time during the trial, they were linked to low/no-cost PrEP services or directly provided PrEP and remained in the trial
- All sites had approved PrEP plans for both the pre-screening and post-enrollment periods

Clinical Research Sites

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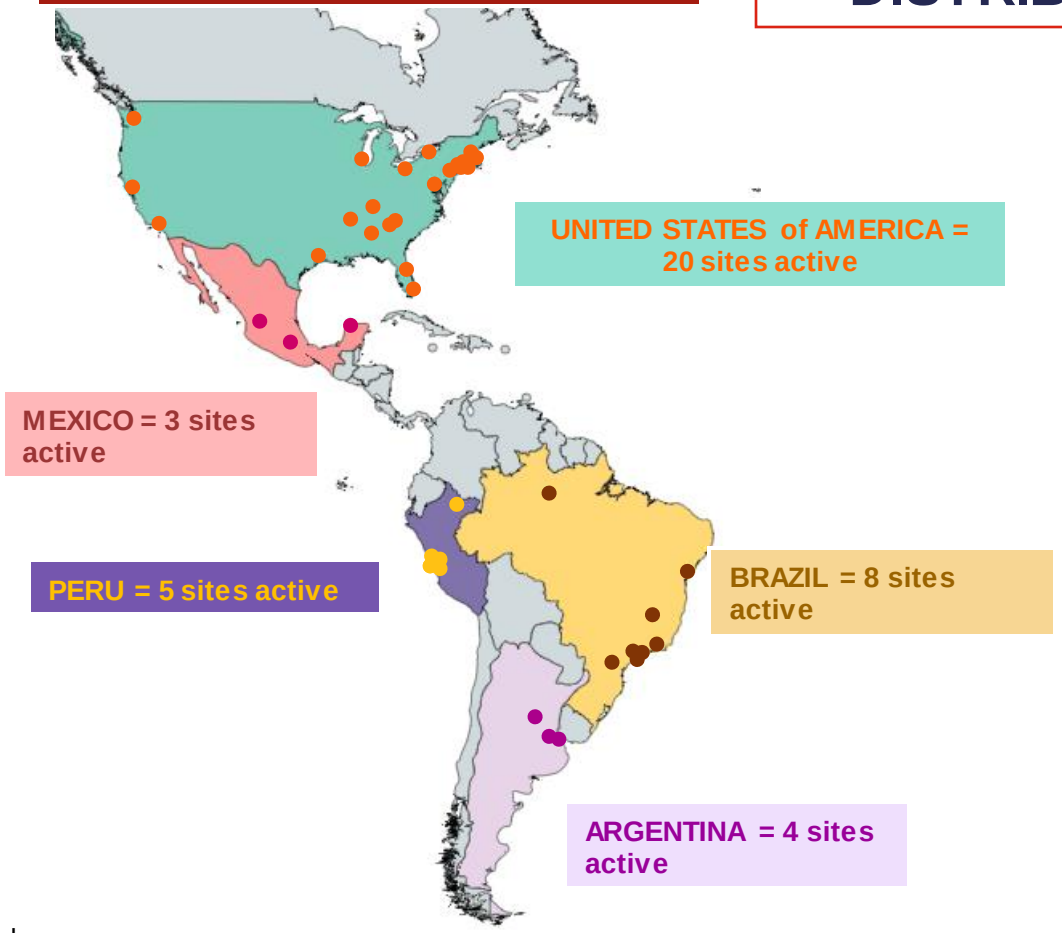
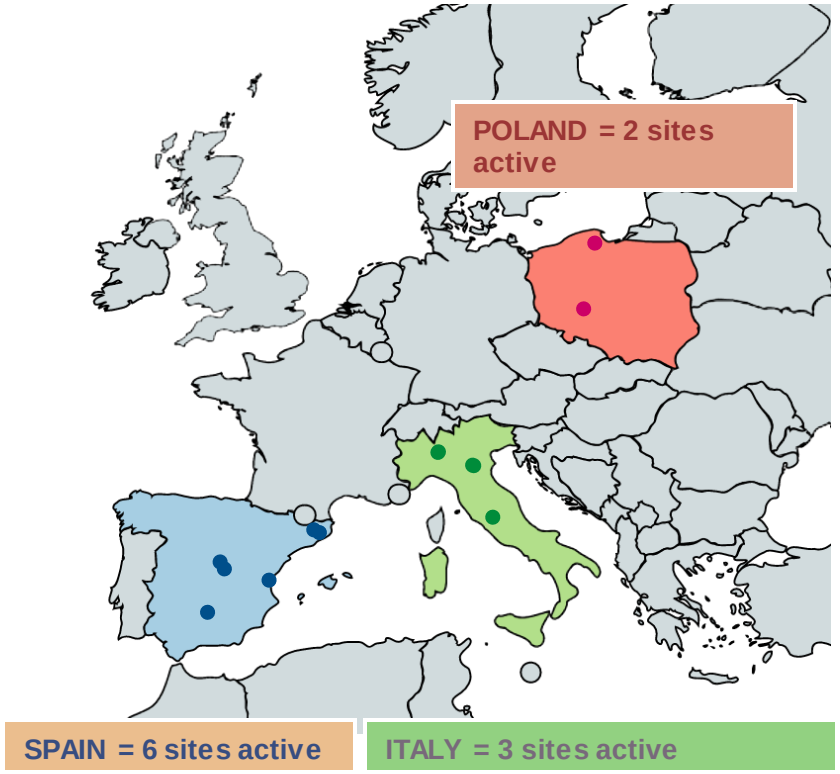
GLOBAL SITE DISTRIBUTION

AMERICAS



EUROPE



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Mosaico Recruitment in Peru

- Study awareness and participation promotion in LGBT+ dating web sites, social media, and study website
  - In-house developed online recruitment tool for high-risk self-assessment
- LGBT+ social media influencers engaged to promote community participation within their networks
- HIV prevention Heroes Tour campaign
- Referrals from participants
- Facilitation of transportation to the sites
- Community consultation
- Community Advisory Board consultation and support

Barcelona Checkpoint + Barcelona PrEP Point

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Key factors:

- ✓ Peer-led
- ✓ Safe environment
- ✓ Positive sexuality
- ✓ Point of Care testing

- Activism about PrEP access in 2015 + support to purchases online
- Currently the biggest PrEP provider in Spain: 3,328 initiations (feb. 2023)
- Fast recruitment for Clinical Trial + highest retention rate
- Easy-PrEP: create tools to improve the motivational PrEP cascade, increase the PrEP uptake and autonomy for decision taking

- Since 2006, Increase HIV screening + Same-day confirmation and CD4 + Fast linkage/treatment
- Change paradigm: Regular testing + AHI with PCR + same-day treatment
- Emotional support HIV + ChemSex support
- Guarantees for access to Care and Treatment (undocumented persons)
- Include other STI, and focus on asymptomatic infections + vaccinations (VHA/B, VPH, MPOX)

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Baseline Characteristics

- Most of the participants had a male gender identity at screening
  - 8.5% were transgender 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%)

* Includes cross dresser, non-binary, fluid gender, gender non-conforming,queer

Cumulative HIV Infections (mITT)

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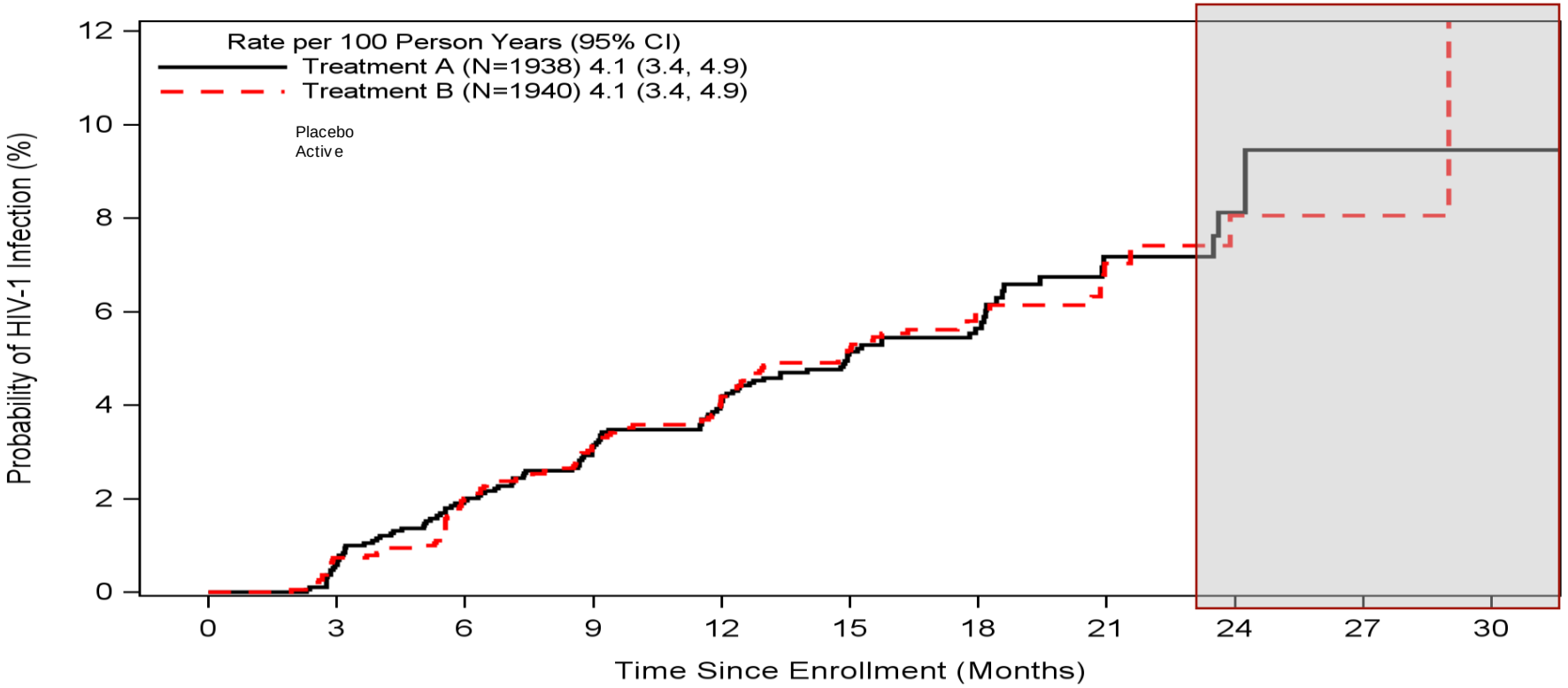

Number at risk

A	1938	1893	1836	1774	1729	1385	801	338	96	17	10
B	1940	1895	1844	1771	1727	1379	798	323	89	11	9

Cumulative number of HIV-1 infections

A	0	11	37	58	76	94	100	110	112	113	113
B	0	14	38	60	78	95	105	110	112	112	113

For VE% calculation the data was cut-off at month 23.7. Thereafter, the estimate is considered unstable due to too few subjects at risk

mITT criteria

- Randomized
- At least one vax
- HIV negative at first vax

PrEP Use

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	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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Safety Summary

- No safety issues with the vaccine regimen were identified
- In the vaccine group, 78% of participants reported local and 79% systemic reactogenicity (Mostly grade 1 and 2)
- Unsolicited adverse events were reported by 37% of the participants in both arms
- Serious adverse events were observed in 3.8% of the vaccine 3.4% of the placebo arms (Related SAE were observed in 2 participants in the vaccine arm and 1 participant in the placebo arm)
- Eight non-related fatalities occurred (5 in placebo and 3 in the vaccine arm)
- Five AESIs were reported in the study with 3 in the vaccine arm and 2 in the placebo arm (Thrombotic events, in the vaccine arm, all were >150 days post-vaccination or with known precipitant
- No cases of thrombosis with concurrent thrombocytopenia were observed

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Conclusions

- **The Mosaico study recruited a diverse cohort of MSM and transgender persons, after counseling and linkage to PrEP for those who would accept this prevention modality**
- **No safety issues with the vaccine regimen were identified but the regimen was not efficacious in preventing HIV acquisition.**
- **Despite ongoing risk reduction counseling and linkage to PrEP, HIV incidence, particularly in young participants in Latin America, was very high. This is a population in great need of additional effective HIV prevention modalities.**
- **The PrEP strategy could be use in future clinical trials.**

HVTN 706/HPX3002 (Mosaico) Protocol Team Acknowledgements

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Janssen Team

- Sabrina Spinosa Guzman, Protocol Leadership Chair
- Ludo Lavreys, Study Responsible Physician
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janssen PHARMACEUTICAL COMPANIES OF Johnson&Johnson

HVTN 706/HPX3002 (Mosaico) Protocol Team Acknowledgements

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HVTN Team

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- Jim Kublin, Principal Staff Scientist
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DAIDS

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MHRP

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