

# ALVAC<sup>®</sup>-HIV and AIDSVAX<sup>®</sup> B/E Prime-Boost HIV-1 Preventive Vaccine Regimen

## Final Results of the Phase III Community-based Trial in Thailand

Supachai Rerks-Ngarm, Punnee Pittisutthithum, Sorachai Nitayaphan, Jaranit Kaewkungwal, Joseph Chiu, Merlin Robb, Robert Paris, Arthur Brown, Elizabeth Adams, Sanjay Gurunathan, Donald Francis, Chirasak Khamboonruang, Prasert Thongcharoen, Nelson L. Michael, Prayura Kunasol, Jerome Kim

for the MOPH-TAVEG Collaboration



---

*Primary data to be published online by the New England Journal of Medicine 20 October 2009 at 1050 CET.*

*The* NEW ENGLAND  
JOURNAL *of* MEDICINE

Vaccination with ALVAC and AIDSVAX to Prevent HIV-1  
Infection in Thailand

Supachai Rerks-Ngarm, M.D., Punnee Pittisutthithum M.D., D.T.M.H., Sorachai Nitayaphan, M.D., Ph.D.,  
Jaranit Kaewkungwal Ph.D., Joseph Chiu, M.D., Robert Paris, M.D., Nakorn Preamsri, M.D.,  
Chawetsan Namwat, M.D., Mark de Souza, Ph.D., Elizabeth Adams, M.D., Michael Benenson, M.D.,  
Sanjay Gurunathan, M.D., Jim Tartaglia, Ph.D., John G. McNeil, M.D., Donald P. Francis, M.D., D.Sc.,  
Donald Stablein, Ph.D., Deborah L. Birx, M.D., Supamit Chunsuttiwat, M.D., Chirasak Khamboonruang, M.D.,  
Prasert Thongcharoen, M.D., Ph.D., Merlin L. Robb, M.D., Nelson L. Michael, M.D., Ph.D., Prayura Kunasol, M.D.,  
and Jerome H. Kim, M.D., for the MOPH-TAVEG Investigators\*

# RV 144

---

- Trial Objectives and Design
- Demographics
- Results

# Trial Objectives

---

## Primary

- To determine whether immunization with ALVAC<sup>®</sup>-HIV (vCP1521) boosted by AIDSVAX<sup>®</sup> B/E gp120 B/E protects Thai volunteers from HIV infection.
- To determine effect of immunization on viral load after inter-current infection.

## Secondary

- To determine effect of immunization on CD4 cell count after inter-current infection.
- To confirm the safety of this vaccine combination.
- To evaluate whether participation is associated with behavior change increasing risk of HIV infection.

# Co-primary Endpoints

---

- Acquisition Endpoint
  - ~50% reduction in the relative risk of infection
  
- Viral Load Endpoint or early Viremia
  - 0.4-log HIV RNA reduction

# Study Vaccines

---

## ALVAC<sup>®</sup>-HIV (vCP1521)

- Recombinant canarypox vector vaccine genetically engineered to express **HIV-1 gp120 (subtype E: 92TH023)** linked to the transmembrane anchoring portion of **gp41 (subtype B: LAI)**, and **HIV-1 gag and protease (subtype B: LAI)**.

## AIDSVAX<sup>®</sup> B/E

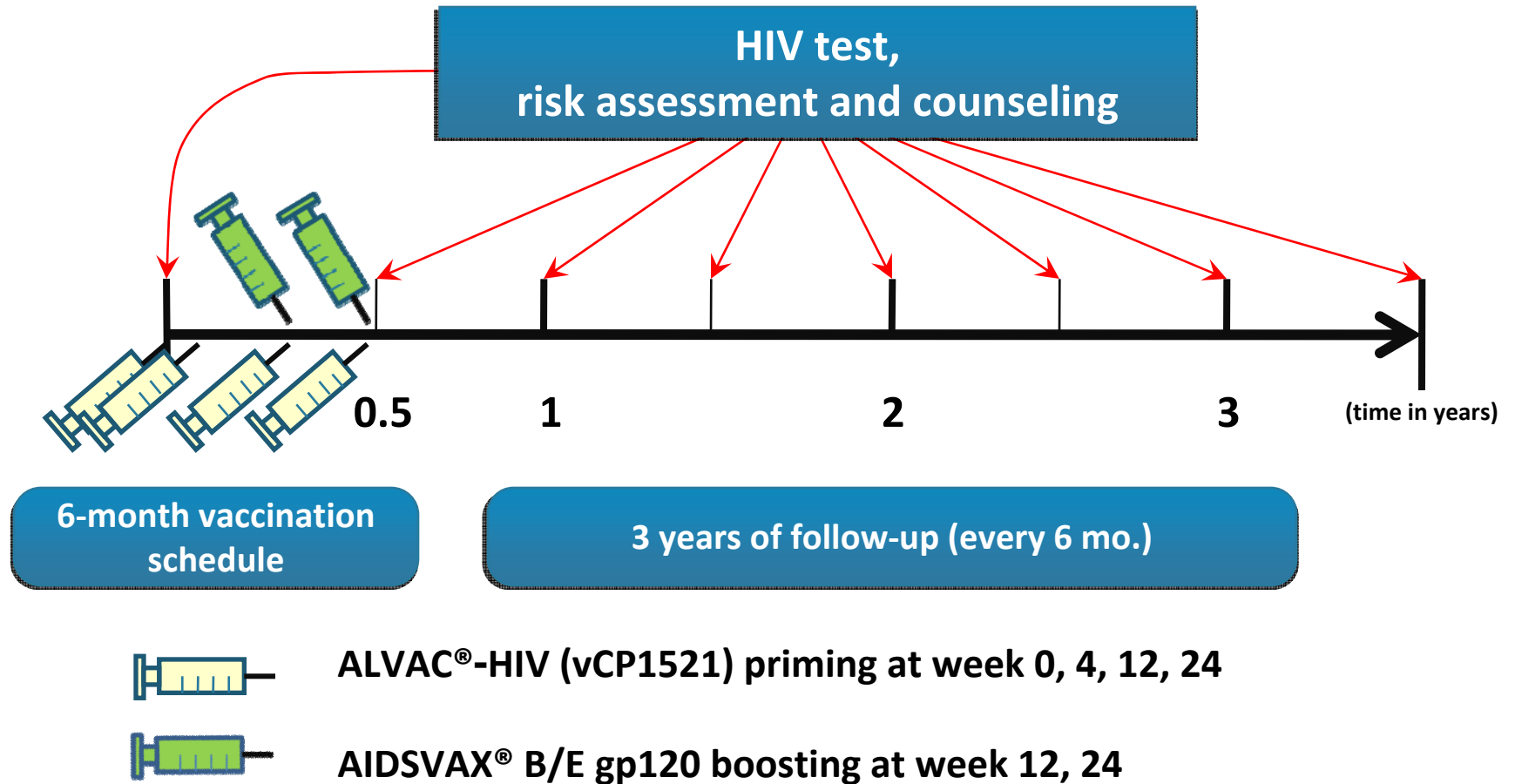
- Bivalent HIV gp120 envelope glycoprotein vaccine containing a **subtype E** envelope from the HIV-1 strain **CM244** and a **subtype B** envelope from the HIV-1 strain **MN**.

# Design

---

- Community-based, randomized, double-blind, placebo-controlled trial (vaccine: placebo 1:1)
- Volunteers: HIV negative, 18-30 years of age
- Excluded: chronic disease, pregnancy or breastfeeding
- 6-month period of study vaccinations
- HIV testing every 6 months for 3 years post-vaccination

# Vaccination and Follow-up Schedule





# Important Milestones

---

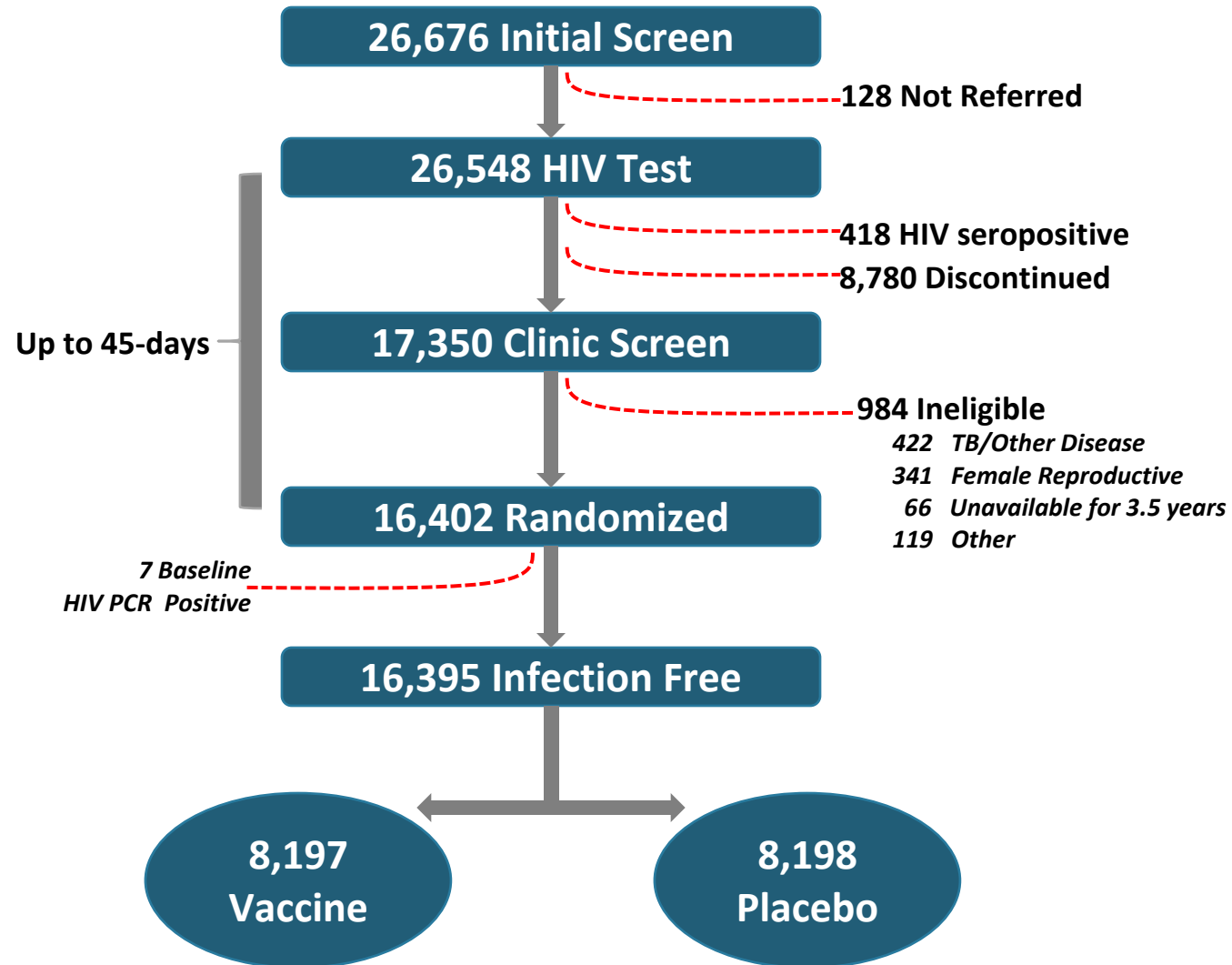
24 September 2003	<b>Screening began</b>
20 October 2003	<b>First vaccination</b>
30 December 2005	<b>Enrollment completed</b>
31 July 2006	<b>Vaccination completed</b>
July 2007	<b>DSMB Interim Analysis (based on mITT statistical plan)</b>
Spring 2009	<b>Communication Plan finalized</b> <i>Commitment to ensuring that the Thai people would be the first to learn the outcome irrespective of the final result</i>
June 2009	<b>Study Follow-up Complete</b>

# RV 144

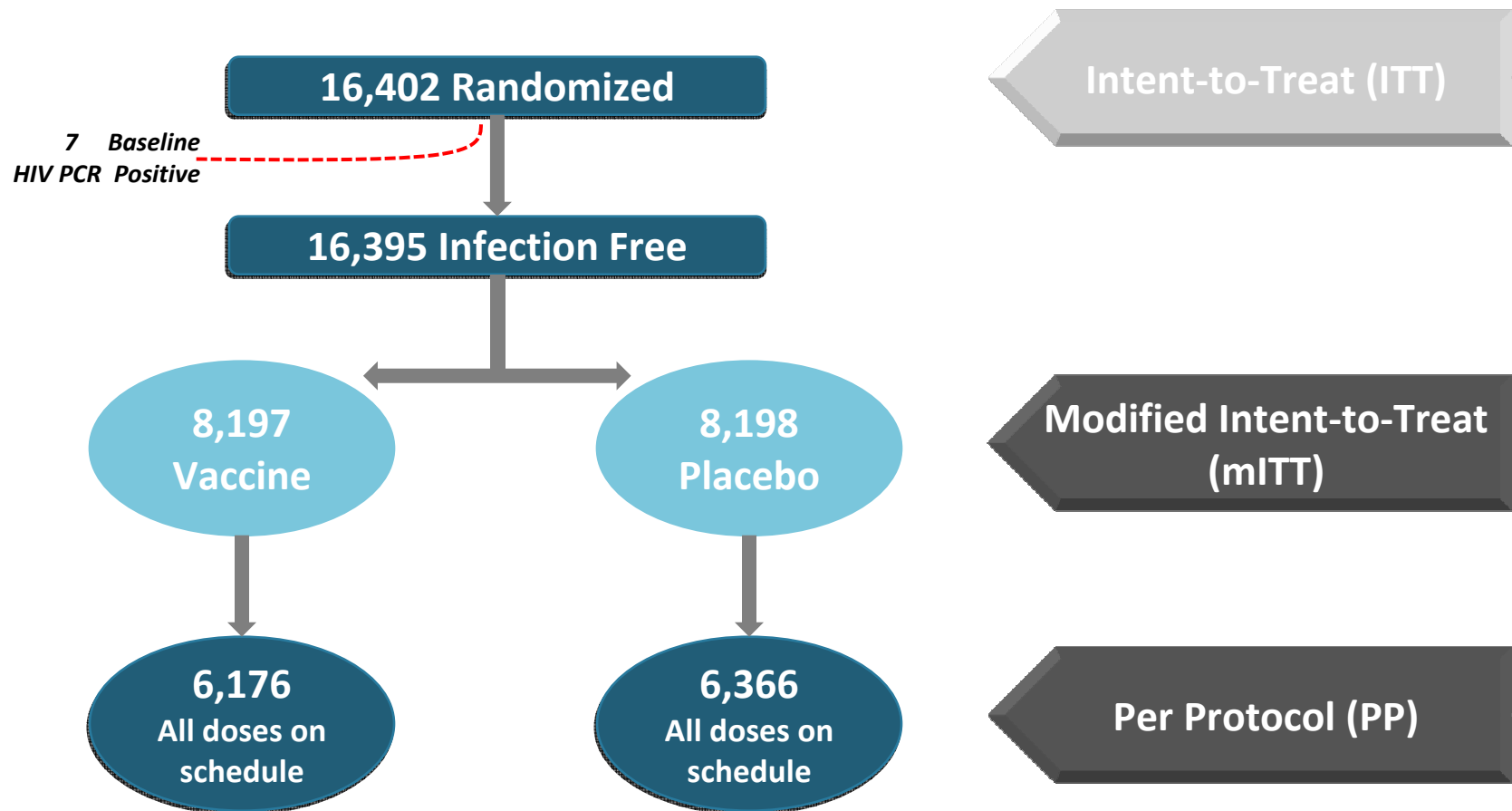
---

- Trial Objectives and Design
- Demographics
- Results

# From Screening to Vaccination

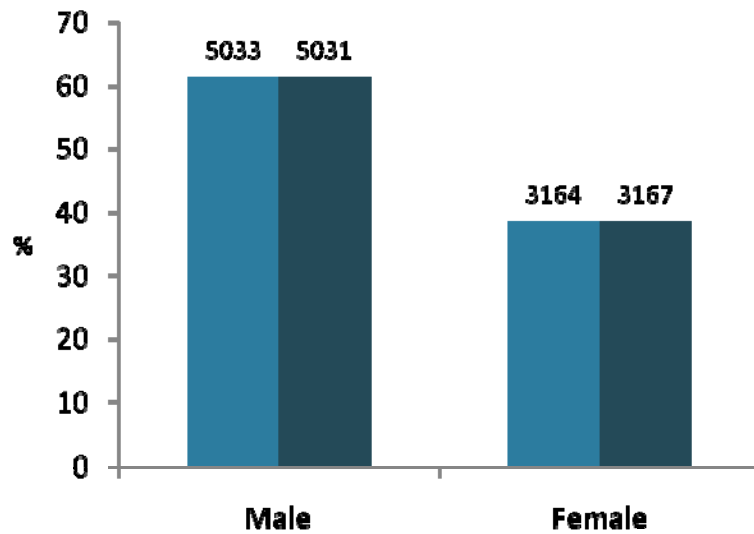


# Definition of Analytical Methods

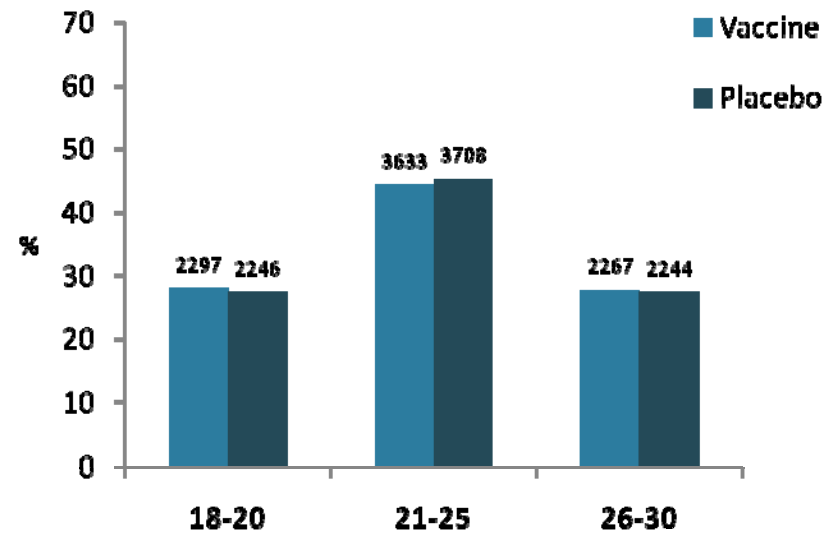


# Baseline Demographics

## Gender

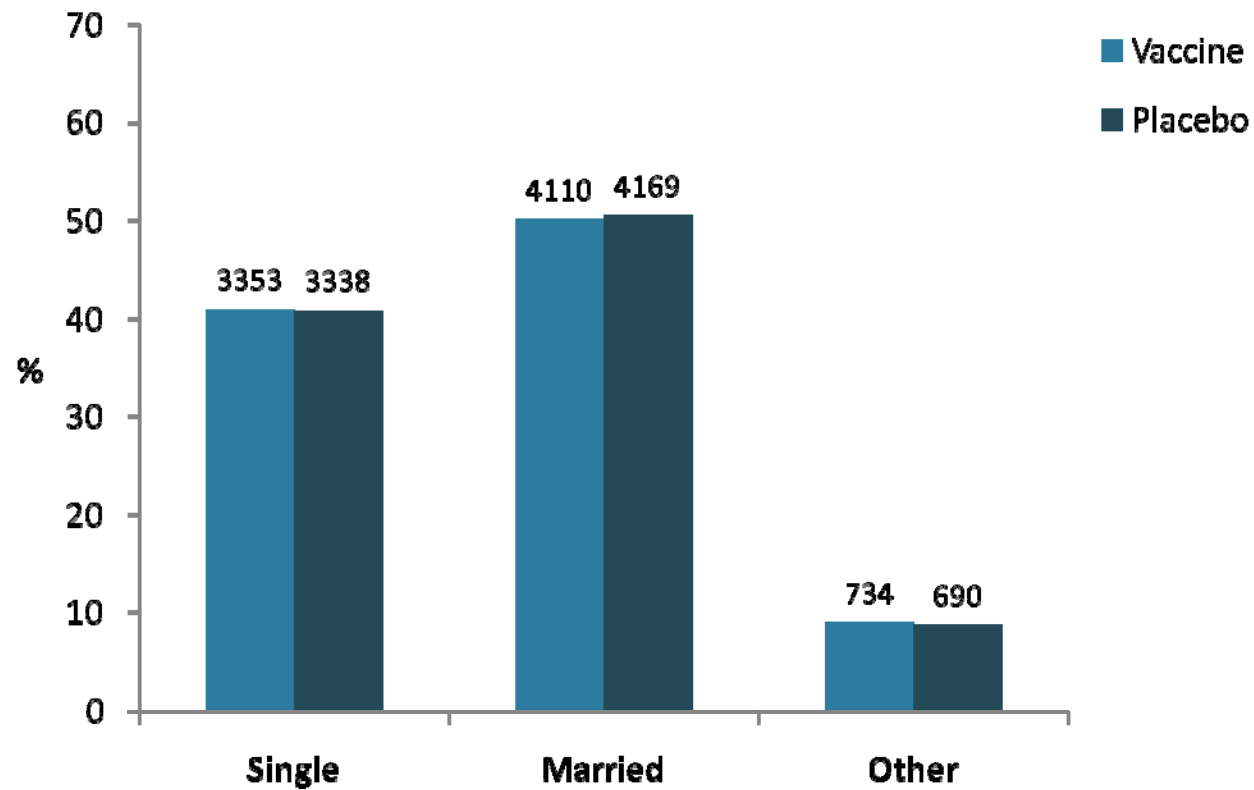


## Age



# Baseline Demographics

## Marital Status



*Other: Widowed, Separated, Divorced*

# Definition of Risk Behavior

---

- High Risk: Self-assessment as high risk OR self-report of one or more high-risk behavior(s) in the previous six months
  - Needle-sharing
  - STI symptoms
  - Sex with HIV-positive partner
  - No condom use during high-risk encounters
  - Occupation entertainment
  - Occupation CSW
  - Jail drug injection
  - Multiple sex partners

# Baseline Demographics

	Vaccine n (%)	Placebo n (%)
--	------------------	------------------

## *Sexual Partner Frequency*

0 Sex Partners	1864 (22.7)	1801 (22.0)
1 Sex Partner	5428 (66.2)	5495 (67.0)
>1 Sex Partners	619 (7.6)	620 (7.6)
No Answer	280 (3.4)	273 (3.3)
Missing Value	6 (0.1)	9 (0.1)

## *Other Risk Behaviors (from a list of 8 criteria)*

Same-gender partner	184 (2.3%)	182 (2.2%)
Needle-sharing	68 (0.8%)	65 (0.8%)



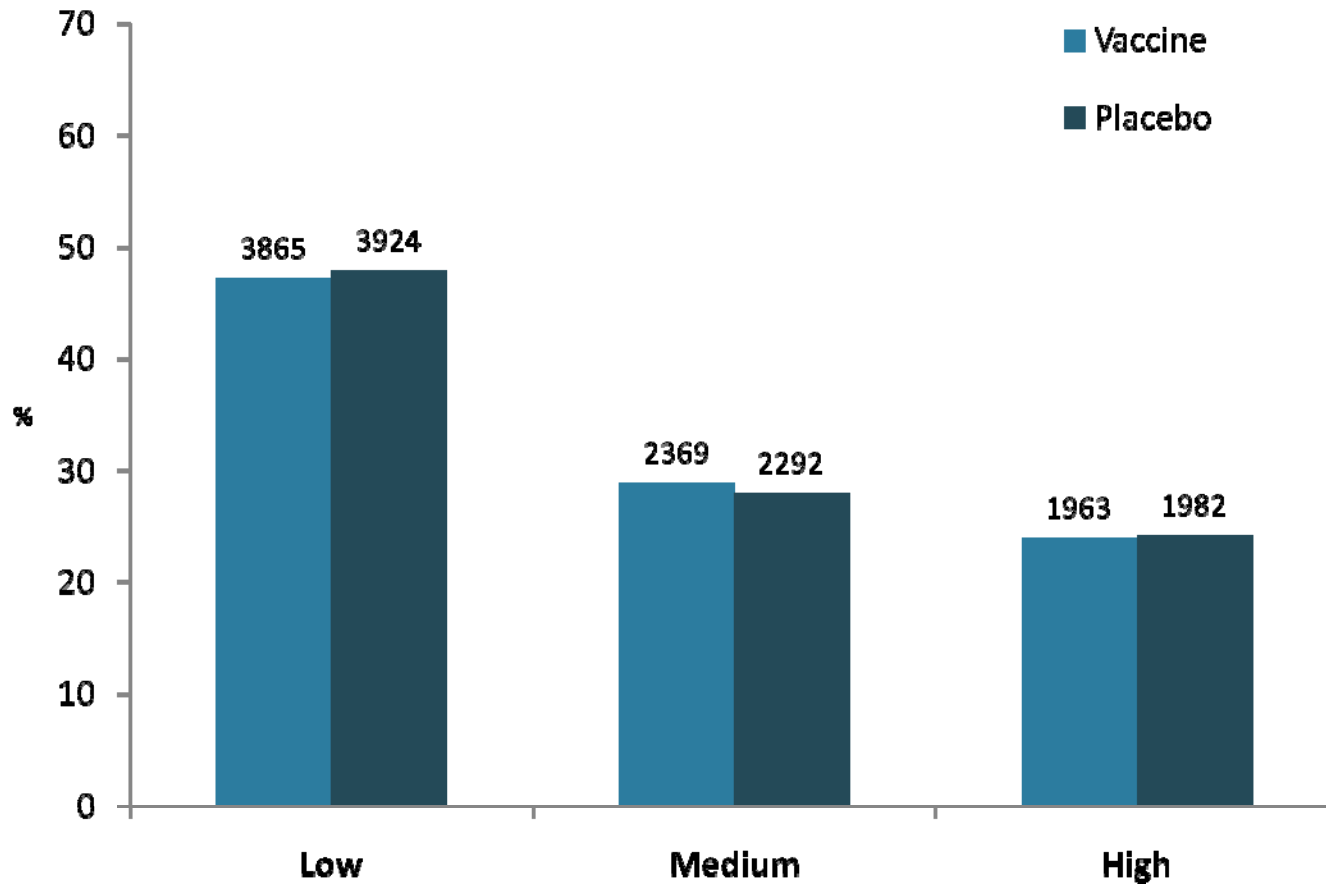
# Definition of Risk Behavior

---

- Low Risk
  - Self-assessment as low risk AND self report of no high-risk behavior in the previous six months
  
- Medium Risk
  - Neither low risk nor high risk (as defined above)

# Baseline Demographics

## Risk Behavior

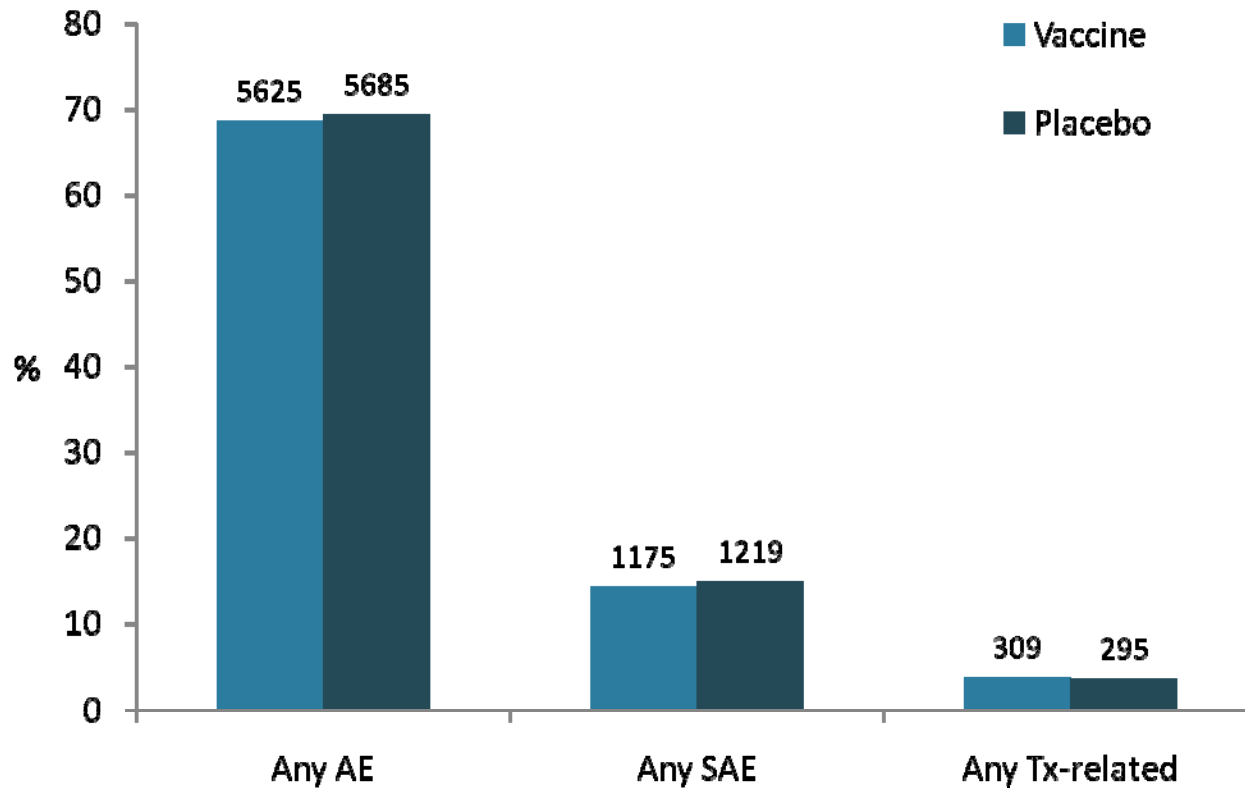


# RV 144

---

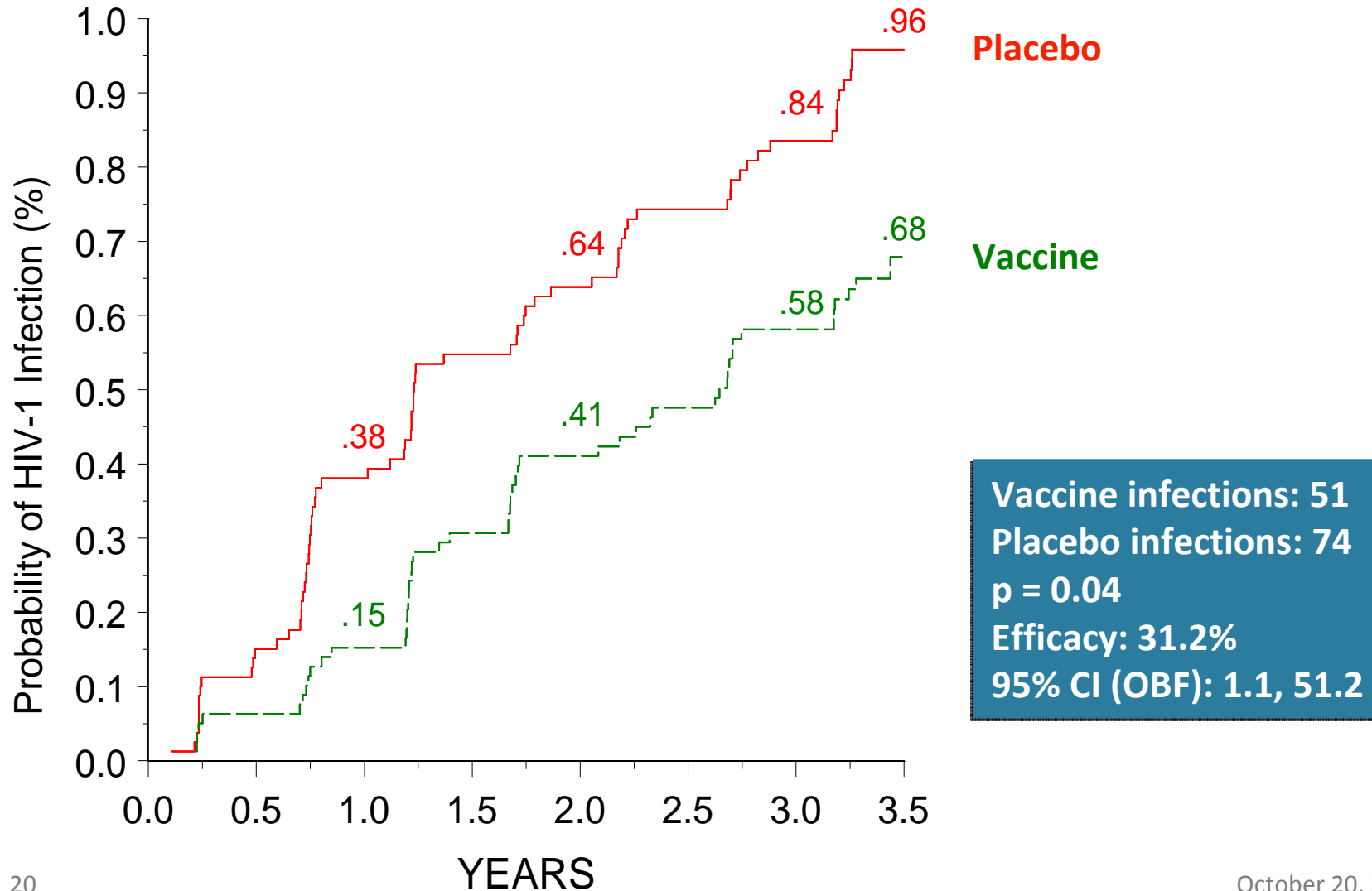
- Trial Objectives and Design
- Demographics
- Results

# Safety and Reactogenicity

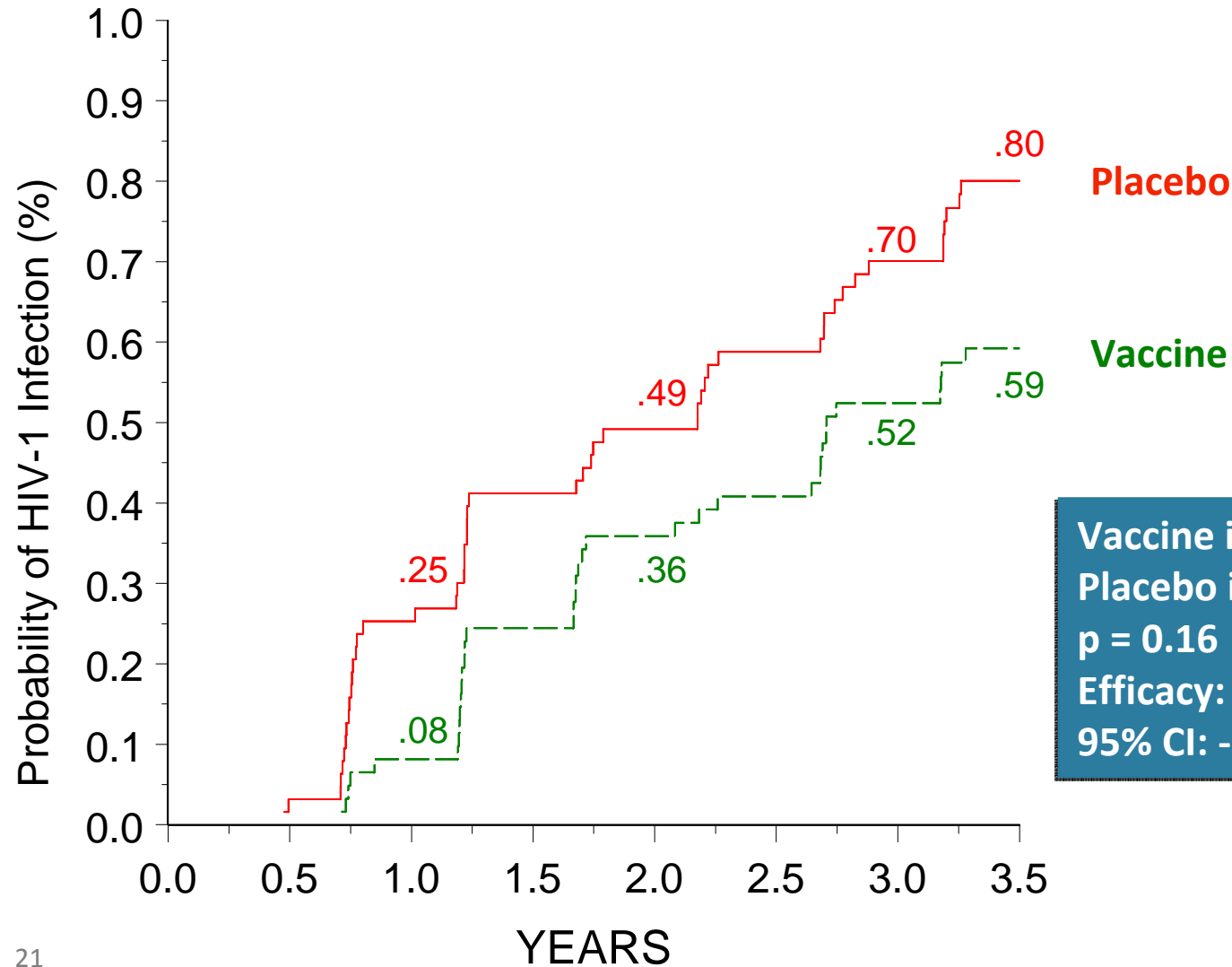


**The vaccine regimen was safe and well tolerated.**

# Acquisition Endpoint: Modified Intent-to-Treat (mITT)

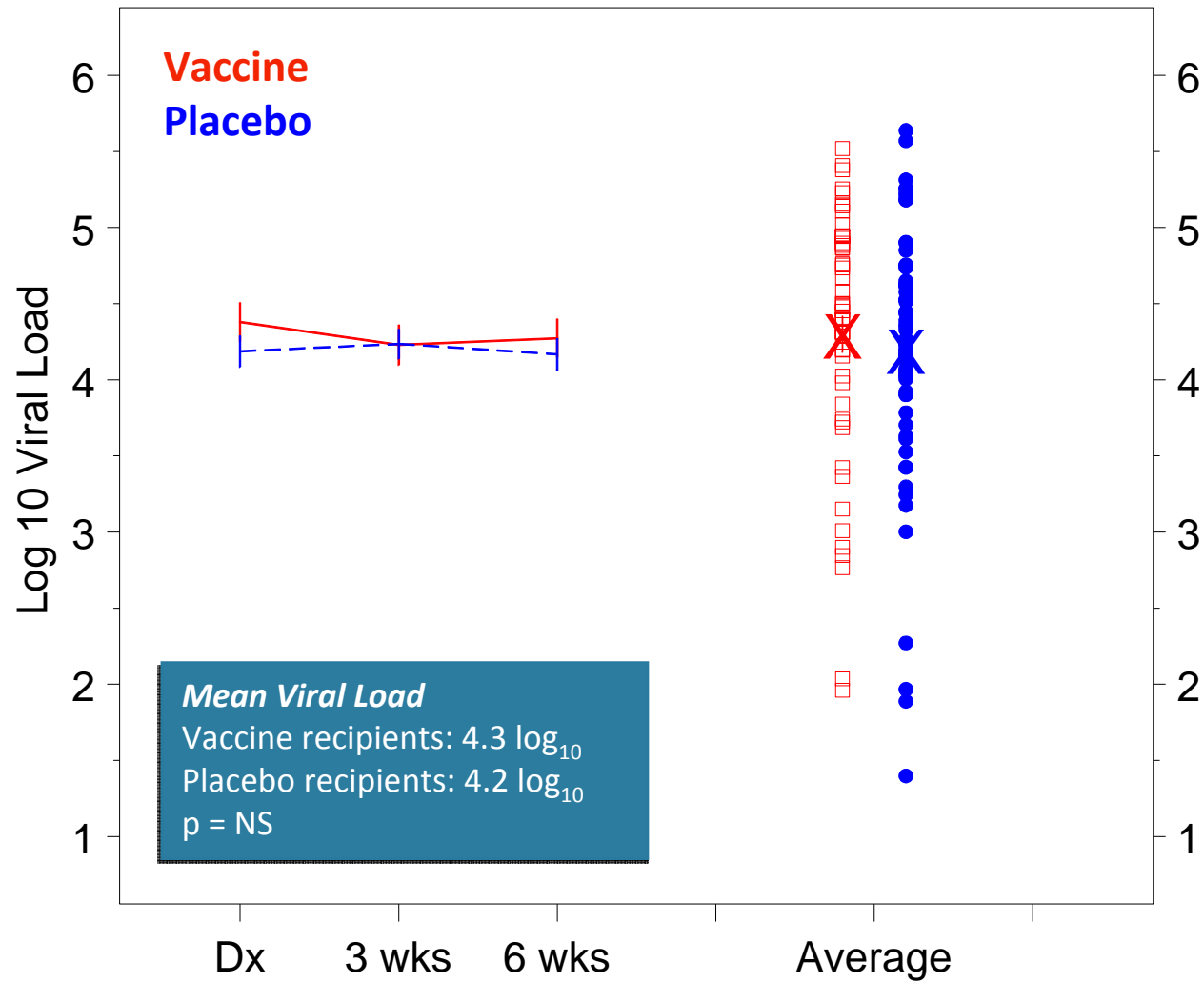


# Acquisition Endpoint: Per Protocol (PP)



Vaccine infections: 36  
Placebo infections: 50  
 $p = 0.16$   
Efficacy: 26.2%  
95% CI: -13.3, 51.9

# Early Viremia Endpoint



# Conclusions

---

1. The observed vaccine efficacy in the mITT analysis was 31.2% [ $p = 0.04$ , 95% CI (OBF) 1.1, 52.1].
2. PP and mITT results were qualitatively consistent.
3. There is no difference in early viremia between vaccine and placebo recipients.
4. The vaccine regimen is safe and well tolerated.
5. Self-reported behavioral risk was the same in vaccine and placebo groups.



# Acknowledgements

---

- **RV144 volunteers and community members**
- AFRIMS – US and Thai Component
- Division of AIDS, National Institute of Allergy and Infectious Diseases, NIH
- Faculty of Tropical Medicine, Mahidol University
- Global Solutions for Infectious Diseases
- Henry M. Jackson Foundation for the Advancement of Military Medicine
- Ministry of Public Health, Thailand
- sanofi pasteur
- U.S. Military HIV Research Program, Walter Reed Army Institute of Research; U.S. Army Medical Research and Materiel Command