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ALVAC®-HIV and AIDSVAX® B/E Prime-Boost HIV-1 Preventive Vaccine Regimen

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

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for the MOPH-TAVEG Collaboration

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The NEW ENGLAND JOURNAL of MEDICINE

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

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- Trial Objectives and Design
- Demographics
- Results

Trial Objectives

Primary

- To determine whether immunization with ALVAC ®-HIV (vCP1521) boosted by AIDSVAX® 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®-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)**.

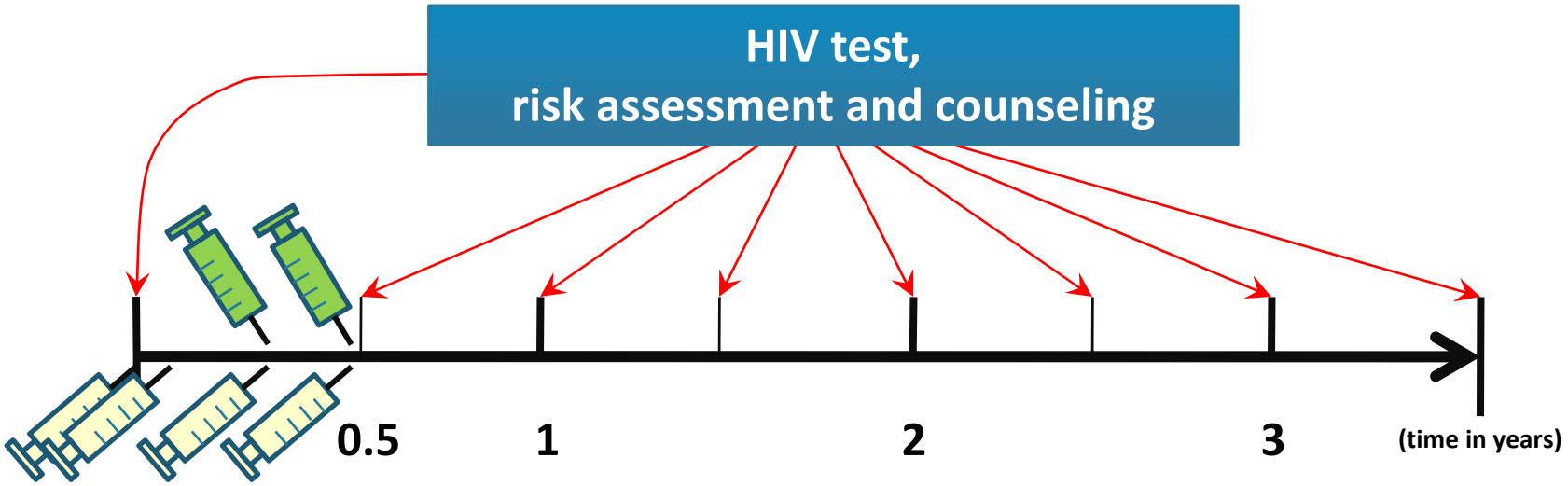
AIDSVAX® B/E

- 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



6-month vaccination schedule

3 years of follow-up (every 6 mo.)

ALVAC®-HIV (vCP1521) priming at week 0, 4, 12, 24

AIDSVAX® B/E gp120 boosting at week 12, 24

Important Milestones

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

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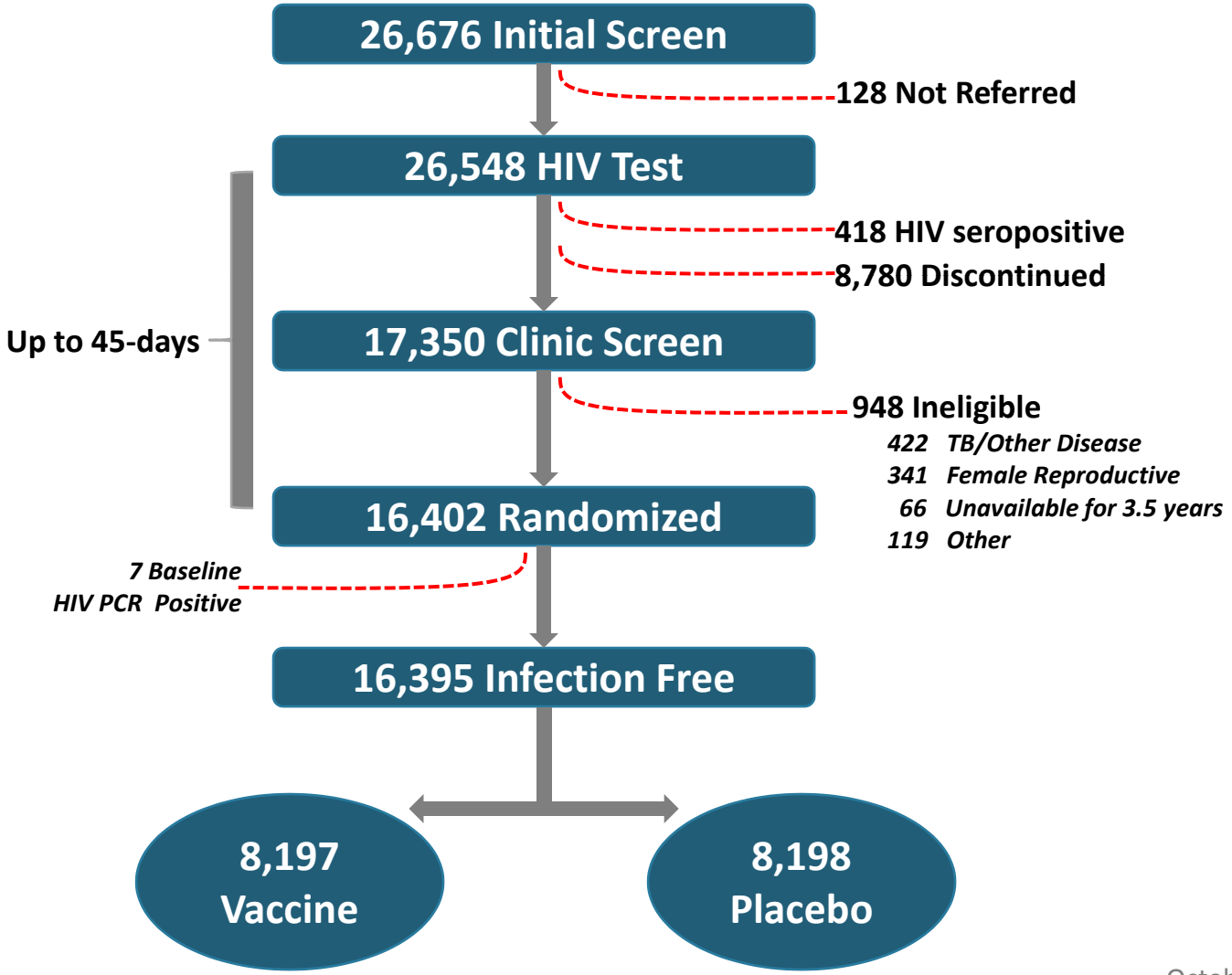
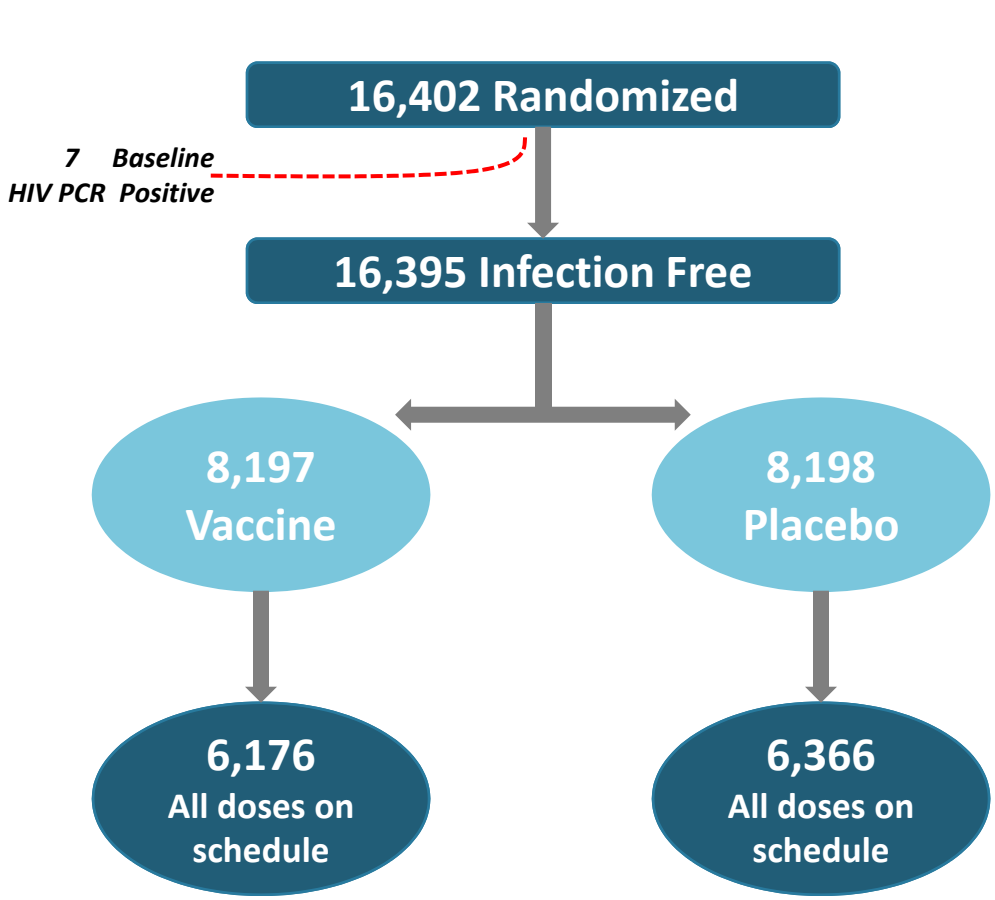
From Screening to Vaccination



Definition of Analytical Methods



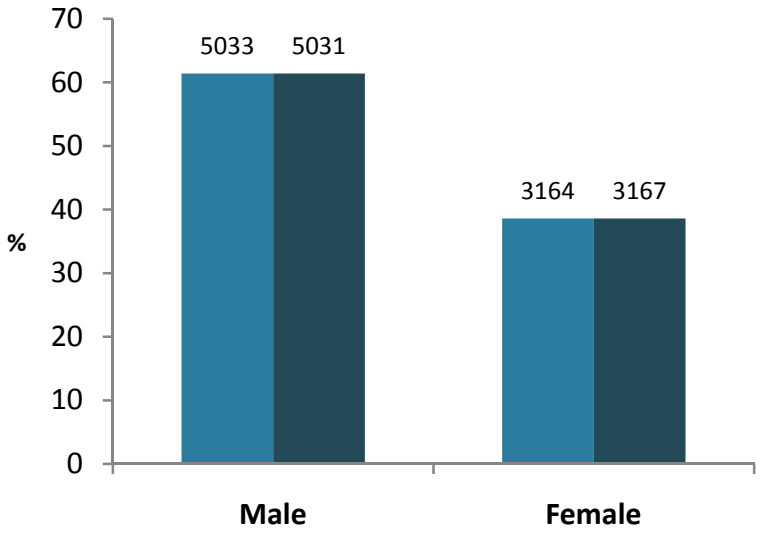
Intent-to-Treat (ITT)

Modified Intent-to-Treat (mITT)

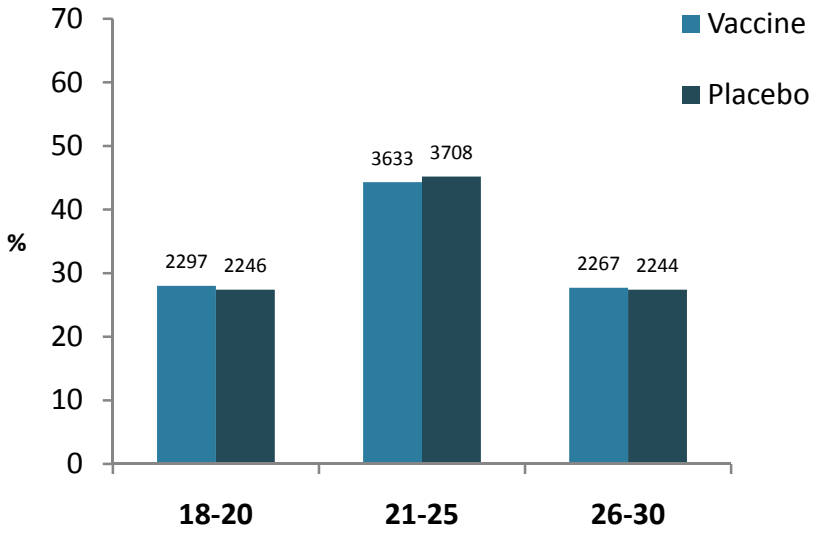
Per Protocol (PP)

Baseline Demographics

Gender

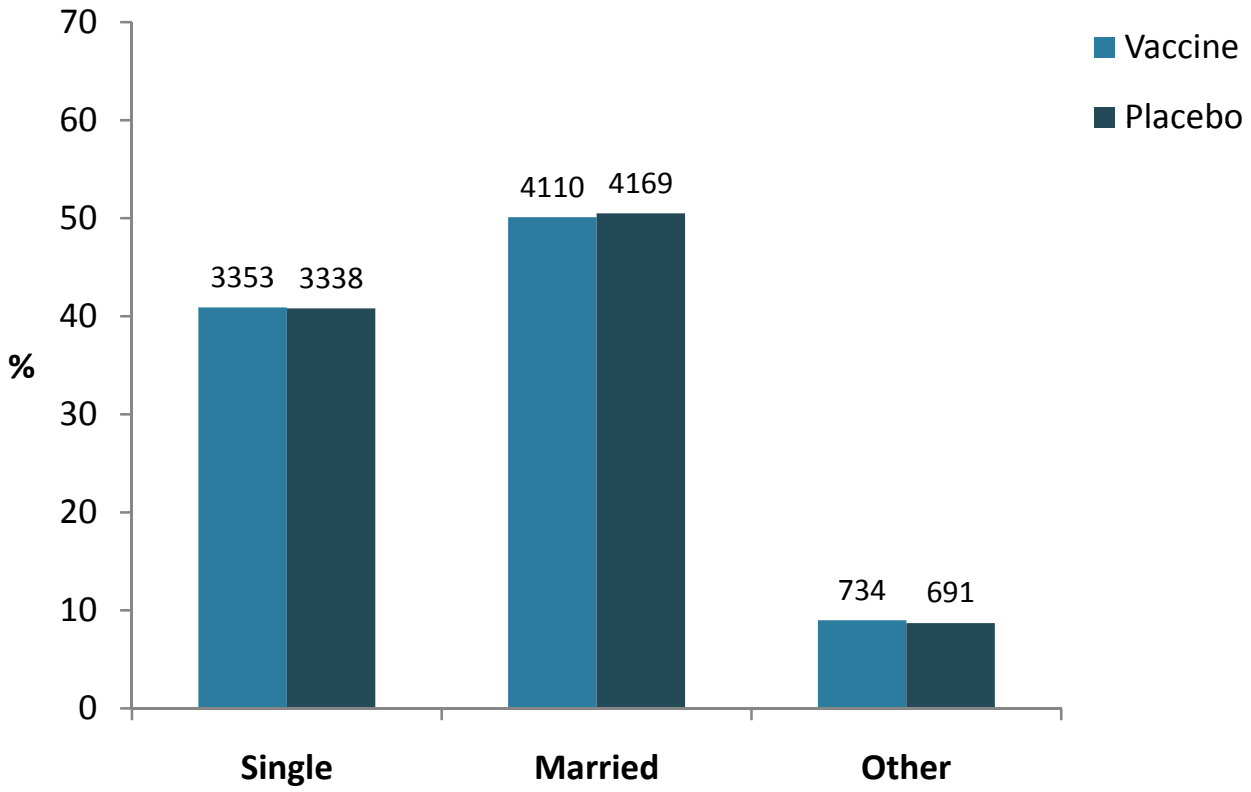


Age



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

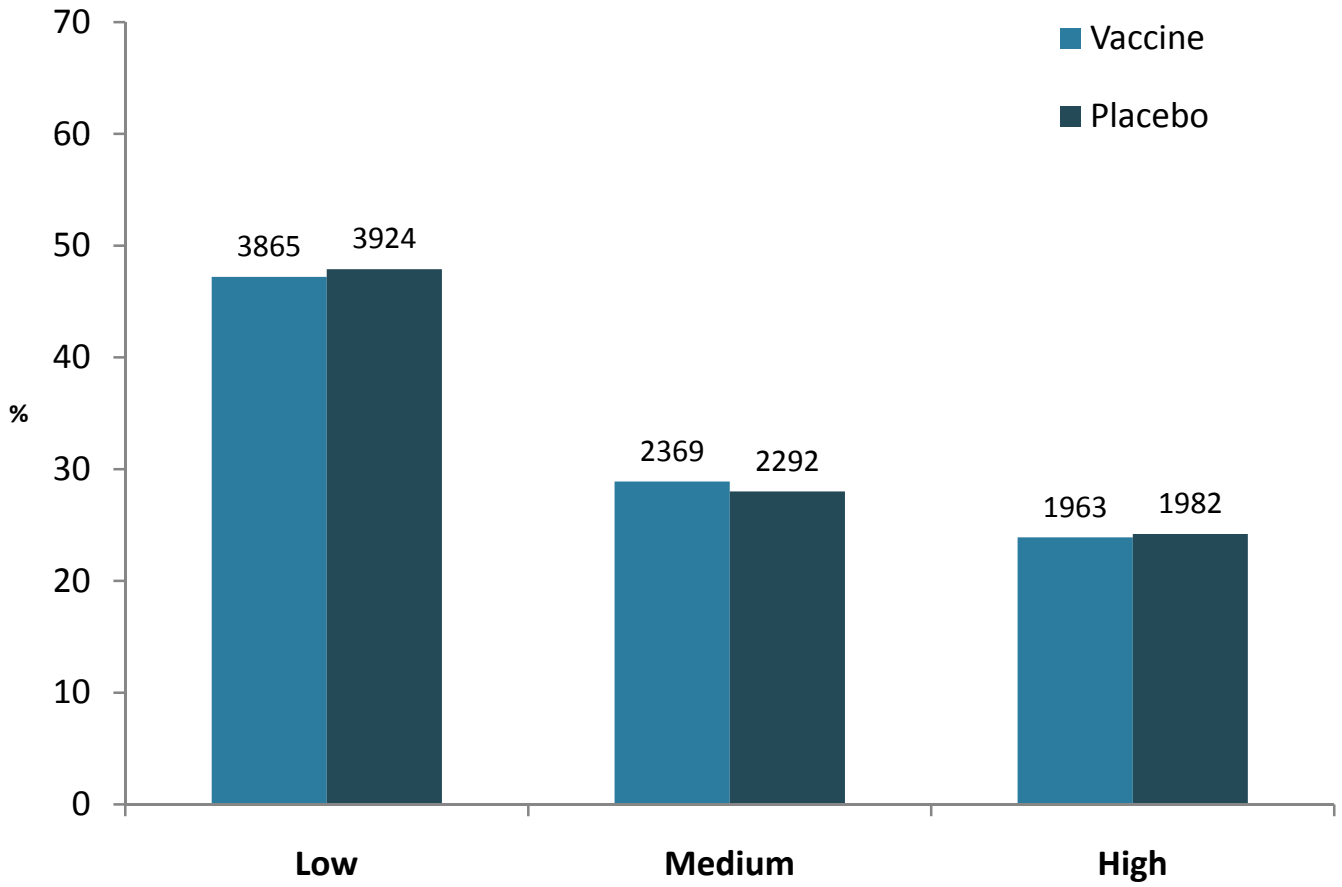
	Vaccine n (%)	Placebo n (%)
Sexual Partner Frequency		
0 Sex Partners	1864 (22.7)	1801 (22.0)
1 Sex Partner	5428 (66.2)	5495 (67.0)
>1 Sex Partners	619 (7.6)	620 (7.6)
No Answer	280 (3.4)	273 (3.3)
Missing Value	6 (0.1)	9 (0.1)
Other Risk Behaviors ***(from a list of 8 criteria)***		
Same-gender partner	184 (2.2%)	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



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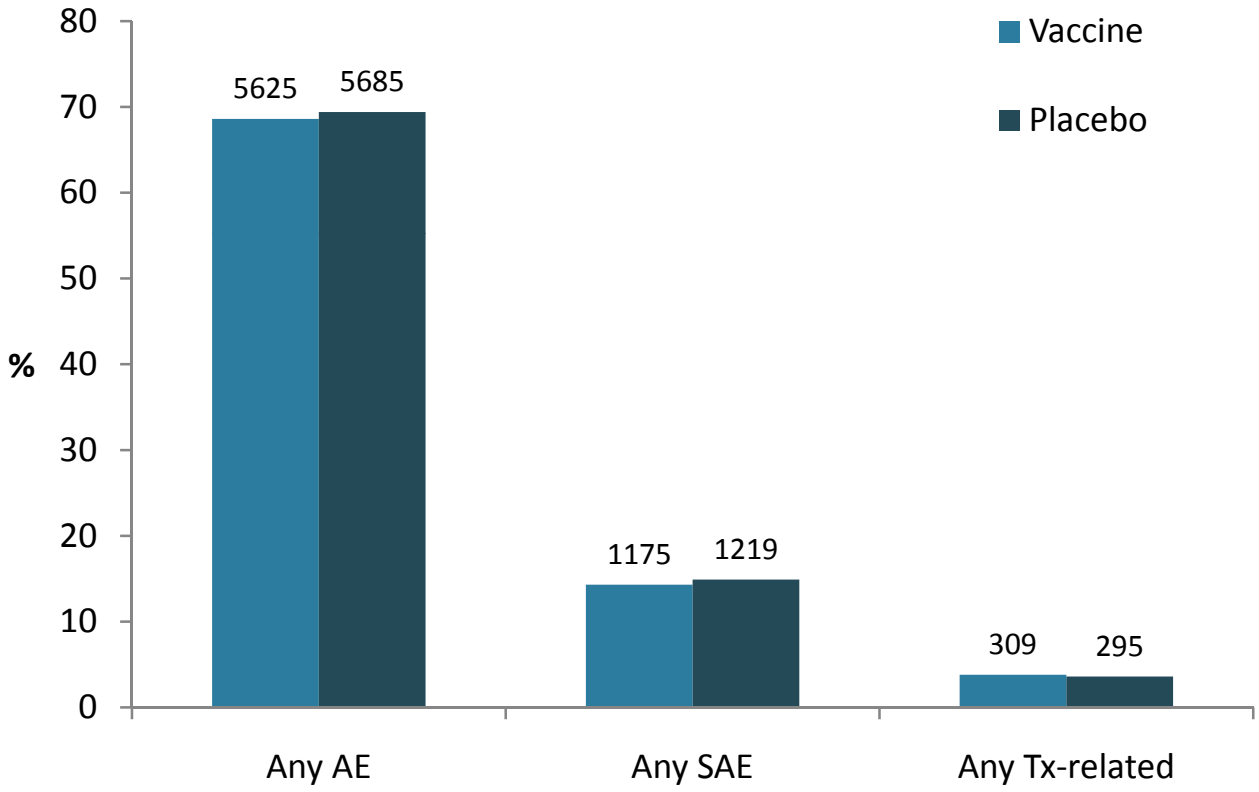
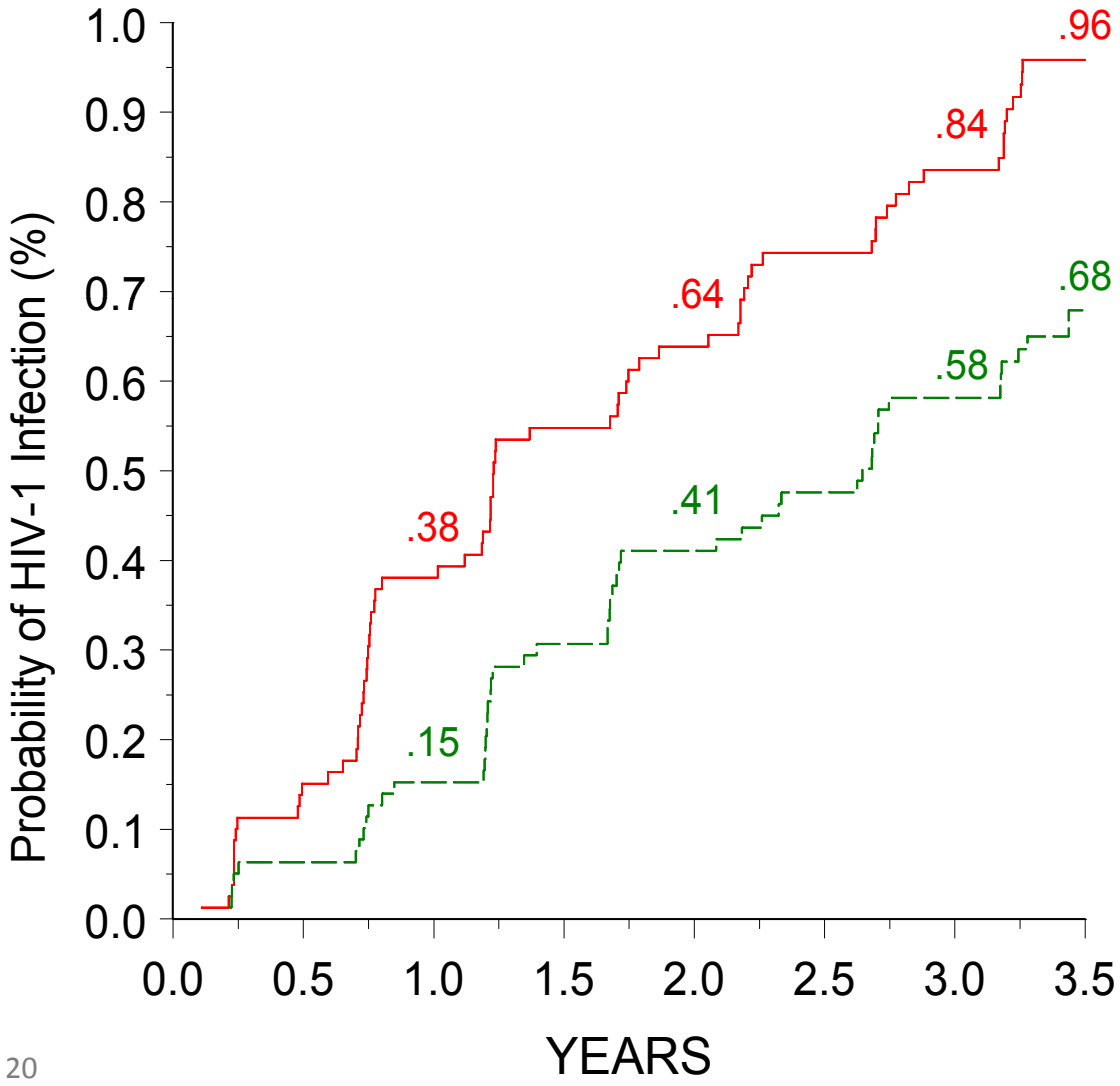
Safety and Reactogenicity



The vaccine regimen was safe and well tolerated.

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

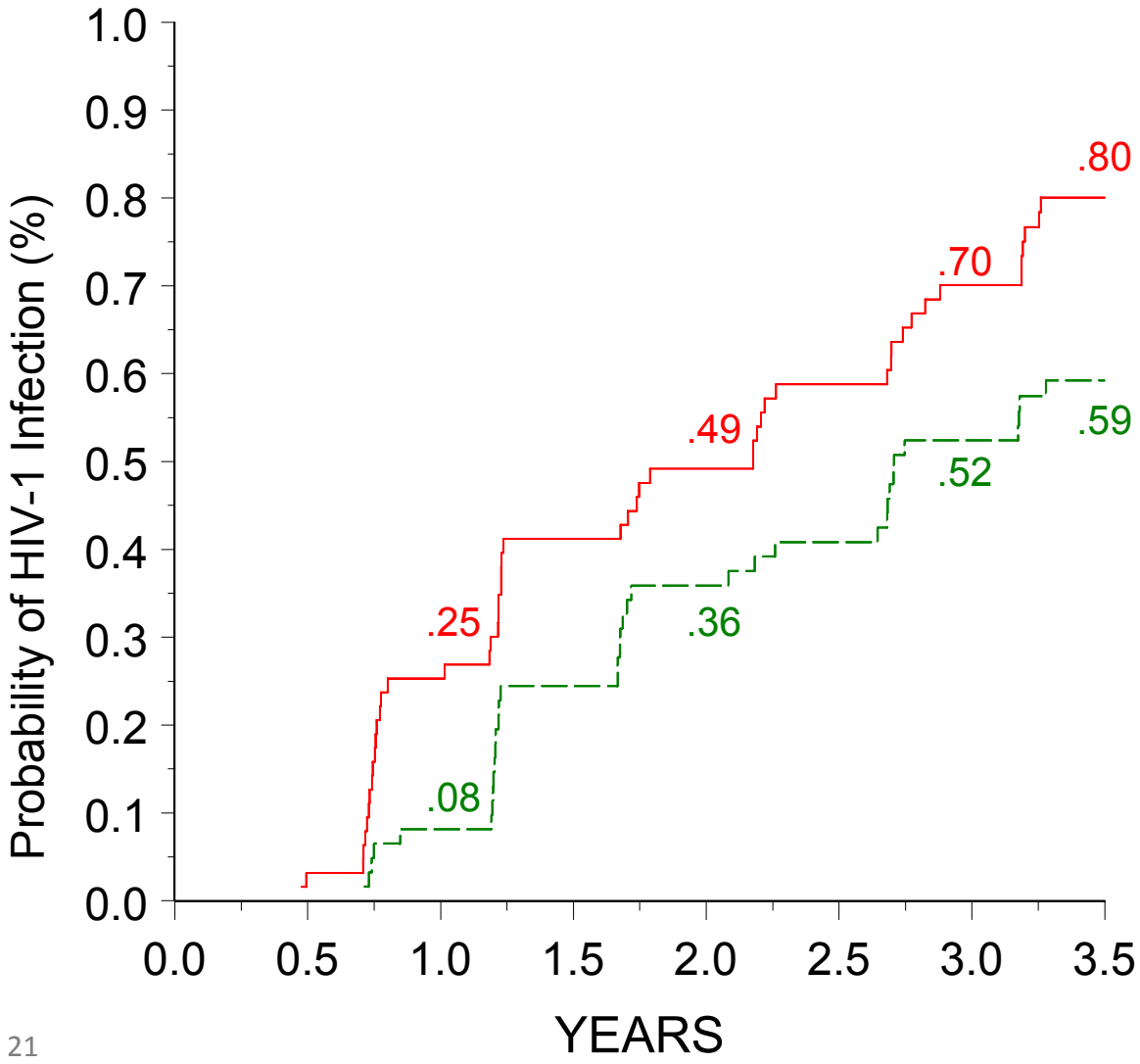


Placebo

Vaccine

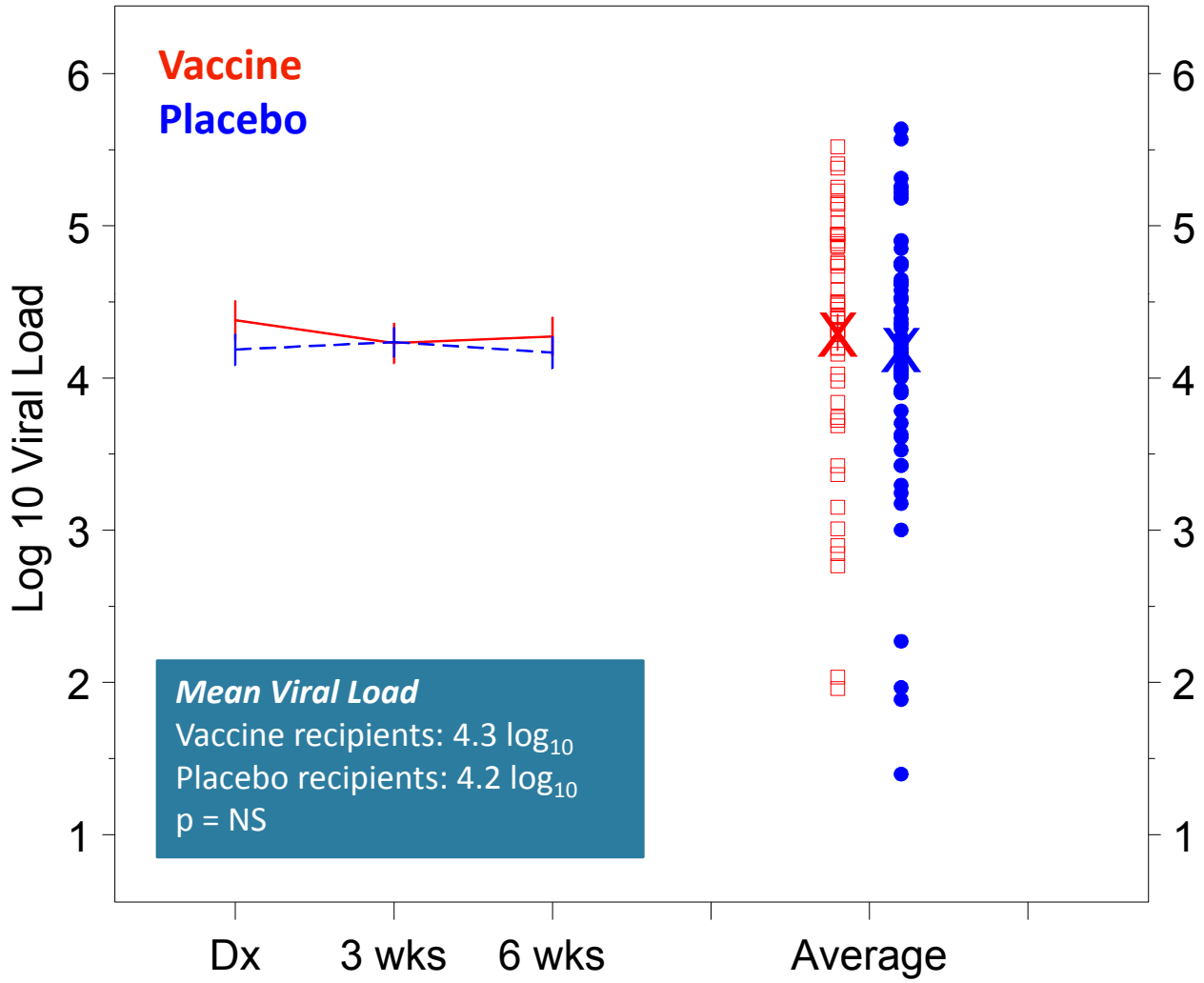
Vaccine infections: 51
Placebo infections: 74
p = 0.04
Efficacy: 31.2%
95% CI (OBF): 1.1, 51.2

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

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