

***Extended Evaluation of  
the Virologic, Immunologic, and Clinical Course of  
Volunteers Who Became HIV-1 Infected  
During Participation in a Phase III Vaccine Trial (RV152)***

**Final Results**

**Vaccines and Other Prevention Strategies  
AIDS Vaccine Conference 2011**

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for the MOPH-TAVEG Collaboration



# Outline

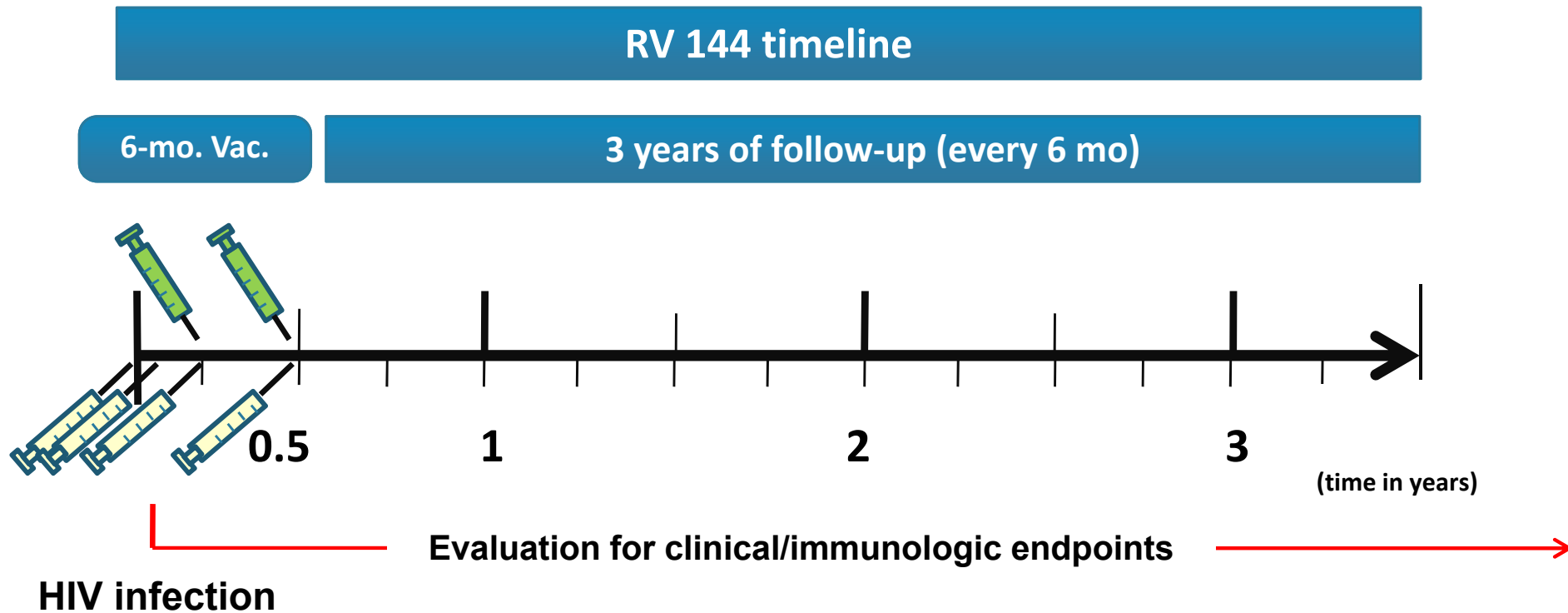
- Background, Trial Objectives, and Design
- Demographics
- Results



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# RV 152 in relation to RV 144



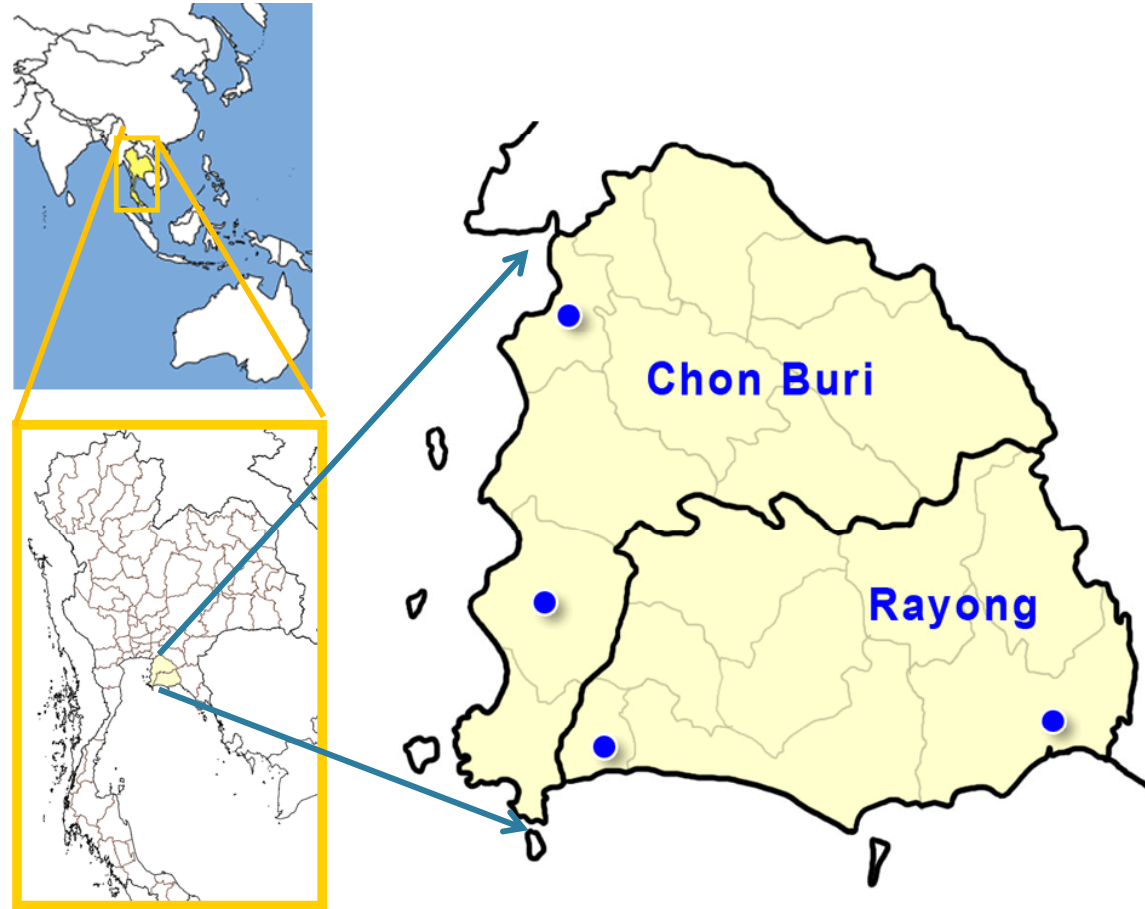
## RV 152 Timeline (every 3 mo. after infection) Concurrent with RV 144

 ALVAC<sup>®</sup>-HIV (vCP1521) priming at week 0, 4, 12, 24

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

# RV 152 Study procedures

- Four sites in two provinces
- Mucosal viral load at visit 1
  - Cervico-vaginal lavage
  - Semen
- Every 3 months visits
  - History and physical exam
  - HIV counseling
  - CD4 and viral load testing
  - Endpoint assessment
- Immunologic assessment every 6 months



# Endpoints/Objectives

## ■ Primary Composite Endpoint

- CD4 < 350 cells/ $\mu$ L (verified by two measurements at least two-weeks apart)
- AIDS-defining illness (first documented event)
- Initiation of ARVs (per Thai National Guidelines)

## ■ Secondary Objectives

- Long-term clinical outcomes—progression of disease (AIDS-defining illness and death)
- Longitudinal trajectory of pre-HAART CD4<sup>+</sup>/viral load
- Mucosal viral load at visit 1



# Statistical Analysis Plan

- **mITT:** HIV-uninfected at first RV144 visit, receipt of at least 1 dose of vaccine and one follow-up visit in RV 152
- **Per protocol:** receipt of all 4 doses and HIV-uninfected at 6-month visit in RV 144
- **Time-to-event analyses** evaluated the time between the estimated date of HIV-1 infection and endpoints measuring HIV-1 progression
- **The primary analysis** evaluated a vaccine efficacy parameter,  $VE_p(T_A)$ , defined as the percent reduction (vaccine vs. placebo) in the cumulative probability of the primary composite endpoint by  $T_A$  months after the estimated date of infection, with  $T_A$  pre-specified at 30, 42, 54, and 66 months

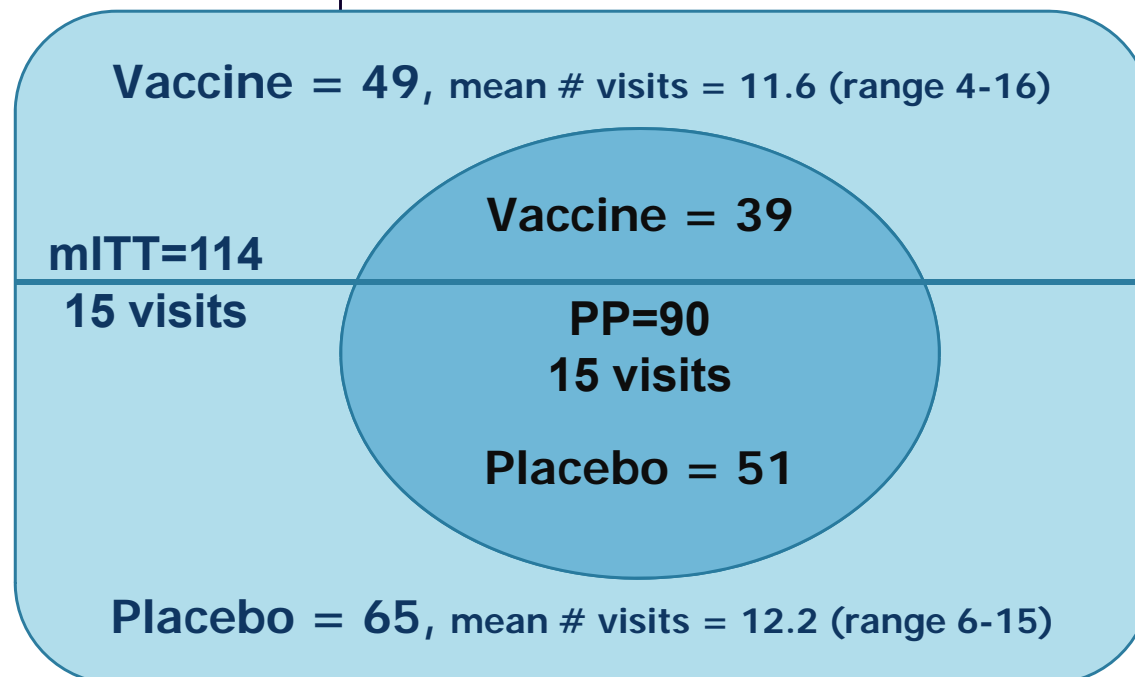


# From RV144 to RV152

16,402 Randomized to RV144

132 infected in RV144

120 enrolled to RV152



**mITT cohort**  
- Vaccine or placebo  
at least 1 time

**PP cohort**  
- Vaccine or placebo  
all 4 times per schedule

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# RV 152 mITT participant demographics

	Total(n=114) # (%)	Vaccine(n=49) # (%)	Placebo(n=65) # (%)	P-value
<b>Sex at birth</b>				
Male	67 (58.8)	30 (61.2)	37 (56.9)	0.64
Female	47 (41.2)	19 (38.8)	28 (43.1)	
<b>Age</b>				
<=20	22 (19.3)	12 (24.5)	10 (15.4)	0.27
21-25	51 (44.7)	18 (36.7)	33 (50.8)	
>=26	41 (36.0)	19 (38.8)	22 (33.8)	
<b>Risk Group</b>				
Low	45 (39.5)	17 (34.7)	28 (43.1)	0.41
Medium	28 (24.6)	11 (22.4)	17 (26.2)	
High	41 (36.0)	21 (42.9)	20 (30.8)	
<b>Calendar Year of Infection Diagnosis</b>				
2004-2005	30 (26.3)	13 (26.5)	17 (26.2)	0.09
2006	39 (34.2)	13 (26.5)	26 (40.0)	
2007	27 (23.7)	17 (34.7)	10 (15.4)	
2008-2009	18 (15.8)	6 (12.2)	12 (18.5)	
<b>Receiving Treatment During Pregnancy</b>				
Yes	13 (27.7)	7 (36.8)	6 (21.4)	0.25
No	34 (72.3)	12 (63.2)	22 (78.6)	



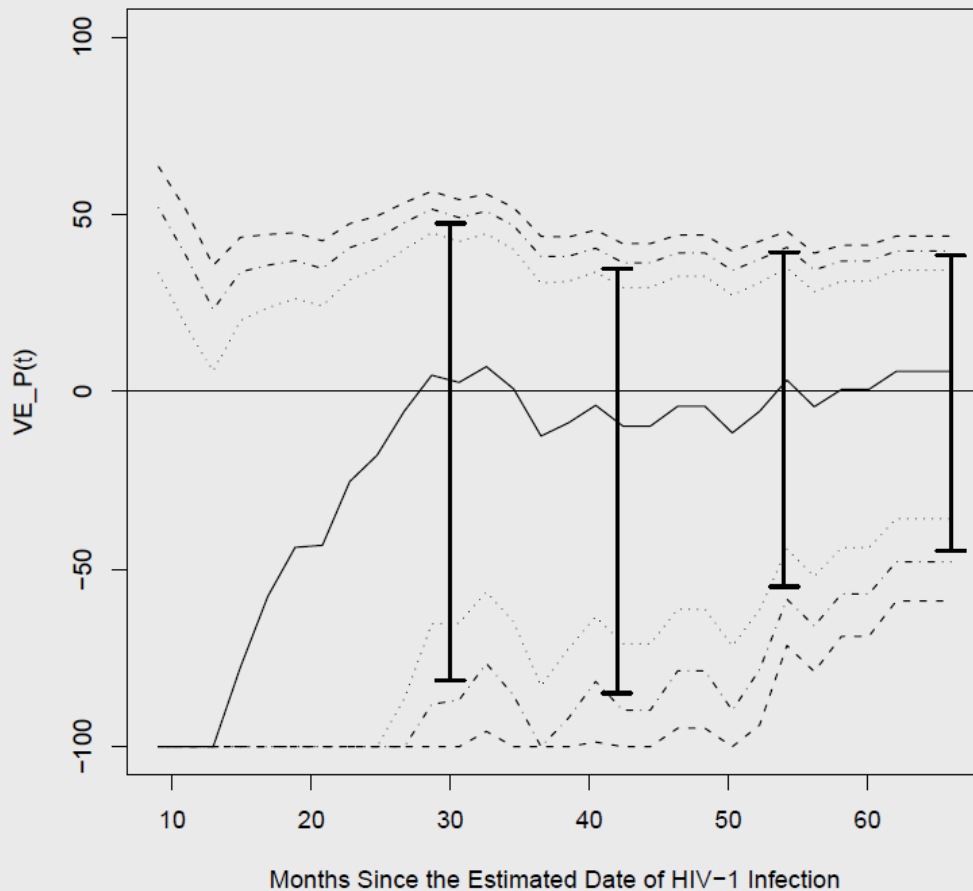
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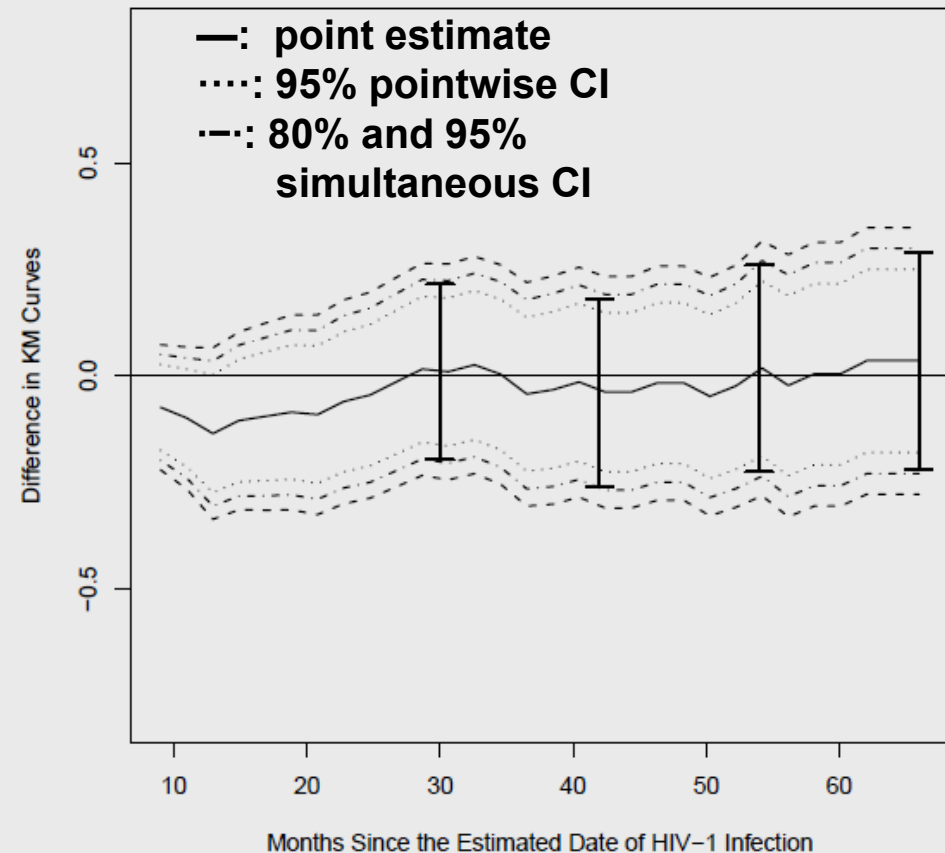


# Vaccine effect on primary composite endpoint in mITT cohort over time

(a) Estimated vaccine effect on disease progression



(b) Estimated survival probability difference

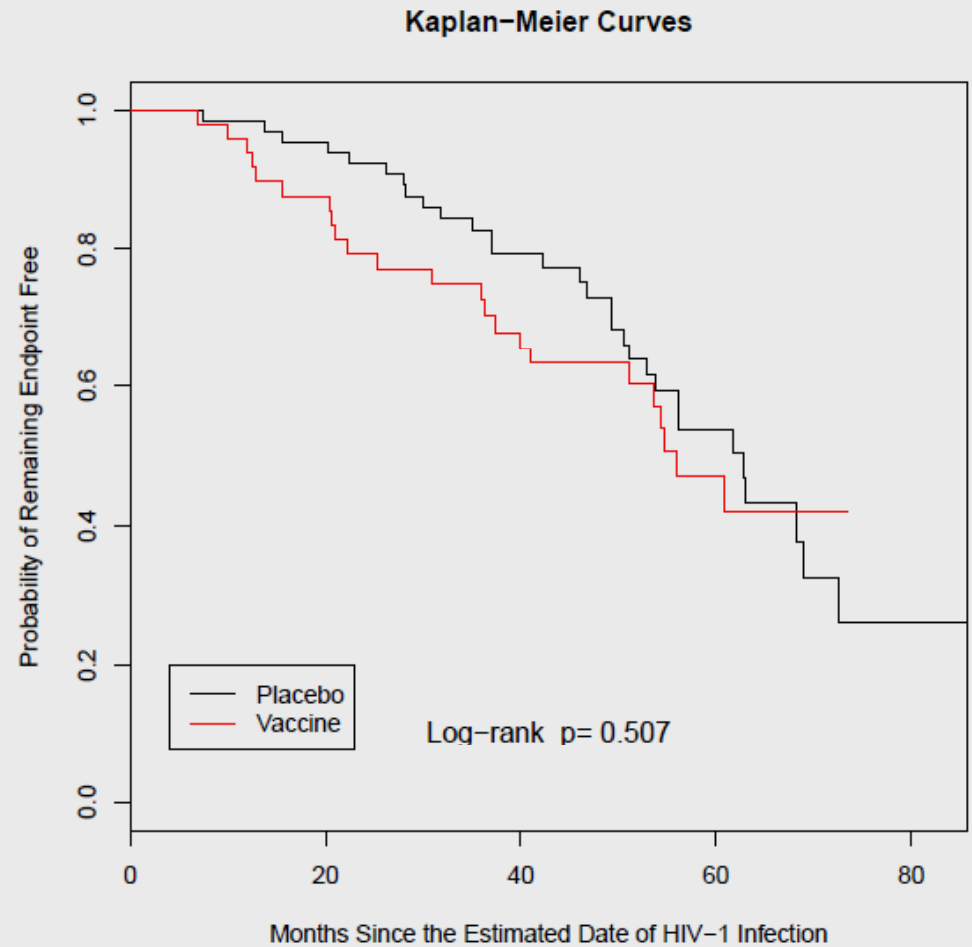
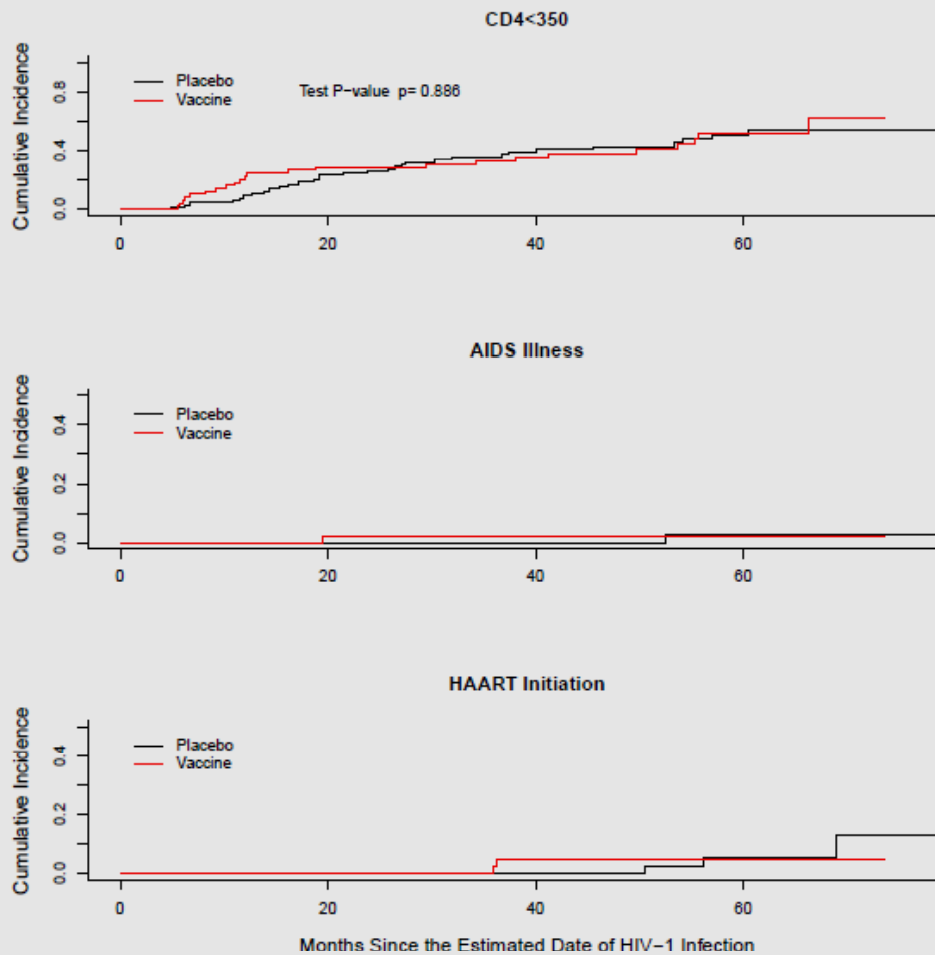


\*The primary analysis assesses the vaccine effect at the fixed time-points 30, 42, 54, and 66 months after the estimated date of HIV-1 infection, with 95% simultaneous confidence intervals (bold vertical segments are simultaneous 95% confidence intervals for the four pre-specified post-infection time-points, 30, 42, 54, 66 months).

# No vaccine effect on component primary endpoints or HAART initiation over time

(a) Component endpoints

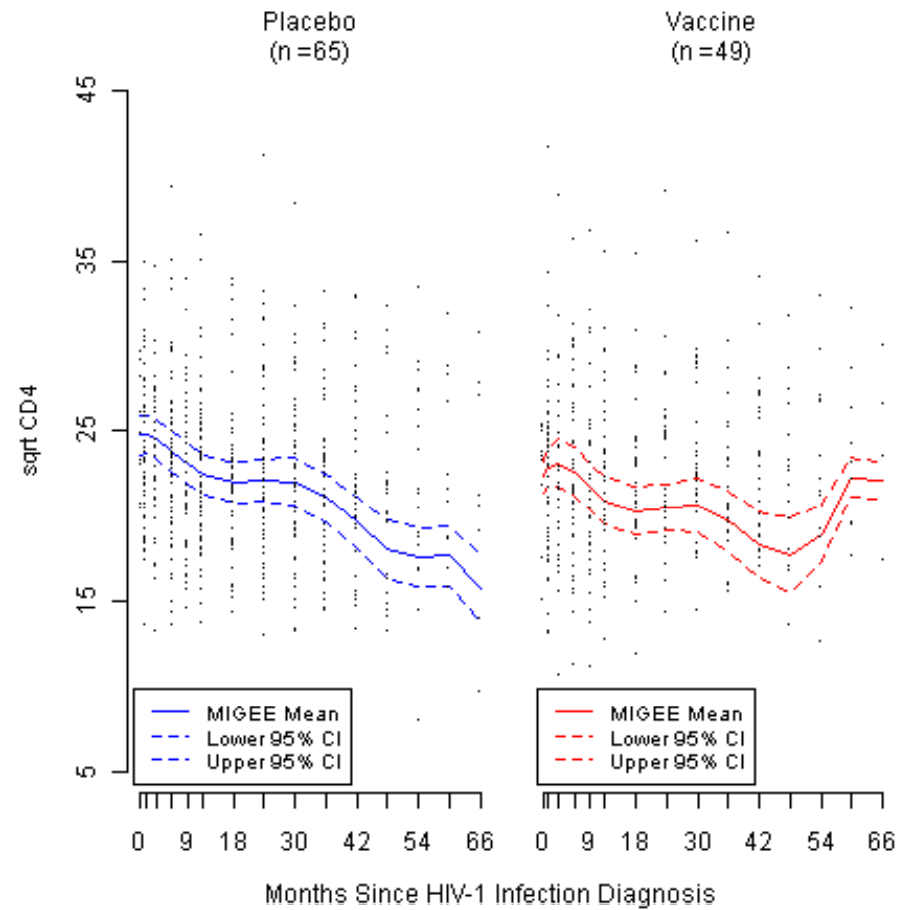
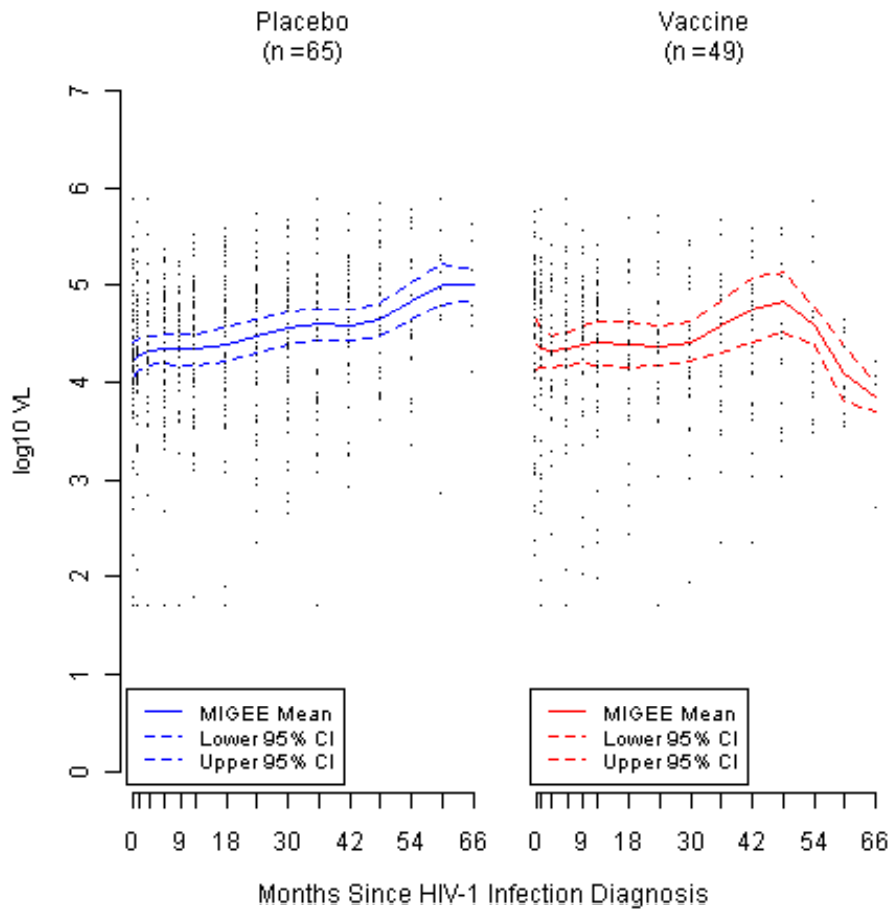
(b) HAART initiation



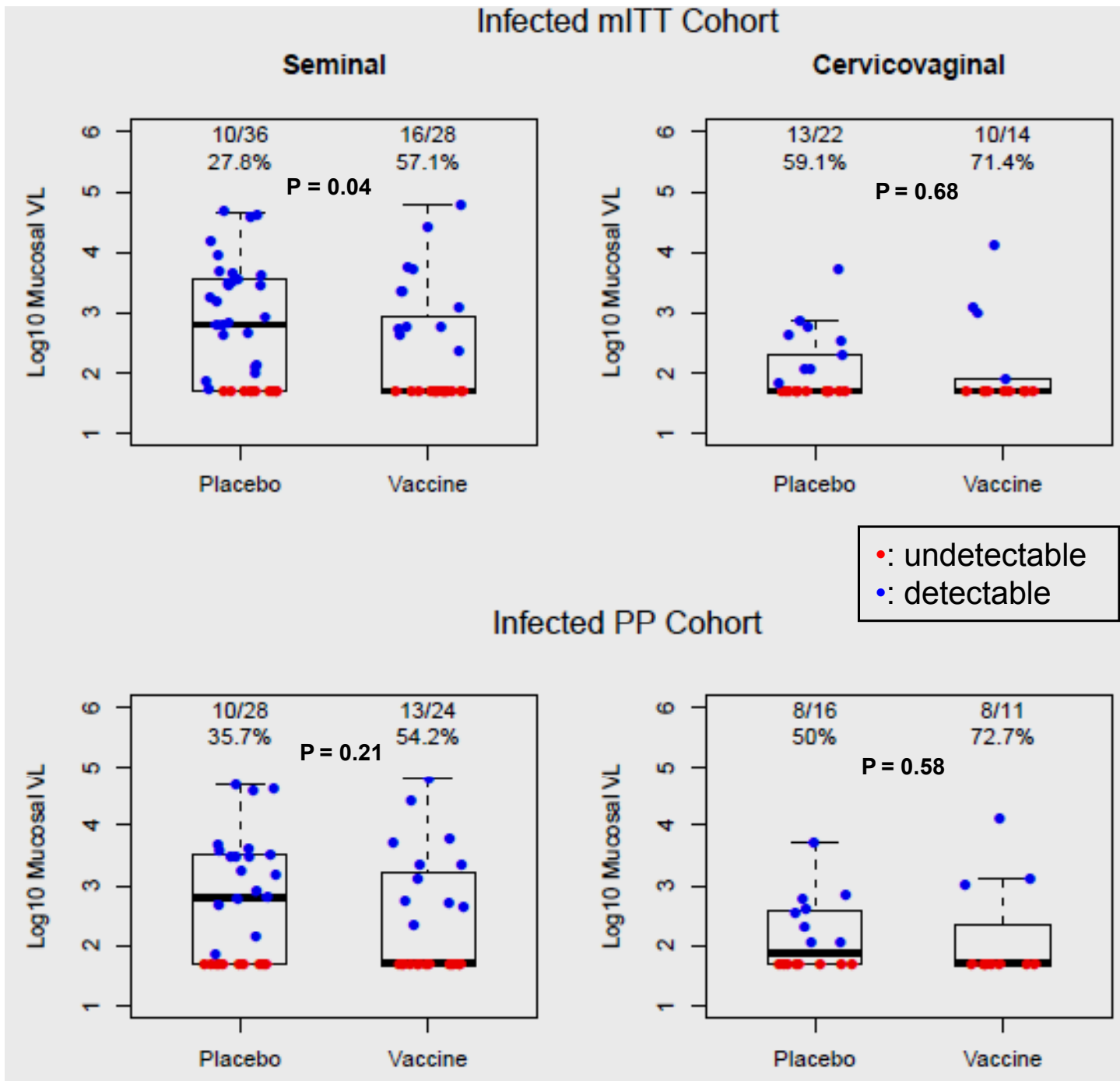
# Pre-HAART mean viral loads and mean CD4+ T cell counts diverge at 48 month after HIV-1 infection diagnosis (mITT cohort)

(a) pre-HAART  $\log_{10}$  viral loads

(b) pre-HAART square-root CD4+ T cell counts



# Lower pre-HAART viral loads in mucosal fluid in vaccine compared to placebo recipients



# Summary

- The vaccine regimen is safe
- There was no evidence of a vaccine effect on the composite endpoint
- No difference between vaccine and placebo plasma viral load at 12 (4.38 log<sub>10</sub>/mL:4.34 log<sub>10</sub>/mL, p=0.90) or 18 months after infection (4.32 log<sub>10</sub>/mL:4.44 log<sub>10</sub>/mL, p=0.69)
- Divergence in viral load and CD4 trajectory between vaccine vs. placebo recipients beyond month 48
- Vaccination was associated with lower viral loads in the seminal fluid (p=0.04); [P14.13 LB]



# ACKNOWLEDGEMENTS

- RV144 and RV152 volunteers and community members
- Participants in Phase I/II ALVAC and AIDSVAX B/E trials

