HIV Vaccines: A Clinician's Perspective

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June 22, 2022

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Disclosures

I have no disclosures.

AETC Program National Centers and HIV Curriculum

- **National Coordinating Resource Center –** serves as the central web –based repository for AETC Program training and capacity building resources; its website includes a free virtual library with training and technical assistance materials, a program directory, and a calendar of trainings and other events. Learn more: https://aidsetc.org/
- **National Clinical Consultation Center –** provides free, peer-to-peer, expert advice for health professionals on HIV prevention, care, and treatment and related topics. Learn more: https://nccc/ucsf.edu
- **National HIV Curriculum –** provides ongoing, up –to-date HIV training and information for health professionals through a free, web –based curriculum; also provides free CME credits, CNE contact hours, CE contact hours, and maintenance of certification credits. Learn more: www.hiv.uw.edu

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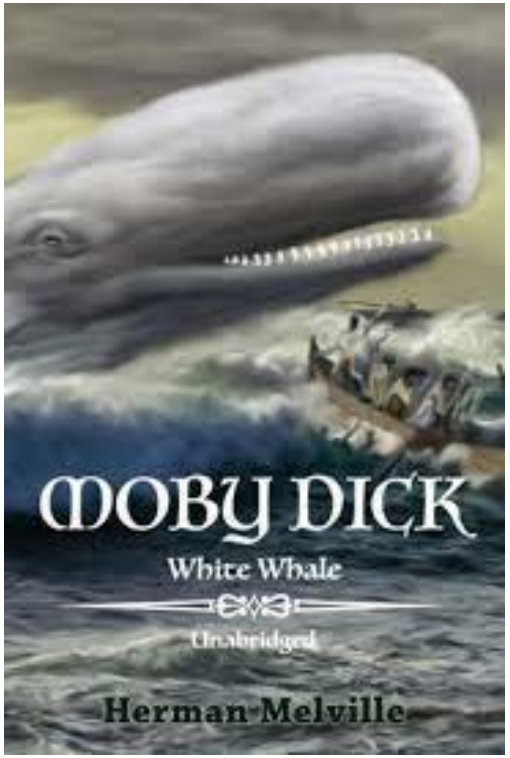
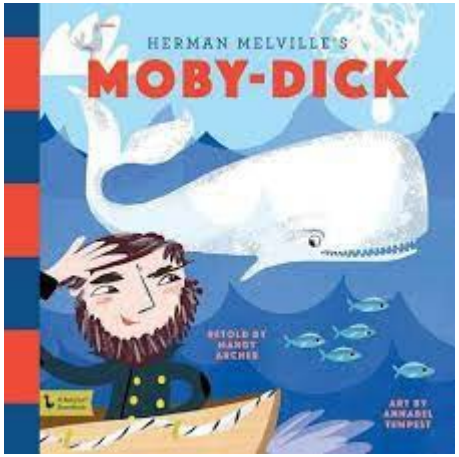
Objectives

- Review landmark clinical trials in the HIV Vaccine Space
- Discuss the evolution of the HIV Vaccine Landscape
- Discuss current challenges facing HIV Vaccine Development





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The NEW ENGLAND JOURNAL of MEDICINE

Perspective

JULY 2, 2020

A HALF-CENTURY OF PROGRESS IN HEALTH: THE NATIONAL ACADEMY OF MEDICINE AT 50

Four Decades of HIV/AIDS — Much Accomplished, Much to Do

Anthony S. Fauci, M.D., and H. Clifford Lane, M.D.

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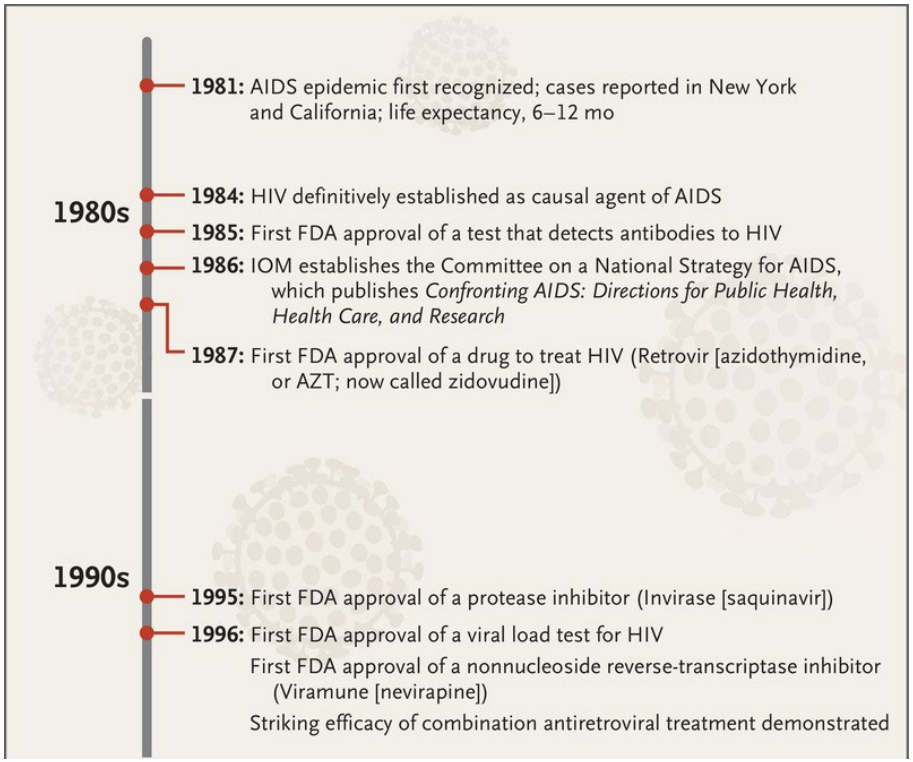
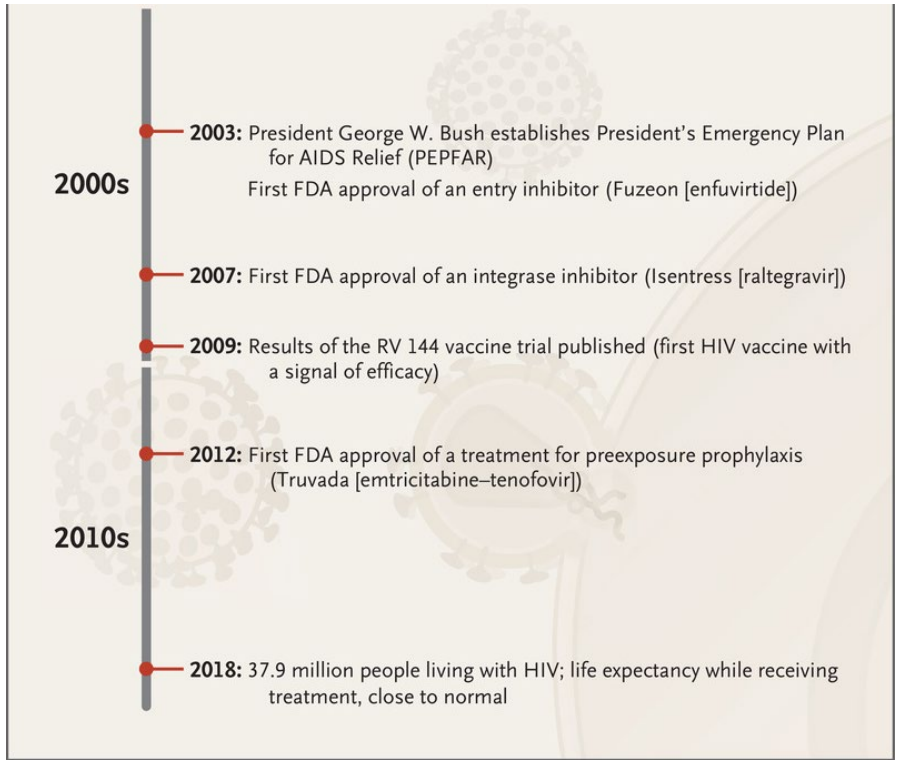
The goal of our historic four-decade-long journey to end the global HIV epidemic, however, will be reached only when we have a safe and effective vaccine and have addressed the remaining implementation challenges. – Dr. Tony Fauci

The goal of our historic four-decade-long journey to end the global HIV epidemic, however, will be reached only when we have a safe and effective vaccine and have addressed the remaining implementation challenges.





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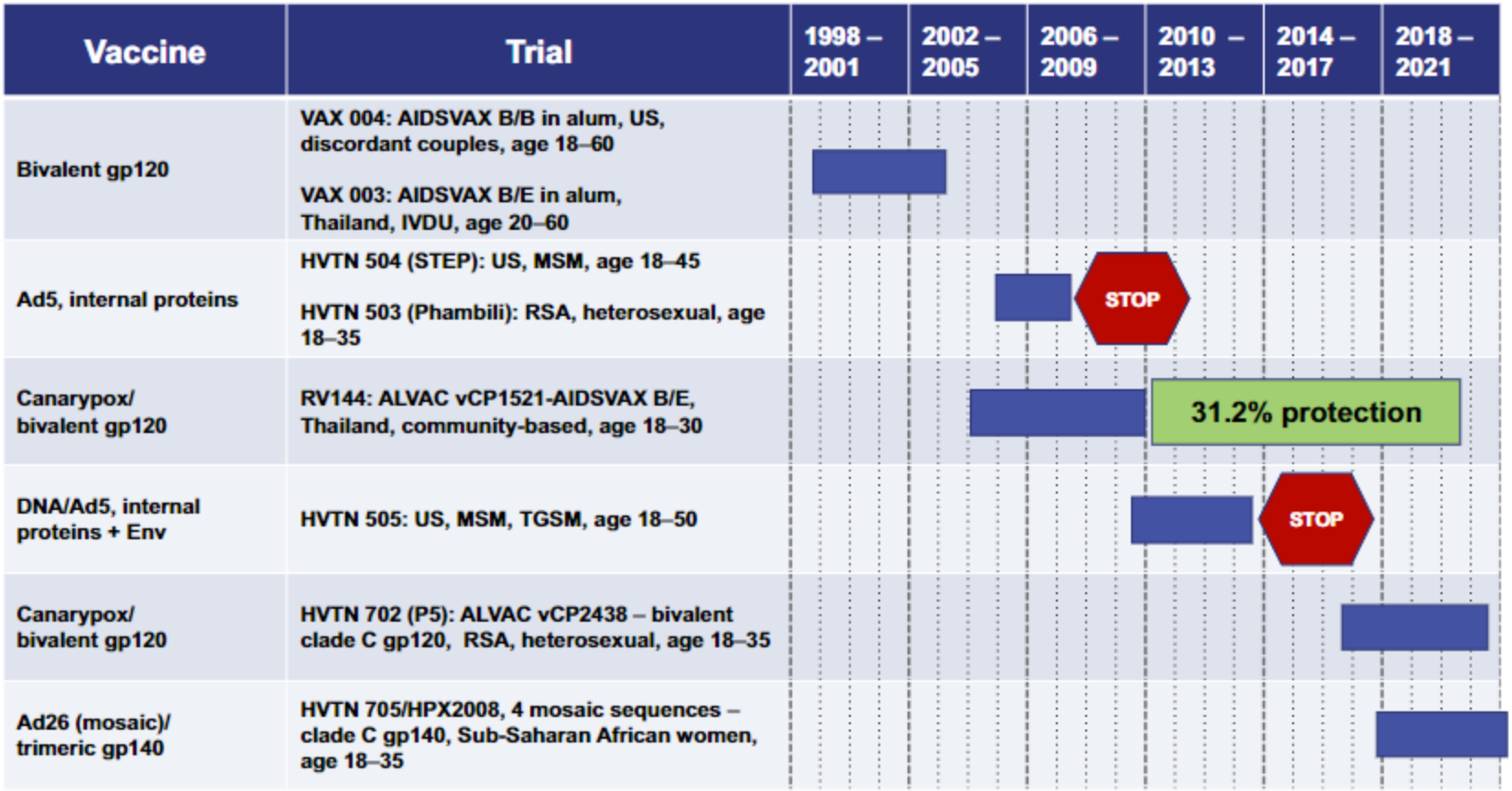

Figure 1 Timeline for human immunodeficiency virus (HIV) vaccine efficacy trials. Years at the top are for 4-year intervals, individual years are designated by dotted lines. Ad5, adenovirus serotype 5 vector; Ad26, adenovirus serotype 26 vector; ALVAC, canarypox vector; HVTN, HIV Vaccine Trials Network; IVDU, intravenous drug users; MSM, men who have sex with men; RSA, Republic of South Africa; TGSM, male to female transgender individuals who have sex with men; US, United States; VCP, canary pox vector.

[1]GeoVax, Inc., Smyrna, Georgia, USA. Harriet L. Robinson (hrobinson@geovax.com)

Received 22 June 2018; accepted 30 July 2018; advance online publication 9 October 2018.doi:10.1002/cpt.1208

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Randomized, Double-Blind, Placebo-Controlled Efficacy Trial of a Bivalent Recombinant Glycoprotein 120 HIV-1 Vaccine among Injection Drug Users in Bangkok, Thailand

Punnee Pitisuttithum,[1] Peter Gilbert,[4] Marc Gurwith,[5] William Heyward,[5] Michael Martin,[3] Fritz van Griensven,[3] Dale Hu,[6] Jordan W. Tappero,[3] and Kachit Choopanya,[2] for the Bangkok Vaccine Evaluation Group*

[1]Department of Clinical Tropical Medicine, Mahidol University, and [2]Bangkok Metropolitan Administration, Bangkok, and [3]Thailand Ministry of Public Health–US Centers for Disease Control and Prevention Collaboration, Nonthaburi, Thailand; [4]Statistical Center for HIV/AIDS Research and Prevention, Fred Hutchinson Cancer Research Center, Seattle, Washington; [5]VaxGen, Inc., Brisbane, California; [6]US Centers for Disease Control and Prevention, Atlanta, Georgia

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VAX003 - Trial Design

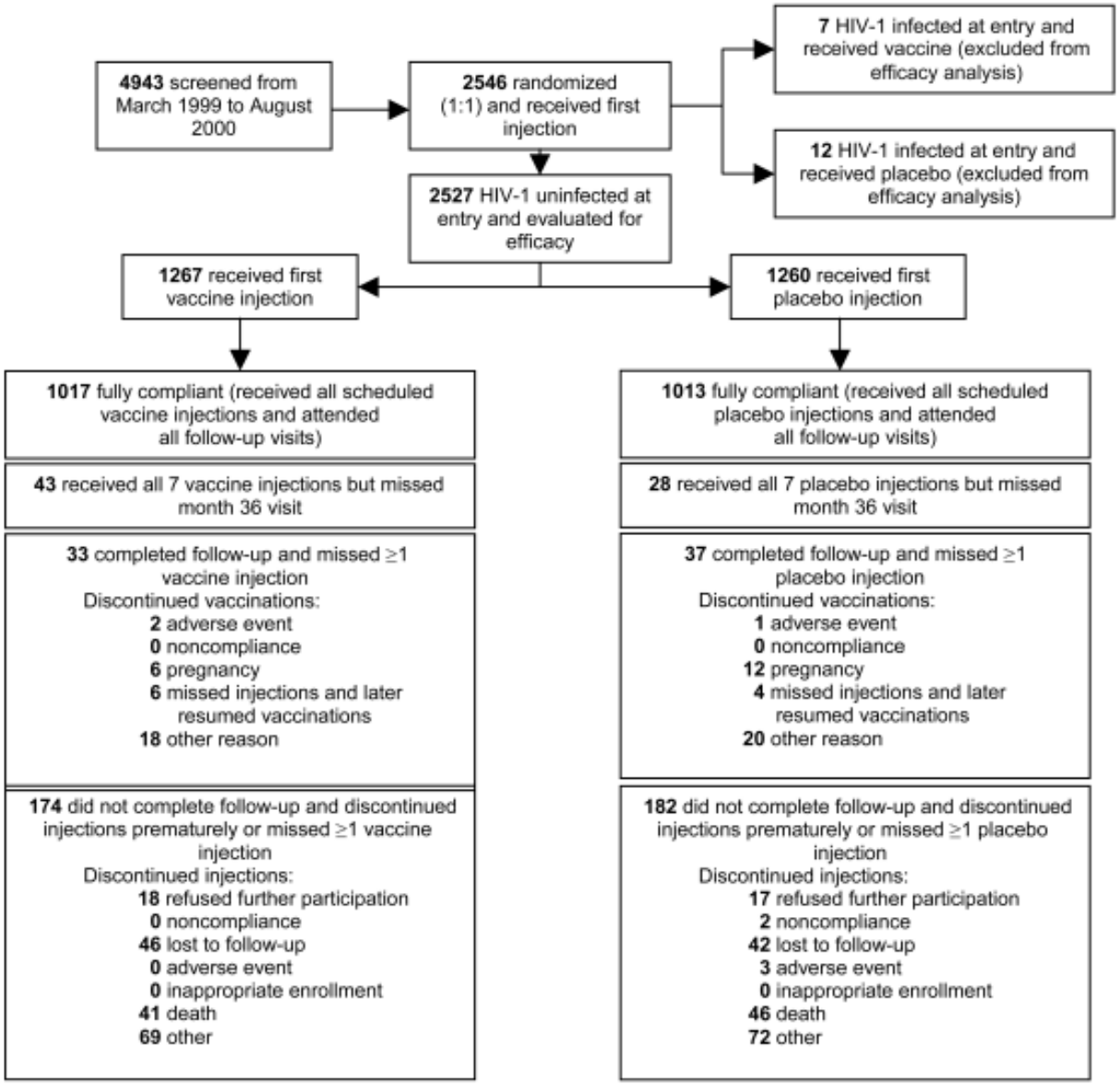
- Randomized, double blind, placebo-controlled vaccine efficacy trial conduced among IVDU attending 17 Bangkok Metropolitan Administration drug-treatment clinics
- Randomized at a 1:1 ratio
- Eligibility Criteria
  - Ages 20 – 60
  - IVDU in the last year
  - Negative for HIV-1 by ELISA screening at baseline

Risk Counseling and Assessment

- At each visit, volunteers were counseled to eliminate HIV risk behavior, including drug injection, needle sharing, and unprotected sexual intercourse.
- Male condoms and bleach to clean injection equipment were provided free of charge
- Questionnaires to assess risk behavior and social harms related to trial participation were administered every 6 months.

Vaccine Product and Administration

- AIDSVAX B/E contains 2 r-gp120 HIV-1 envelope antigens: 1 from a CXCR4-dependent laboratory-adapted subtype B strain (MN), and 1 from a CCR5-dependent primary subtype CRF01_AE isolate
- Vaccine or placebo was injected intramuscularly at months 0, 1, 6, 12, 18, 24, and 36. At each visit, adverse events were assessed and blood was collected, to determine vaccine antibody response and HIV-1 status by ELISA and immunoblotting.



End Points

- HIV-1 infection was the primary end point for vaccine efficacy
- Secondary endpoints were safety and delayed progression of HIV-1 disease
  - Disease progression was based on initiation of ART, onset of AIDS, and CD4/HIV VL endpoints

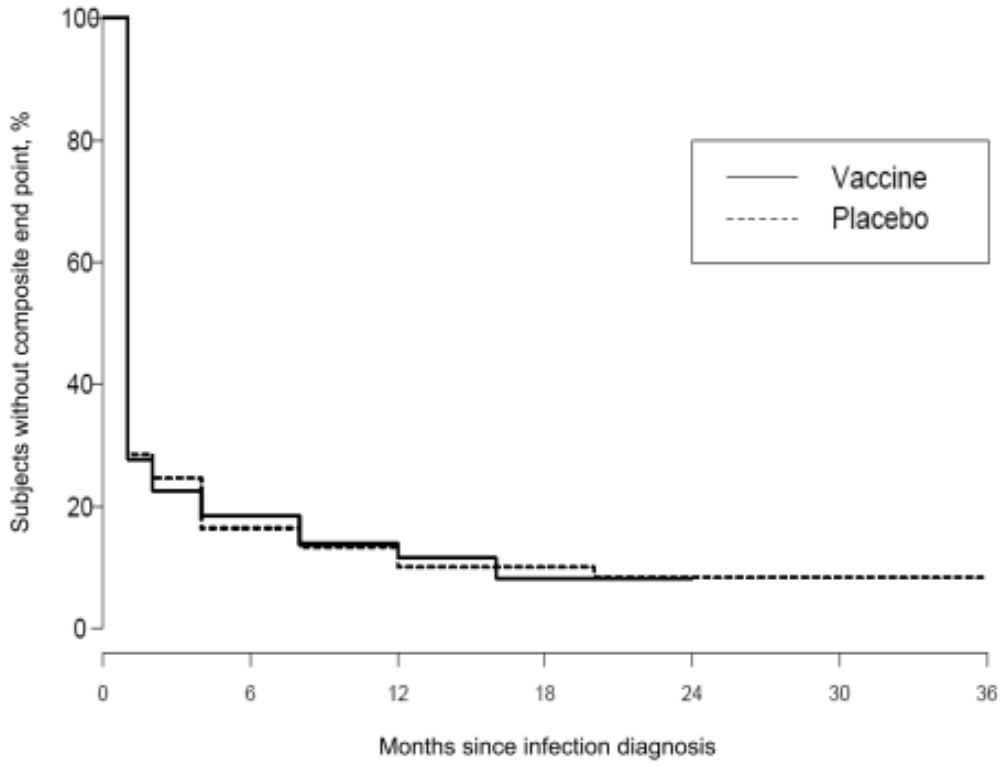


Figure 4. Kaplan-Meier curves for the time from infection diagnosis to the composite end point of drug-treatment initiation or viral failure (>10,000 copies/mL), for study participants in the intention-to-treat cohort who became infected with HIV-1.

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

Supachai Rerks-Ngarm, M.D., Punnee Pitisuttithum, 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 Premsri, M.D., Chawetsan Namwat, M.D., Mark de Souza, Ph.D., Elizabeth Adams, M.D., Michael Benenson, M.D., Sanjay Gurunathan, M.D., et al., for the MOPH–TAVEG Investigators*

The NEW ENGLAND JOURNAL of MEDICINE

NEJM.ORG

December 3, 2009

N Engl J Med 2009; 361:2209-2220

DOI: 10.1056/NEJMoa0908492

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Methods

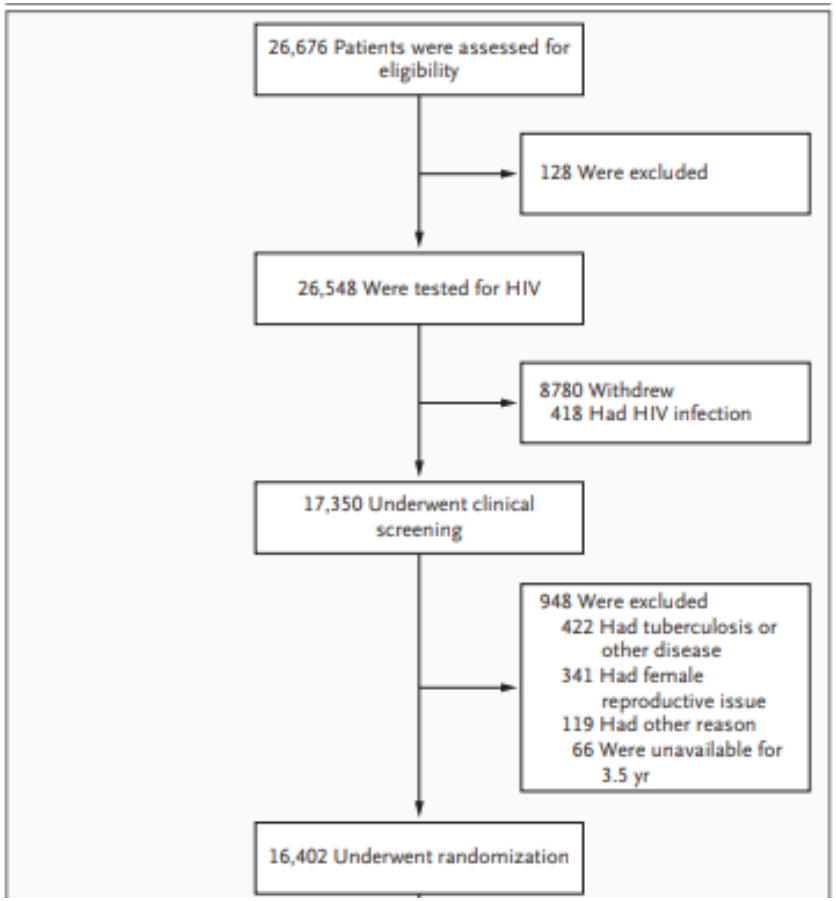
- Community-based, randomized, multicenter, double-blind, placebo-controlled efficacy trial of the prime-boost combination of the vaccines ALVAC-HIV and AIDSVAX B/E
- From Sept 2003 – Dec 2005
- Eligibility
  - 18 – 30 years of age
  - Not infected with HIV
  - Recruited from the community independent of HIV risk
  - Had to pass a test of understanding

Study Procedures

- The study vaccines were administered at baseline (day 0), 4 weeks (prespecified range, 3 to 7), 12 weeks (range, 10 to 15), and 24 weeks (range, 21 to 28). The ALVAC-HIV (vCP1521) vaccine was administered at each of the four visits. Boosting with AIDSVAX B/E occurred at weeks 12 and 24.
- For 3 days after each dose of vaccine, subjects reported local and systemic vaccine reactions on a diary card.

Endpoints

We established the presence of HIV infection on the basis of repeated positive results on enzyme immunoassay and Western blotting, with two confirmatory HIV nucleic acid tests. We performed three measurements of HIV-1 RNA within 6 weeks after serodiagnosis to determine the mean post-infection viral load.



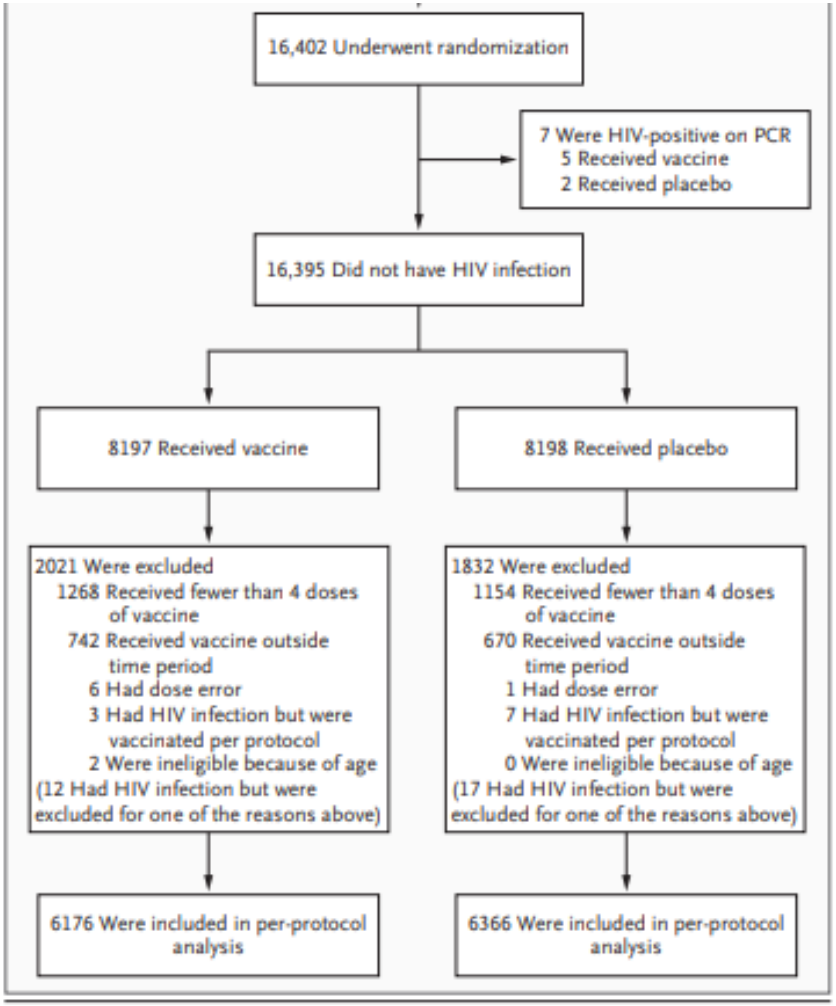


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Table 1. Baseline Characteristics of the Subjects (Modified Intention-to-Treat Population).

Variable	Vaccine (N=8197)	Placebo (N=8198)	All Subjects (N=16,395)
		number (percent)	
Sex			
Male	5033 (61.4)	5031 (61.4)	10,064 (61.4)
Female	3164 (38.6)	3167 (38.6)	6,331 (38.6)
Age group			
≤20 yr	2297 (28.0)	2246 (27.4)	4,543 (27.7)
21–25 yr	3633 (44.3)	3708 (45.2)	7,341 (44.8)
≥26 yr	2267 (27.7)	2244 (27.4)	4,511 (27.5)
Province			
Chon Buri	4107 (50.1)	4107 (50.1)	8,214 (50.1)
Rayong	4090 (49.9)	4091 (49.9)	8,181 (49.9)
Marital status			
Single	3353 (40.9)	3338 (40.7)	6,691 (40.8)
Married	4110 (50.1)	4169 (50.9)	8,279 (50.5)
Divorced	602 (7.3)	541 (6.6)	1,143 (7.0)
Widowed	50 (0.6)	64 (0.8)	114 (0.7)
Separated	82 (1.0)	86 (1.0)	168 (1.0)
No. of sex partners			
0	1864 (22.7)	1801 (22.0)	3,665 (22.4)
1	5428 (66.2)	5495 (67.0)	10,923 (66.6)
>1	619 (7.6)	620 (7.6)	1,239 (7.6)
Did not answer	280 (3.4)	273 (3.3)	553 (3.4)
Missing data	6 (0.1)	9 (0.1)	15 (0.1)
Risk group			
Low	3865 (47.2)	3924 (47.9)	7,789 (47.5)
Medium	2369 (28.9)	2292 (28.0)	4,661 (28.4)
High	1963 (23.9)	1982 (24.2)	3,945 (24.1)
Behavioral risk			
Needle sharing			
No condom use			
With casual partner			
With commercial sex worker			
With same-sex partner			
With HIV-infected partner			
With partner who injects drugs			
With multiple sex partners			
Condom use with HIV-infected partner			
Symptoms of an STD within past 6 mo*			
Drug injection in jail			
Occupation as a commercial sex worker			
Occupation in the entertainment business			

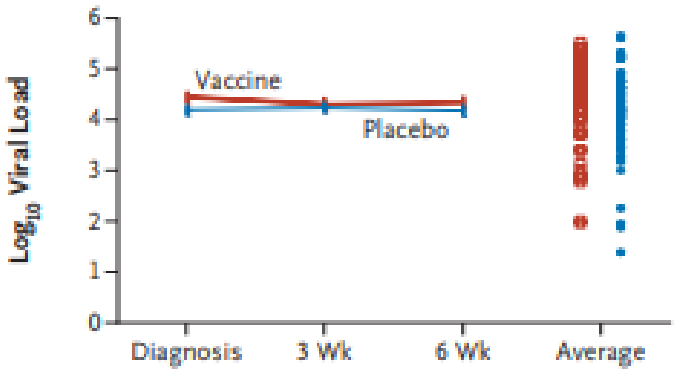

Figure 3. Viral Loads in Subjects with Early HIV-1 Infection.

The receipt of vaccine did not have a significant effect on the viral load in subjects who were found to have early HIV-1 infection. On the left are the mean $\log_{10}$ viral loads at three visits during a 6-week period for subjects who were included in the intention-to-treat analysis. The data points at the right show the distribution of viral loads in the vaccine group (mean, 4.36 $\log_{10}$ copies per milliliter) and the placebo group (mean, 4.21 $\log_{10}$ copies per milliliter) ($P=0.09$). There was no significant between-group difference in viral load in either the per-protocol analysis ($P=0.47$) or the modified intention-to-treat analysis ($P=0.24$).

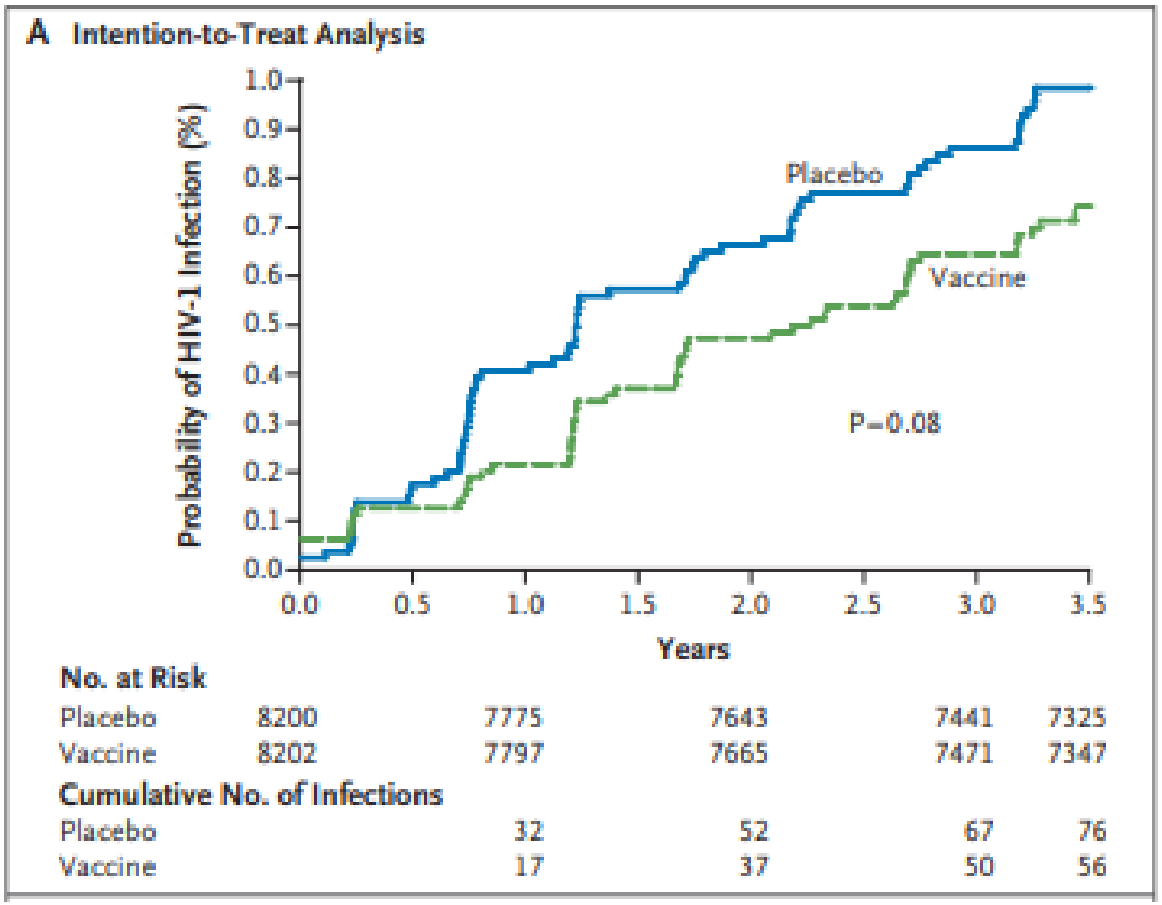

Figure 2. Kaplan–Meier Cumulative Rates of Infection, According to Type of Analysis.

The vaccination regimen was completed approximately 6 months after the first dose was administered. In the intention-to-treat analysis involving 16,402 subjects, the vaccine efficacy was 26.4% (95% confidence interval [CI], −4.0 to 47.9; P=0.08) (Panel A). In the per-protocol analysis involving 12,542 subjects, the vaccine efficacy was 26.2% (95% CI, −13.3 to 51.9; P=0.16) (Panel B). In the modified intention-to-treat analysis involving 16,395 subjects (excluding 7 subjects who were found to have had HIV infection at baseline), the vaccine efficacy was 31.2% (95% CI, 1.1 to 51.2; P=0.04) (Panel C).

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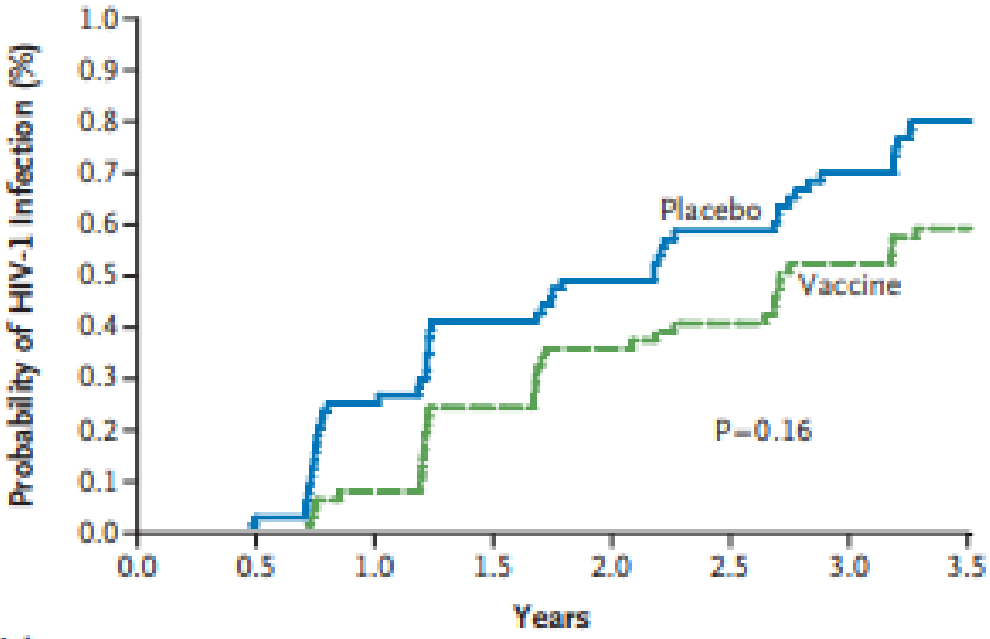
B Per-Protocol Analysis



No. at Risk					
Placebo	6366	6283	6220	6089	6002
Vaccine	6176	6140	6068	5958	5874
Cumulative No. of Infections					
Placebo		16	31	44	50
Vaccine		5	22	32	36

Figure 2. Kaplan–Meier Cumulative Rates of Infection, According to Type of Analysis.

The vaccination regimen was completed approximately 6 months after the first dose was administered. In the intention-to-treat analysis involving 16,402 subjects, the vaccine efficacy was 26.4% (95% confidence interval [CI], −4.0 to 47.9; P=0.08) (Panel A). In the per-protocol analysis involving 12,542 subjects, the vaccine efficacy was 26.2% (95% CI, −13.3 to 51.9; P=0.16) (Panel B). In the modified intention-to-treat analysis involving 16,395 subjects (excluding 7 subjects who were found to have had HIV infection at baseline), the vaccine efficacy was 31.2% (95% CI, 1.1 to 51.2; P=0.04) (Panel C).

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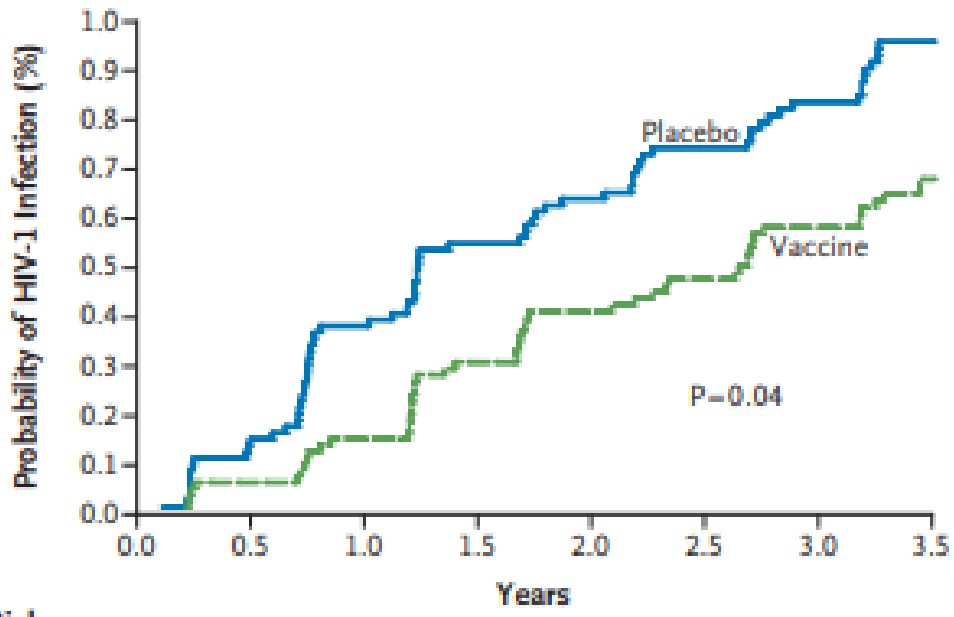
C Modified Intention-to-Treat Analysis



No. at Risk					
Placebo	8198	7775	7643	7441	7325
Vaccine	8197	7797	7665	7471	7347
Cumulative No. of Infections					
Placebo		30	50	65	74
Vaccine		12	32	45	51

Figure 2. Kaplan–Meier Cumulative Rates of Infection, According to Type of Analysis.

The vaccination regimen was completed approximately 6 months after the first dose was administered. In the intention-to-treat analysis involving 16,402 subjects, the vaccine efficacy was 26.4% (95% confidence interval [CI], −4.0 to 47.9; P=0.08) (Panel A). In the per-protocol analysis involving 12,542 subjects, the vaccine efficacy was 26.2% (95% CI, −13.3 to 51.9; P=0.16) (Panel B). In the modified intention-to-treat analysis involving 16,395 subjects (excluding 7 subjects who were found to have had HIV infection at baseline), the vaccine efficacy was 31.2% (95% CI, 1.1 to 51.2; P=0.04) (Panel C).

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Discussion

- However, after the exclusion of the subjects who were infected with HIV-1 before vaccination, the modified intention-to-treat analysis showed a significant, though modest, reduction in the rate of HIV-1 infection, as compared with placebo.

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

Supachai Rerks-Ngarm, M.D., Punnee Pitisuttithum, 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 Premsri, M.D., Chawetsan Namwat, M.D., Mark de Souza, Ph.D., Elizabeth Adams, M.D., Michael Benenson, M.D., Sanjay Gurunathan, M.D., et al., for the MOPH–TAVEG Investigators*

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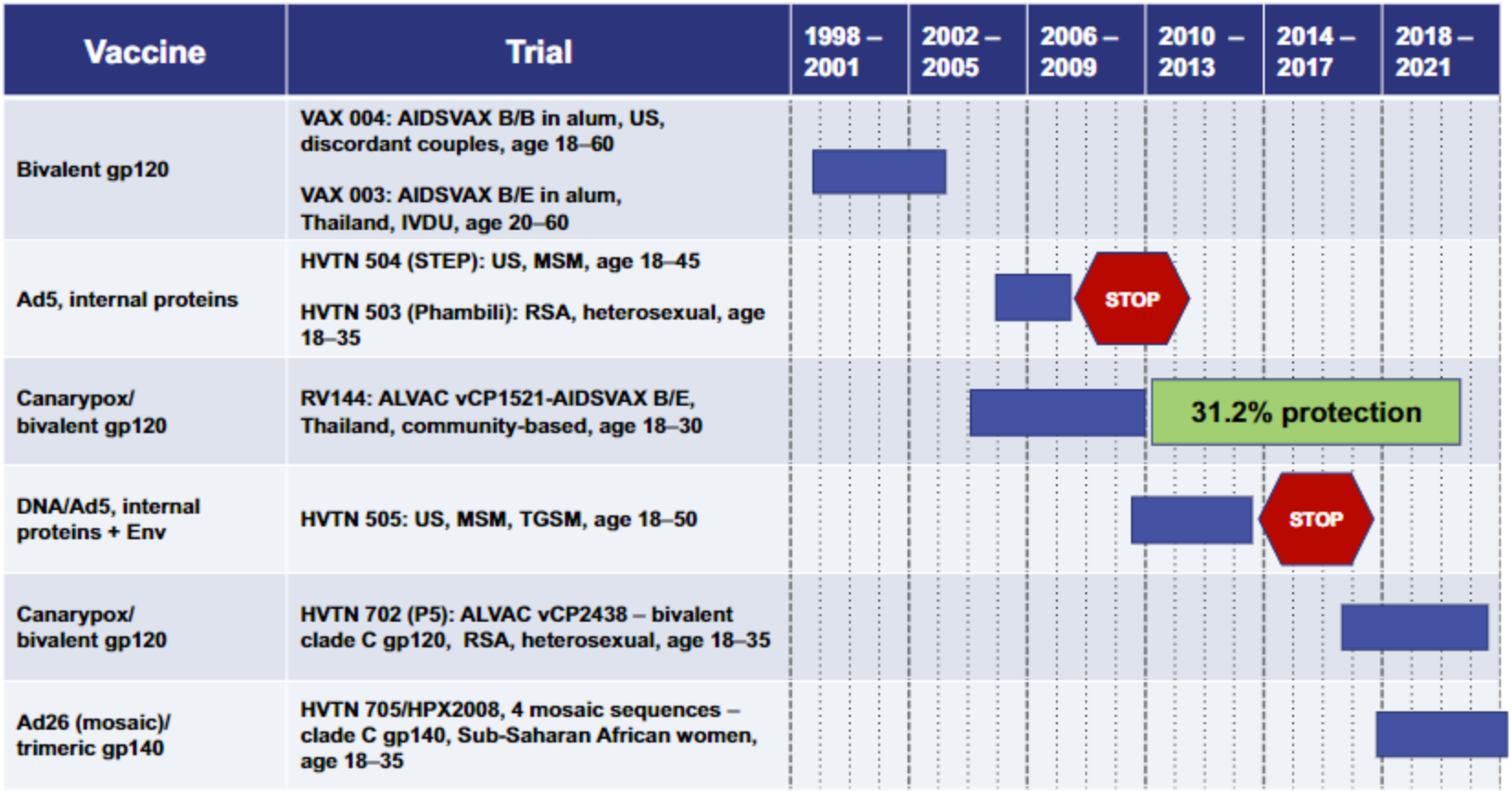

Figure 1 Timeline for human immunodeficiency virus (HIV) vaccine efficacy trials. Years at the top are for 4-year intervals, individual years are designated by dotted lines. Ad5, adenovirus serotype 5 vector; Ad26, adenovirus serotype 26 vector; ALVAC, canarypox vector; HVTN, HIV Vaccine Trials Network; IVDU, intravenous drug users; MSM, men who have sex with men; RSA, Republic of South Africa; TGSM, male to female transgender individuals who have sex with men; US, United States; VCP, canary pox vector.

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Received 22 June 2018; accepted 30 July 2018; advance online publication 9 October 2018.doi:10.1002/cpt.1208

REVIEW

Current approaches to HIV vaccine development: a narrative review

Jiae Kim[1,2], Sandhya Vasan[1,2], Jerome H. Kim[3] and Julie A. Ake[1,§]

[§]**Corresponding author:** Julie A. Ake, Walter Reed Army Institute of Research, 503 Robert Grant Ave, Silver Spring, MD 20910, USA. Tel: 240-506-1915. (Julie.a.ake.mil@mail.mil)

HVTN 502 (STEP) and Phambili (HVTN 503)

- **HVTN 502 (STEP)**
- The STEP trial evaluating a replication defective adenovirus serotype 5 (Ad5) vectored vaccine enrolled MSM, sex workers, and participants with elevated heterosexual risk in the Americas and Australia.
- The trial was halted by the Data Safety Monitoring Board (DSMB) after initial data showed an increase in HIV infection among uncircumcised males and/or Ad5 seropositive vaccinees.
- Interim analysis revealed an infection rate in per protocol male vaccinees double that of placebo recipients.

Efficacy assessment of a cell-mediated immunity HIV-1 vaccine (the Step Study): a double-blind, randomised, placebo-controlled, test-of-concept trial

Susan P. Buchbinder, MD[1], Devan V. Mehrotra, PhD[2], Ann Duerr, MD, PhD, MPH[3], Daniel W. Fitzgerald, MD[4], Robin Mogg, MS[2], David Li, PhD[2], Peter B. Gilbert, PhD[3], Javier R. Lama, MD, MPH[5], Michael Marmor, PhD[6], Carlos del Rio, MD[7], M. Juliana McElrath, MD, PhD[3], Danilo R. Casimiro, PhD[2], Keith M. Gottesdiener, MD[2], Jeffrey A. Chodakewitz, MD[2], Lawrence Corey, MD[3], and Michael N. Robertson, MD[2] the Step Study Protocol Team
[1] HIV Research Section, San Francisco Department of Public Health, San Francisco, CA

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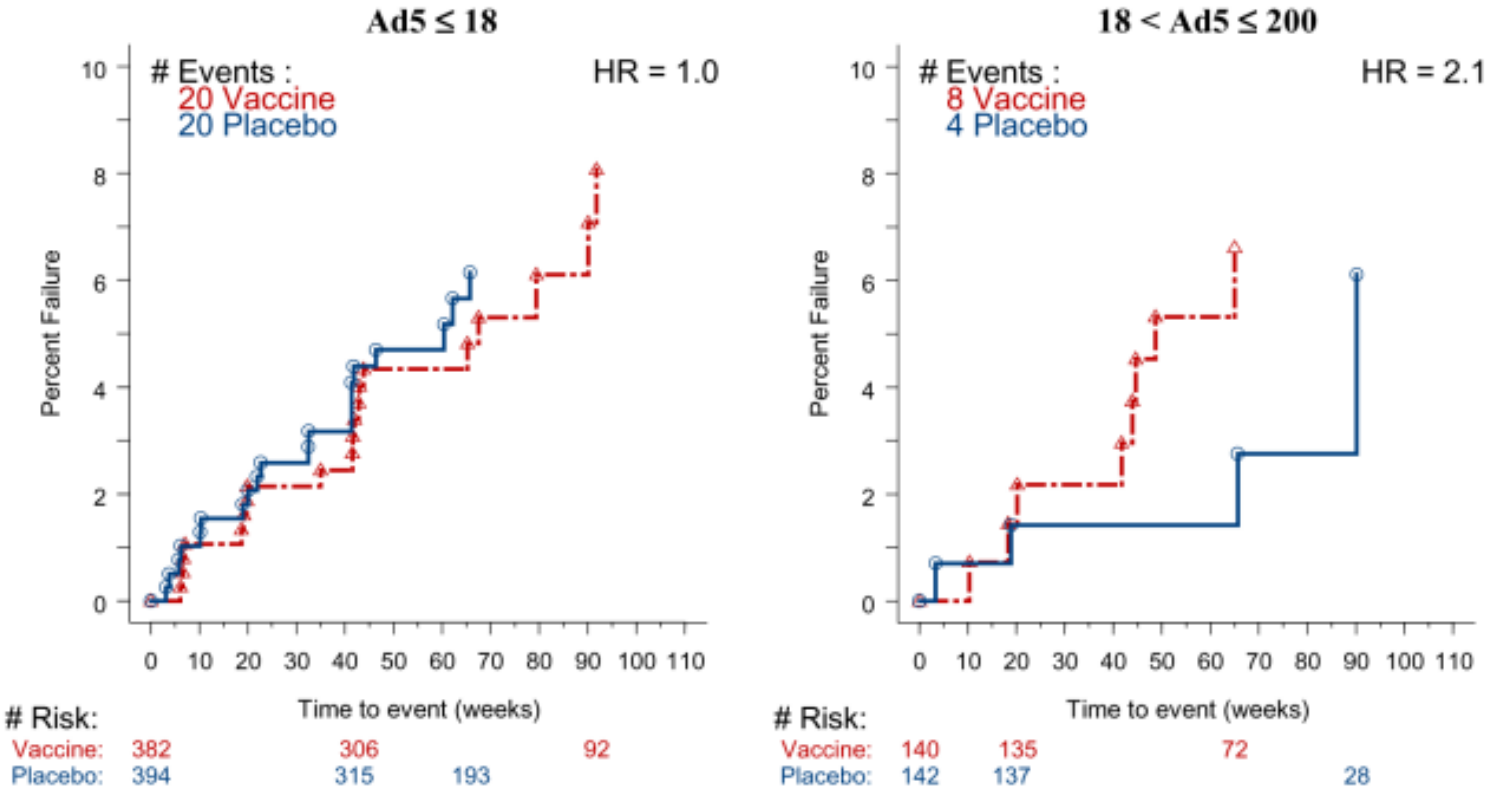
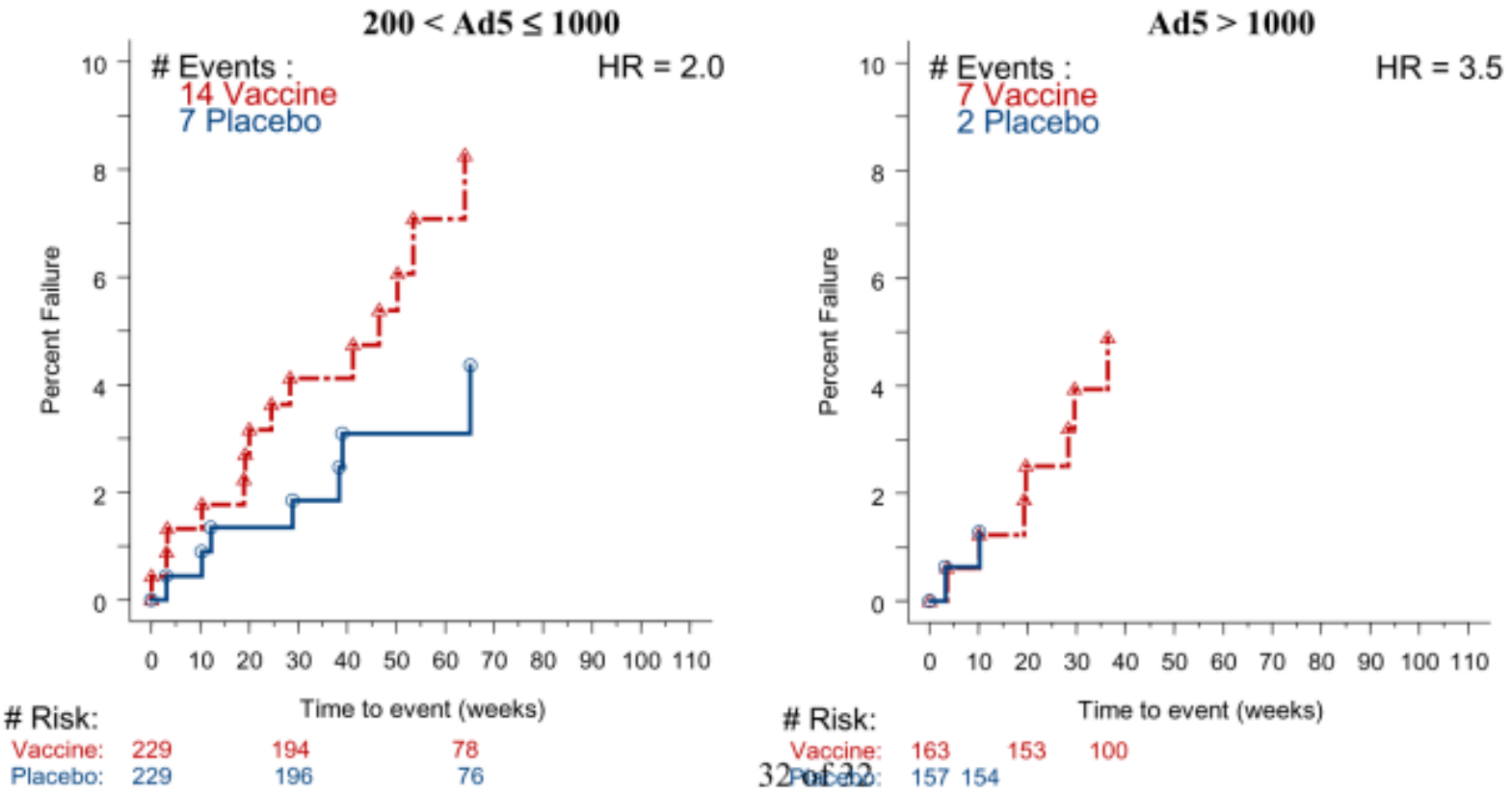


Figure 2. Kaplan Meier plots of HIV infection for male vaccine and placebo groups by A) baseline Ad5 ≤18; B) baseline Ad5 >18 and ≤200; C)baseline Ad5 >200 and ≤1000; and D) baseline Ad5 >1000. Each hazard ratio (HR) is from a univariate Cox regression model.



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HVTN 502 (STEP) and Phambili (HVTN 503)

- The Phambili trial, which enrolled participants in the Republic of South Africa (RSA) was terminated early based on the results of the STEP trial, and preliminary data revealed a higher incidence of HIV infection in the vaccinated group compared to placebo, without impact on viral load or disease progression.
- In vitro experiments demonstrated that Ad5-specific CD4+ T cells are highly susceptible to HIV infection, and that these cells are preferentially lost in HIV-1-positive individuals.
- These studies raised important questions about pre-existing anti-vector immunity and concern about the use of Ad5 vectored vaccines where Ad5 is prevalent.

HVTN 702 - Uhambo Efficacy Trial

ORIGINAL ARTICLE

Vaccine Efficacy of ALVAC-HIV and Bivalent Subtype C gp120–MF59 in Adults

Glenda E. Gray, M.B., B.Ch., Linda-Gail Bekker, M.B., Ch.B., Ph.D., Fatima Laher, M.B., B.Ch., Mookho Malahleha, M.B., Ch.B., M.P.H., Mary Allen, B.S.N., M.S., Zoe Moodie, Ph.D., Nicole Grunenberg, M.D., Yunda Huang, Ph.D., Doug Grove, M.S., Brittany Prigmore, M.S., Jia J. Kee, M.S., David Benkeser, Ph.D., et al., for the HVTN 702 Study Team*

March 25, 2021
N Engl J Med 2021; 384:1089-1100
DOI: 10.1056/NEJMoa2031499

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Methods

- Double-blind, placebo controlled trial at 14 sites in South Africa.
- Oct 26, 2016 – June 21, 2019
- Trial was designed to evaluate vaccine efficacy to prevent HIV-1 infection within 24 months after enrollment (primary endpoint)
- Eligibility
  - 18 – 35 years of age
  - 60 – 75% women
- Standard of care PreP and sexual health counseling was offered throughout the study

Study Product/Intervention

- The vaccine regimen consisted of an ALVAC-HIV vector and an MF59-adjuvanted bivalent subtype C gp120. ALVAC-HIV (vCP2438) (at a dose of 107 50% cell-culture infectious dose) expresses the HIV-1 envelope glycoprotein of the subtype C ZM96.C strain, along with the gp41 transmembrane sequence, gag, and protease from the subtype B LAI strain. Bivalent subtype C gp120 is a combination of 100 µg each of the HIV-1 subtype C gp120 of the TV1.C and 1086.C strains.
- Participants received an intramuscular injection of ALVAC-HIV or placebo at months 0 and 1, which was followed by four injections of ALVAC-HIV plus bivalent subtype C gp120–MF59 or placebo at months 3, 6, 12, and 18.

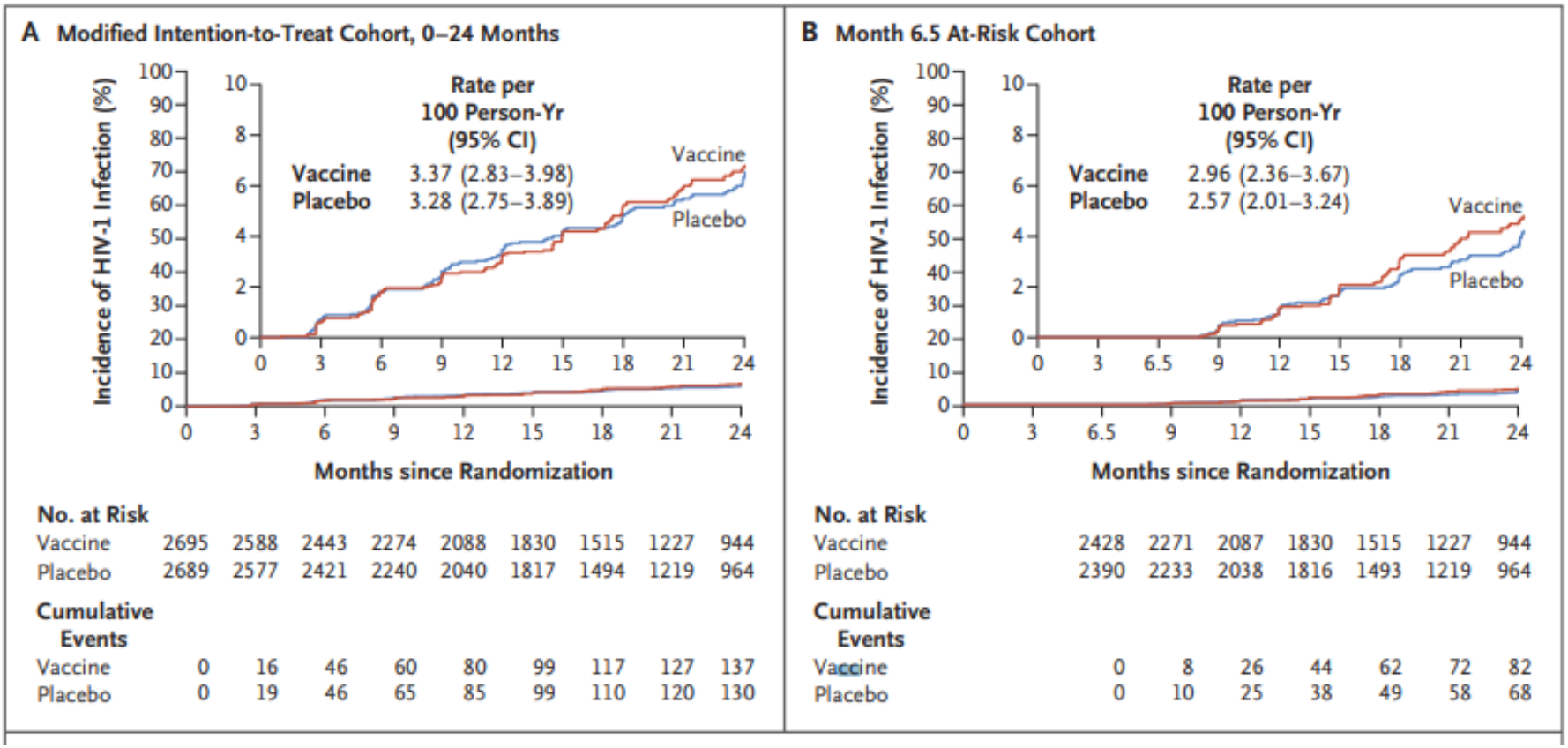
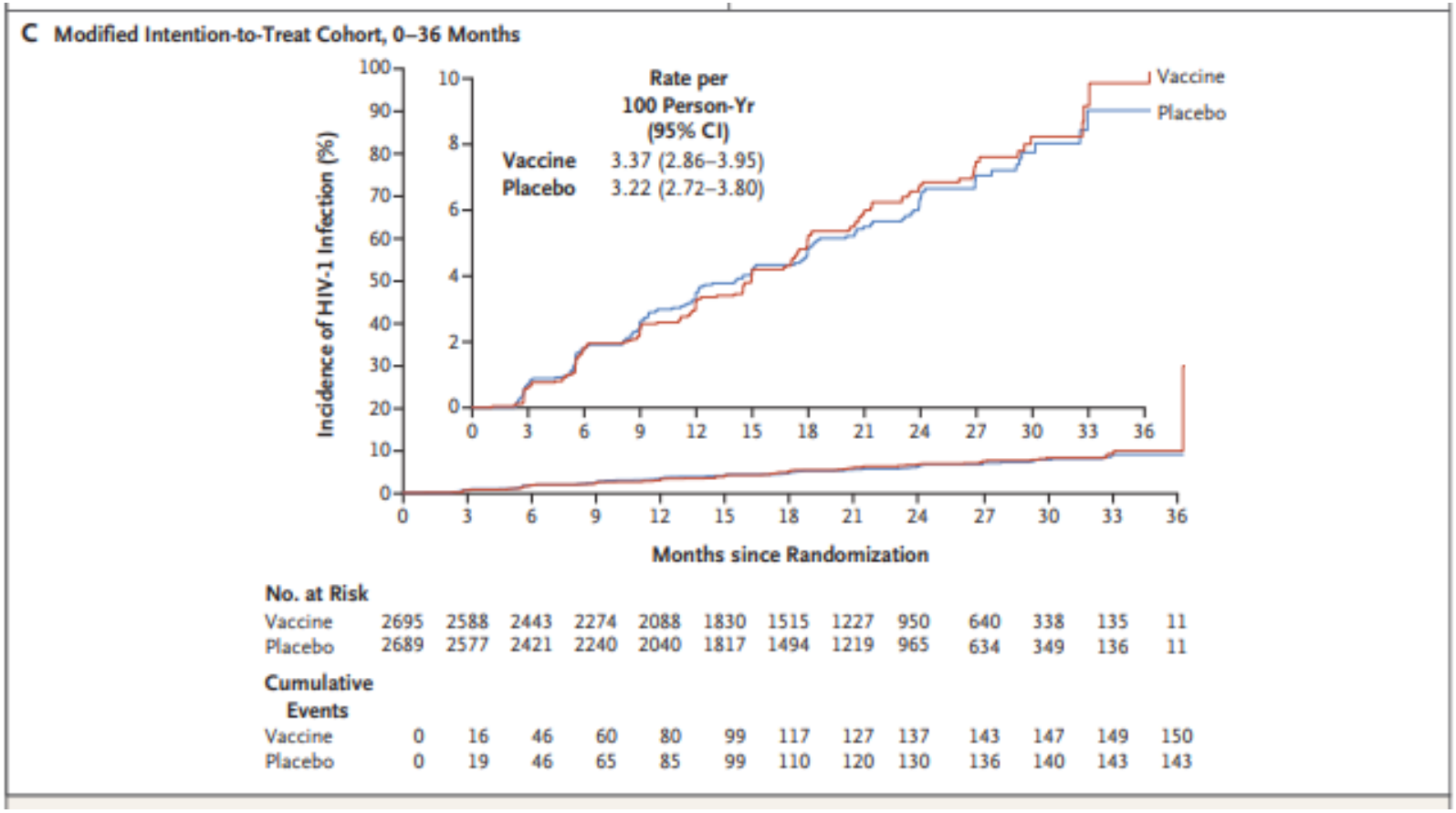


Figure 1. Kaplan–Meier Analysis of HIV-1 Infection in Three Cohorts.

Shown are data for the cumulative incidence of human immunodeficiency virus type 1 (HIV-1) infection among the participants in the modified intention-to-treat cohort who were evaluated during the period from randomization to 24 months (primary analysis cohort) (Panel A), in the cohort of participants who were HIV-1–negative at month 6.5 and were at risk for subsequent HIV-1 infection (month 6.5 at-risk cohort) (Panel B), and in the modified intention-to-treat cohort during the period from randomization to month 36 (Panel C). The apparent uptick in the vaccine curve at month 36 is due to a single infection among the remaining 11 participants at risk. In each panel, the inset shows the same data on an expanded y axis; in Panel C, the vaccine curve at 36 months has been cut off at 10% for graphical presentation.



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PREPVACC Trial – ONGOING!

- International, multicenter, double-blind vaccine study is a three-arm prospective 1:1:1 randomization comparing each of the two experimental combination vaccine regimens **DNA/AIDSVAX (weeks 0,4,24,48) and DNA/CN54gp140 (weeks 0,4) + MVA/CN54gp140 (weeks 24,48) with placebo control.**
- **There will be a concurrent open-label 1:1 randomization to compare daily TAF/FTC (week 0-26) to daily TDF/FTC (weeks 0-26) as pre-exposure prophylaxis.**

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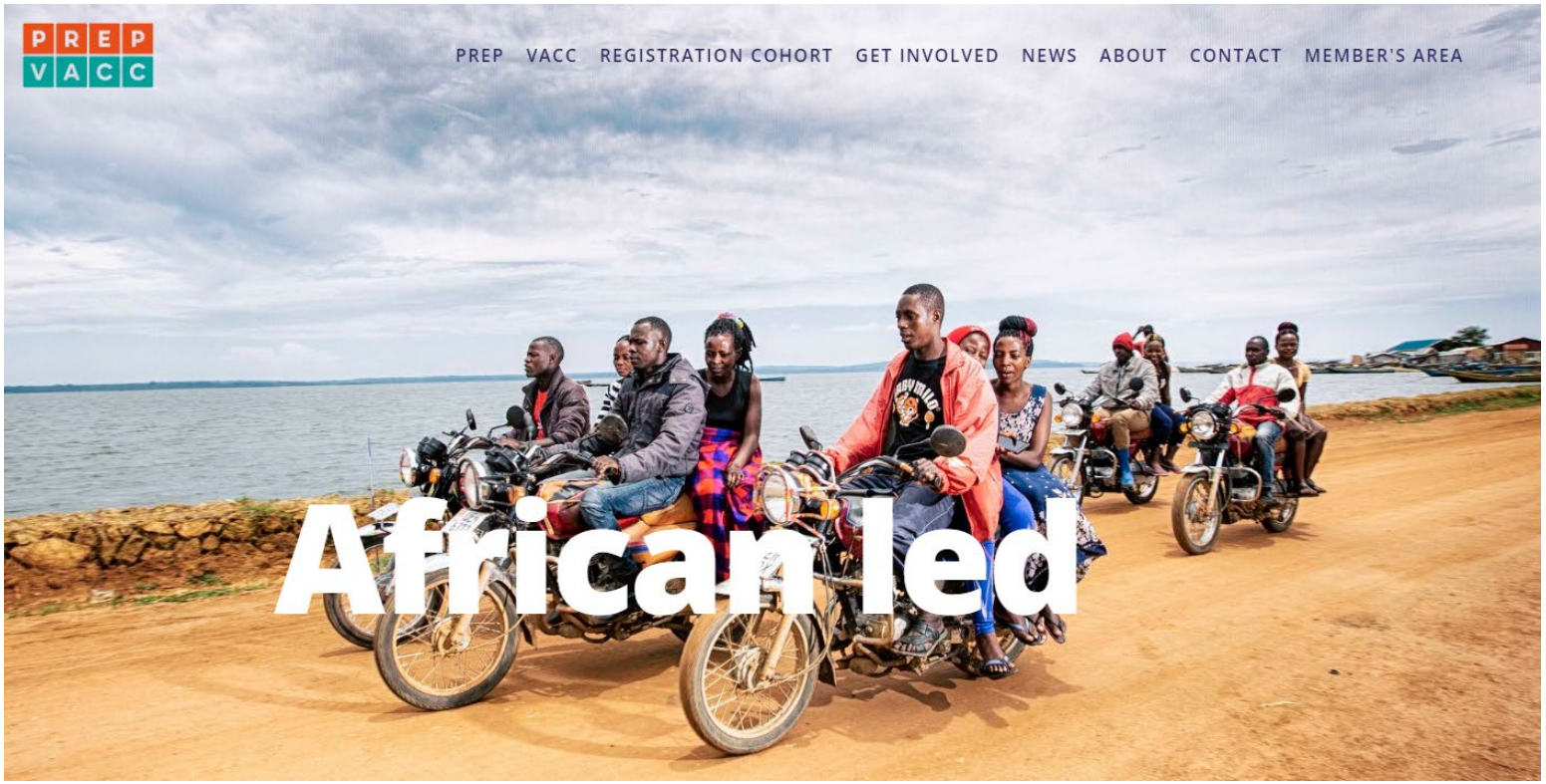

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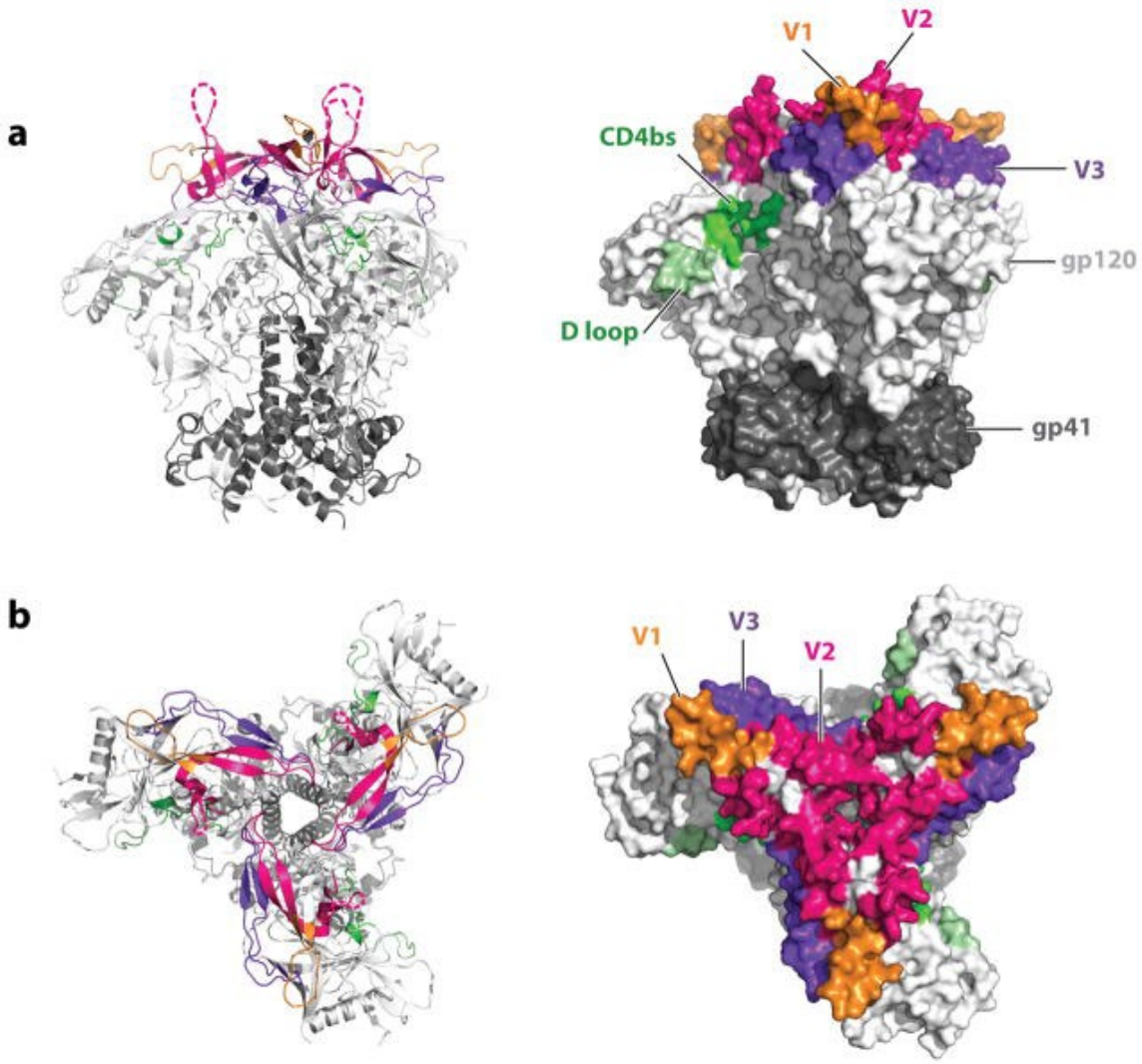
Ad26 mosaic trials

- TRAVERSE
- IMBOKODO
- ASCENT
- MOSAICO

The Problem

- Don’t stand there admiring the problem. I want solutions! – President Barack Obama



Structure of the HIV envelope spike. In a crystal structure of the HIV strain BG505 expressed as SOSIP.664 near-native trimers [PDB 4zmj (31)], the location of some of the most important Env trimer domains is indicated as viewed (*a*) from the side or (*b*) from the top. The gp120 subunits form the blades of a propeller-like structure, whereas the gp41 subunit forms a central stalk and a membrane-proximal, pedestal-like structure. As predicted from other experimental data, hypervariable loops V1 through V3 are located at the apex of the trimer, with hypervariable loop V3 being partially buried under hypervariable loops V1 and V2. These loops are also in proximity to the CD4 receptor binding site that is recessed left in the cleft formed by two propeller blades. Loops that did not resolve in the structure are indicated by a dashed line.

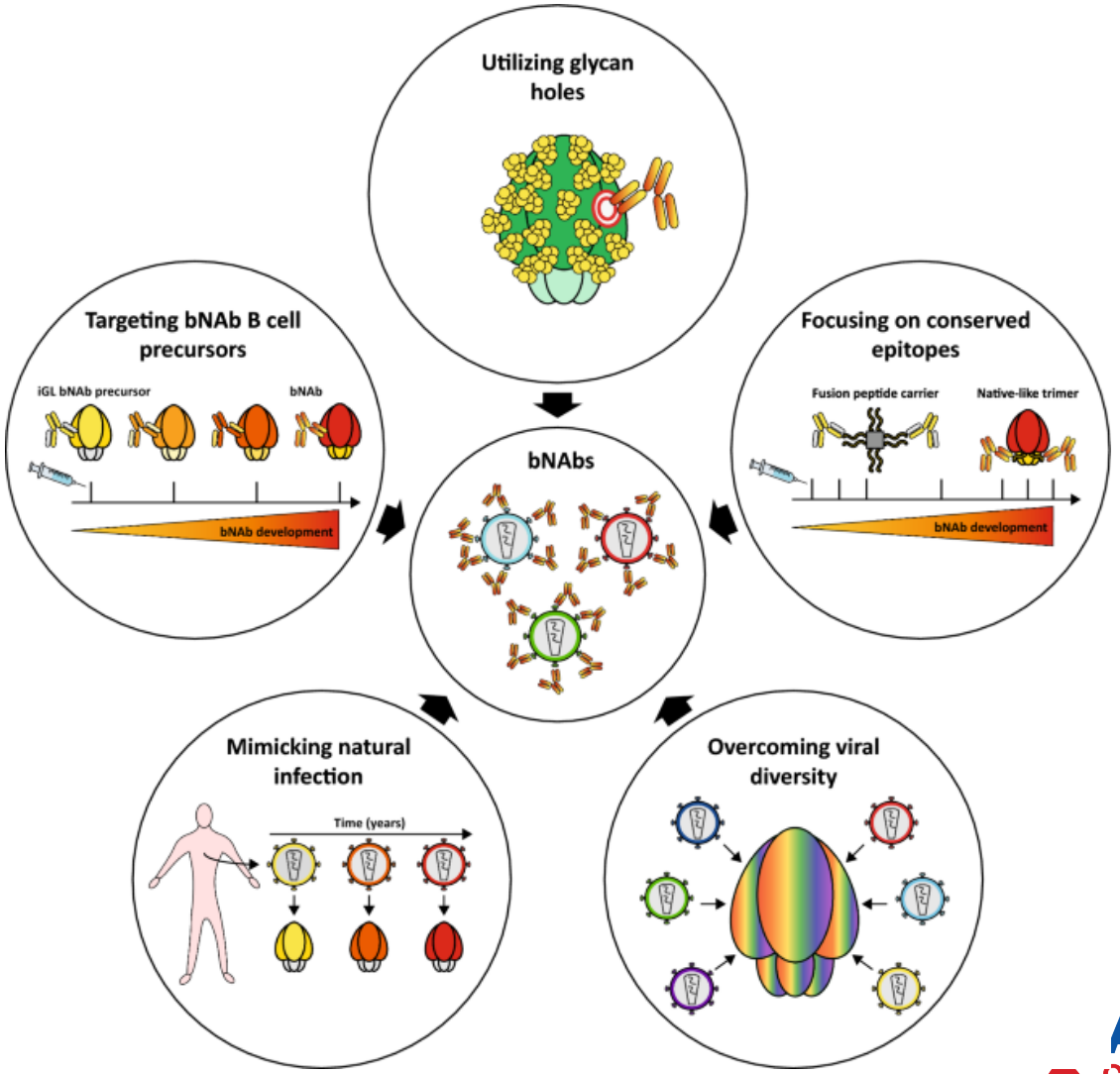
The Problem

- Spacing between envelope spikes is unfavorable for B cell activation that requires antigen cross-linking of B cell receptors.
- Extensive glycosylation of the envelope spike by the host cellular machinery cloaks the virus with a weakly immunogenic, potentially self, antigen and constrains antibody access to neutralizing epitopes.
- Addition and loss of glycosylation sites is actively used by the virus to change the surface of the spike and thwart antibody recognition.

The Problem – Con't

- Functionally essential structures that cannot easily be mutated in order to escape antibody recognition are presented in poorly accessible locations on the quaternary structure [e.g., the CD4 binding site (CD4bs),
- Membrane-proximal external region (MPER)] and may be obstructed by structures that have no essential function and therefore can more readily be mutated in response to antibody pressure [e.g., V1/V2]

Enter: Broadly Neutralizing Antibodies (BnAbs)



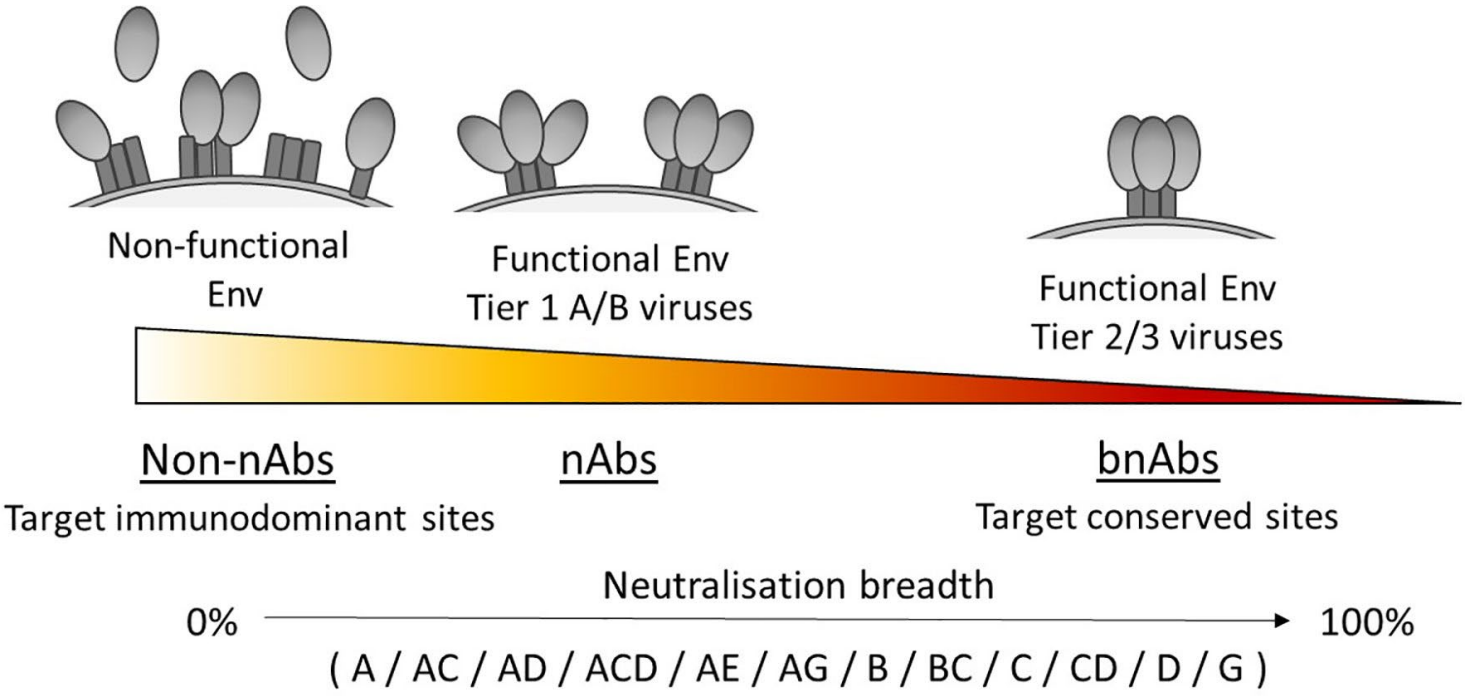


Figure 1 Neutralisation breadth corresponds with the ability to target functional Env trimers in a closed conformation. Tier 1A, tier 1B and tier 2/3 viruses have a predominantly open, intermediate and closed Env trimer conformation respectively and relates to their susceptibility to neutralisation, with tier 2/3 viruses being harder to neutralise. Antibodies that can neutralise tier 2/3 viruses from multiple clades (listed here in alphabetical order) have increased breadth by targeting conserved sites on the Env trimer.

REVIEW article
Front. Immunol., 19 October 2021 | https://doi.org/10.3389/fimmu.2021.708227

To bnAb or Not to bnAb: Defining Broadly Neutralising Antibodies Against HIV-1

Sarah A. Griffith and Laura E. McCoy*

HIV bnAb	Neutralisation breadth	Viruses tested	Potency (µg/ml)	Clades/CRFs neutralised	Reference
N49P7	100%	117	0.44	15	(30)
10E8	98%	118	0.36	14	(24)
4E10*	98%	118	1.81	15	(24)
1-18	97%	116	0.05	15	(73)
12A12	93%	117	0.22	15	(24)
LN01	92%	118	0.96	15	(74)
VRC01	91%	118	0.38	15	(24)
3BNC117	89%	118	0.12	15	(24)
PG9	87%	118	0.15	14	(24)
NIH45-46	86%	117	0.11	15	(24)
VRC13	86%	113	0.27	14	(24)
VRC-CH31	84%	115	0.32	15	(24)
PG16	83%	118	0.08	15	(24)
PGDM1400	83%	118	0.02	15	(24)
PGV04	81%	116	0.32	15	(24)
PGT145	78%	118	0.13	15	(24)
PGT151	73%	118	0.04	15	(24)
1B2530	72%	113	3.62	14	(24)
PGT128	68%	118	0.06	13	(24)
8ANC195	68%	118	1.23	15	(24)
CH103	67%	113	2.28	14	(24)

*The neutralisation breadth (percentage of viruses neutralised) and the number of clades/CRFs neutralised in the 118 PV panel was captured from the antibody isolation paper or LANL HIV CATNAP tool (24), bnAbs with data for >95% of PVs in the 118 PV panel were included. Potency is given as the geometric mean IC_{50} of viruses neutralised. The total number of virus clades/CRFs in the 118 PV panel is 15, categorised according to the LANL HIV CATNAP tool. *First generation bnAbs isolated prior to 2009 are marked by an asterisk.*

Higher neutralisation breadth, number of viruses tested and potency are indicated by a darker shade of green, yellow and red respectively.

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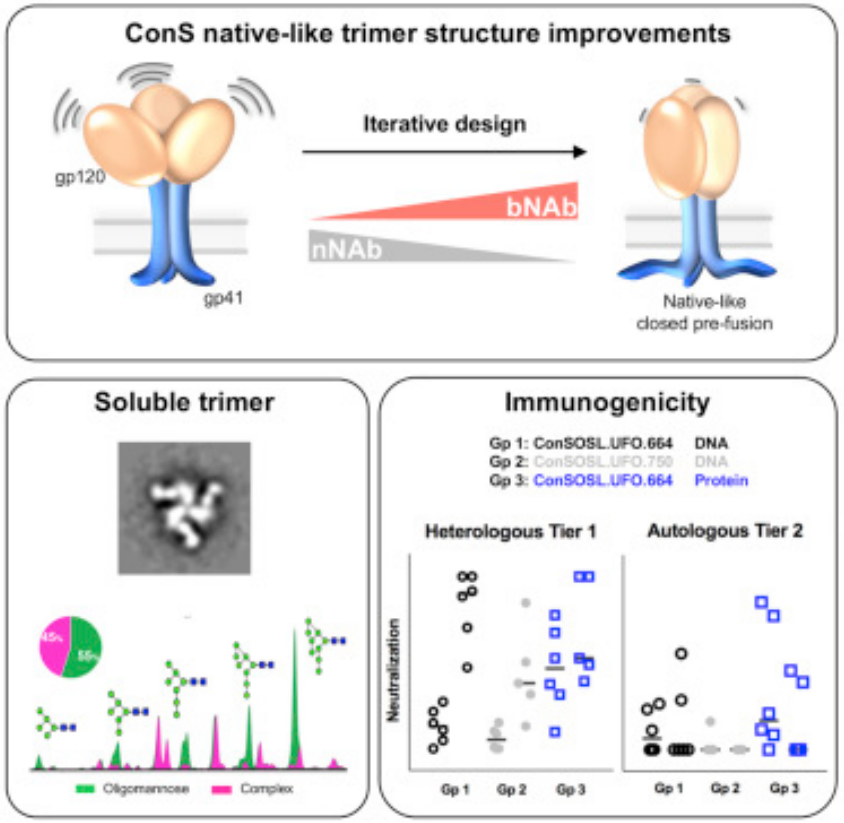
Future Directions

- Native-like trimers are a platform for developing complex antigens and eliciting BNaBs



Cell Reports
Volume 24, Issue 12, 18 September 2018, Pages 3324-3338.e5
CellPress

Article

Rational Design of DNA-Expressed Stabilized Native-Like HIV-1 Envelope Trimers

Yoann Aldon [1], Paul F. McKay [1], Joel Allen [2], Gabriel Ozorowski [3], Réka Felföldiné Lévai [4], Monica Tolazzi [5], Paul Rogers [1], Linling He [3], Natalia de Val [3], Katalin Fábián [4], Gabriella Scarlatti [5], Jiang Zhu [3], Andrew B. Ward [3], Max Crispin [2, 6], Robin J. Shattock [1, 7]

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"If it was up to the NIH to cure polio through a centrally directed program instead of independent investigator driven discovery, you'd have the best iron lung in the world, but not a polio vaccine." - **Samuel Broder**, former Director of the National Cancer Institute.

Questions about a potential vaccine

- How many shots in the series?
- How will the vaccine fit into the existing PreP landscape?
- Will the vaccine efficacy affect recommendations about target populations?
- What kind of disinformation will affect vaccine uptake?
- Will the vaccine produce stigma?

Thank You!

This [project/publication/program/website, etc.] [is/was] supported by the Health Resources and Services Administration (HRSA) of the U.S. Department of Health and Human Services (HHS) under grant number U1OHA30535.. The contents are those of the author(s) and do not necessarily represent the official views of, nor an endorsement, by HRSA, HHS, or the U.S. Government. For more information, please visit HRSA.gov.

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