XII Workshop Nazionale
INNOVAZIONE E RICERCA PER LA PRATICA CLINICA
TERAPIA E PREVENZIONE DELL' INFEZIONE DA HIV E MICRORGANISMI EMERGENTI
9-10 Giugno 2021
VIRTUAL EDITION

A che punto è la vaccinazione contro HIV

Antonella Castagna

Disclosures

I have received funding for Advisory Boards, Speaker Panels and for preparation of educational materials from the following:

Gilead Sciences
ViiV Healthcare
Janssen-Cilag
Merck Sharp & Dohme
Theratechnologies

UNAIDS

FACT SHEET 2021

Preliminary UNAIDS 2021 epidemiological estimates

GLOBAL HIV STATISTICS

37.6 million [30.2 million–45.0 million] people globally were living with HIV in 2020.

1.5 million [1.1 million–2.1 million] people became newly infected with HIV in 2020.

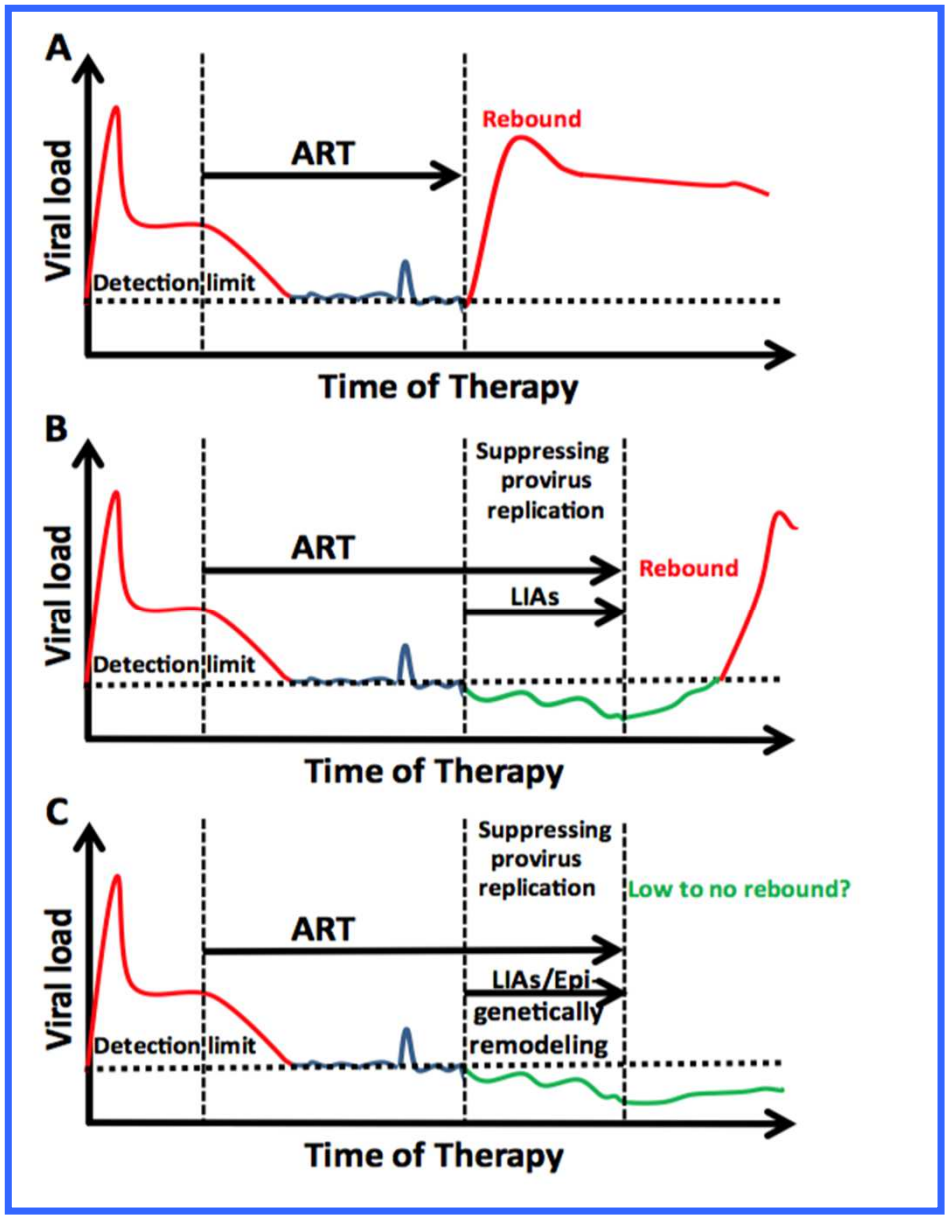
690 000 [480 000–1 million] people died from AIDS-related illnesses in 2020.

27.4 million [26.5 million–27.7 million] people were accessing antiretroviral therapy in 2020.

77.5 million [54.6 million–110 million] people have become infected with HIV since the start of the epidemic.

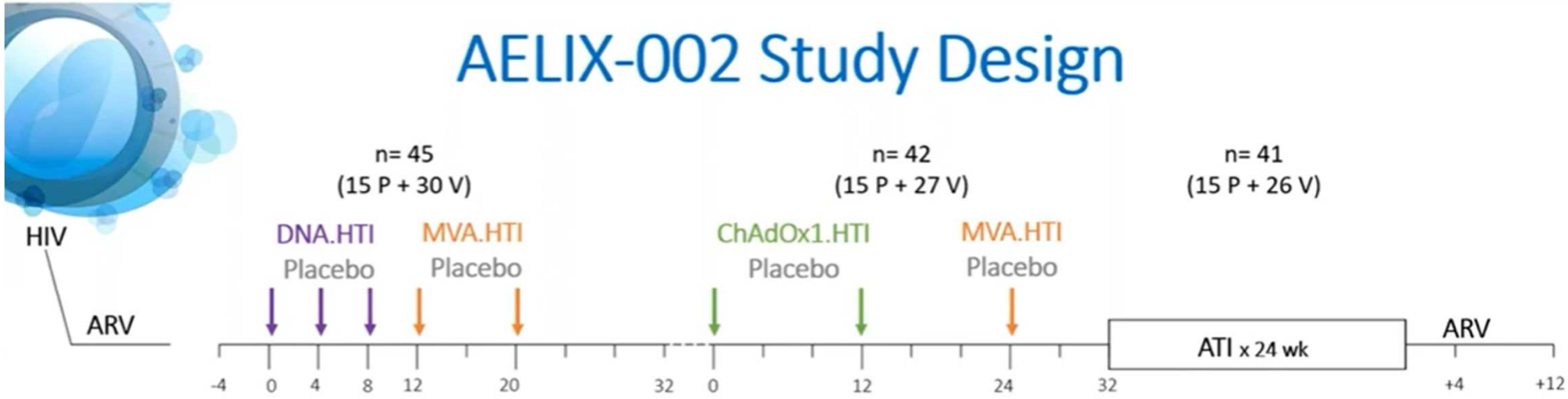
34.7 million [26.0 million–45.8 million] people have died from AIDS-related illnesses since the start of the epidemic.

Strategy to induce silencing of latent HIV reservoirs



ME Elsheickh, Ebio Med 2019

AELIX-002 Study Design



MAIN INCLUSION/EXCLUSION criteria

- **Early-ART with 3-drug regimen**
  <6months after documented HIV acquisition
- **Virological**
  >1y pVL undetectable
- **Immunological**
  CD4 count >400 cells/mm^3 for 6m
  Nadir >200 cells/mm3

ART RESUMPTION CRITERIA DURING ATI

- **Clinical**
  ARS
- **Virological**
  pVL of HIV-1 RNA >100,000 copies/mL
  pVL of HIV-1 RNA > 10,000 copies/mL for 8 weeks
- **Immunological**
  CD4 count <350 cells/mm^3 for 2 consecutive determinations

AELIX THERAPEUTICS

FIGHT AIDS AND INFECTIOUS DISEASES FOUNDATION

IrsiCaixa

BCN checkpoint

Mothe B. *et al*
LB 02669 – *v*CROI2021

Demographics

Demographics	Placebo n=15	Vaccine n=30
Age, years	34 (20 - 51)	37 (23 - 57)
Male gender, n (%)	15 (100%)	29 (96.7%)
Time from estimated HIV acquisition to ART initiation (days)	55 (12 - 125)	64 (6 - 140)
Fiebig stage at ART initiation, n (%)		
I	1 (6.7%)	1 (3.3%)
II	0 (0%)	2 (6.7%)
III	2 (13.3%)	0 (0%)
IV	0 (0%)	2 (6.7%)
V	5 (33.3%)	19 (63.3%)
VI	7 (46.7%)	6 (20%)
pVL at ART initiation, log_{10} copies/mL	4.9 (3.7 – 7)	4.7 (2.9 – 7)
Time with undetectable pVL (months)	18 (13 - 56)	27 (12 - 55)
Absolute CD4 (cells/mm^3)	826 (549 - 2156)	727 (553 - 1333)
CD4/CD8 ratio	1.1 (0.5 – 2.66)	0.99 (0.5 – 3.3)
Any Beneficial HLA class I alleles *(B2705, B5701, B1517, B1503)*	3 (20%)	7(23.3%)

Data expressed as median (range) except when noted

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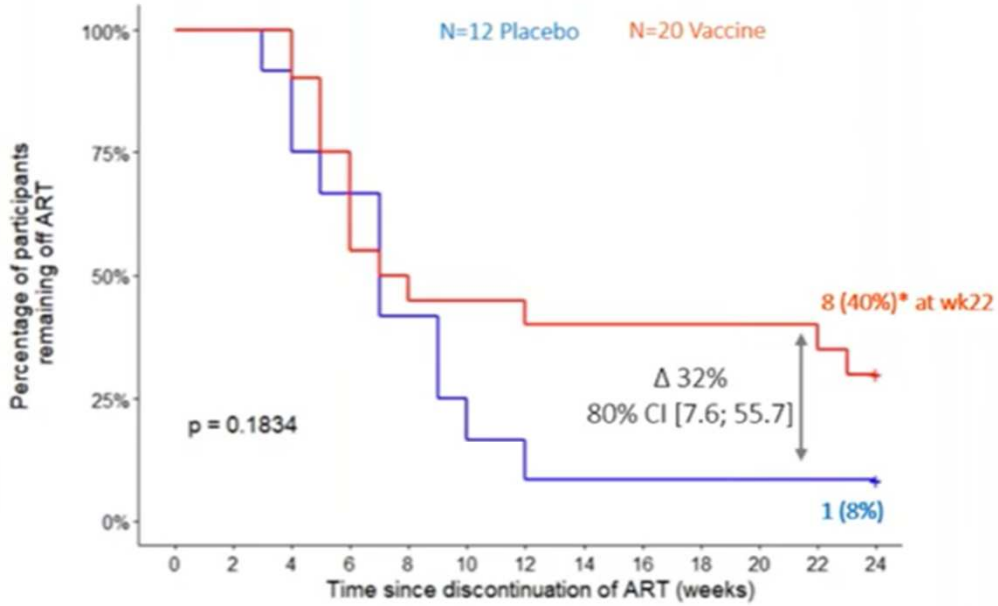
LB 02669 – vCROI2021

Higher Proportion of Vaccinees off ART

Participants Without Beneficial HLA class I alleles



** 2 last vaccinees dropped out due to COV-19 without meeting pre-specified ART resumption criteria*

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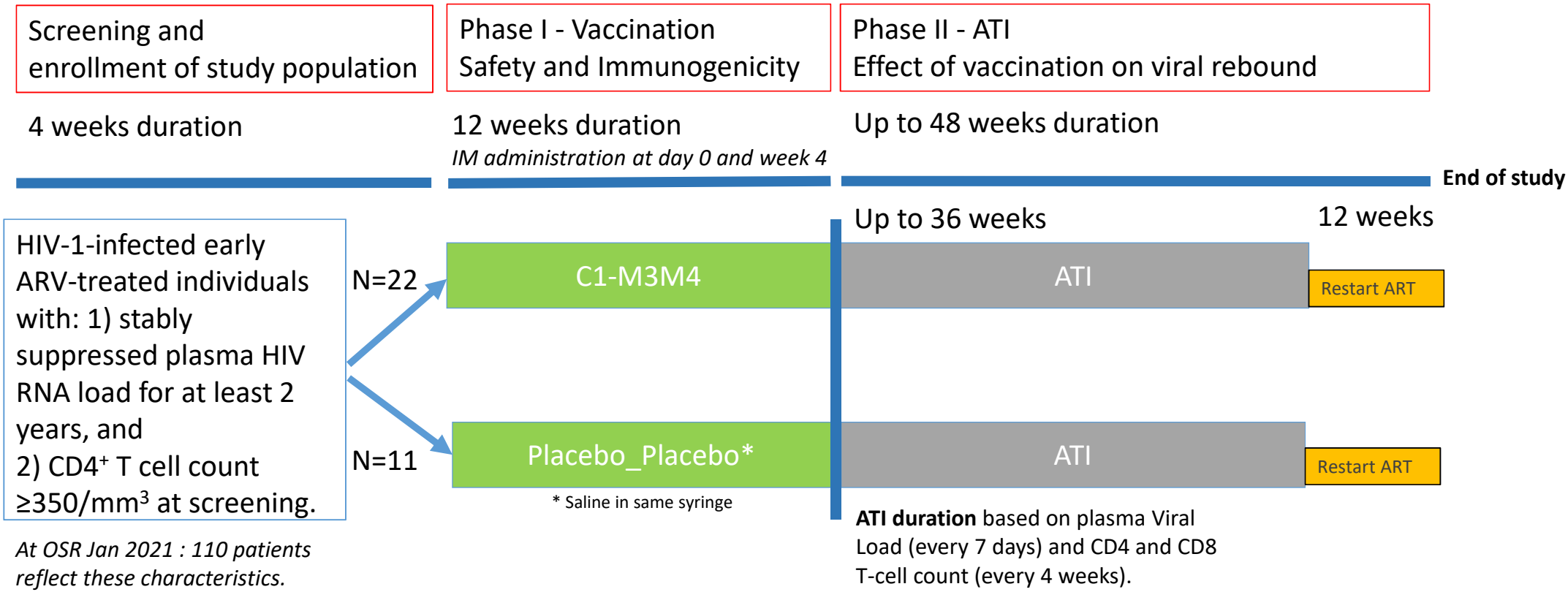
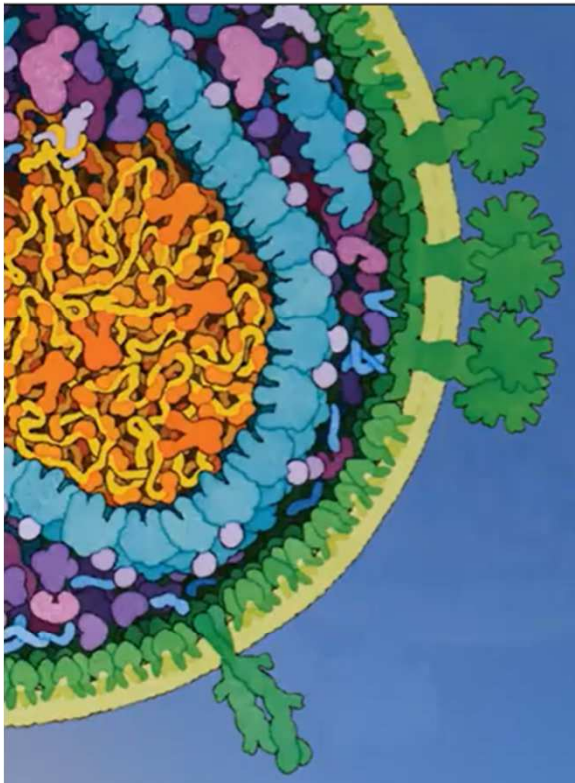
HIV-CORE 007 _ Study Schema

Phase I : Randomized, placebo-controlled, single-blind, proof-of-concept study on vaccination with C1-M3M4
Phase II : Open-label, proof-of-concept study with an Analytical Treatment Interruption (ATI)



At OSR Jan 2021 : 110 patients reflect these characteristics.



ORAL ABSTRACT

PD-1 Immune Checkpoint Blockade Enhances Vaccine Potential in a Chronic SIV/Macaque Model

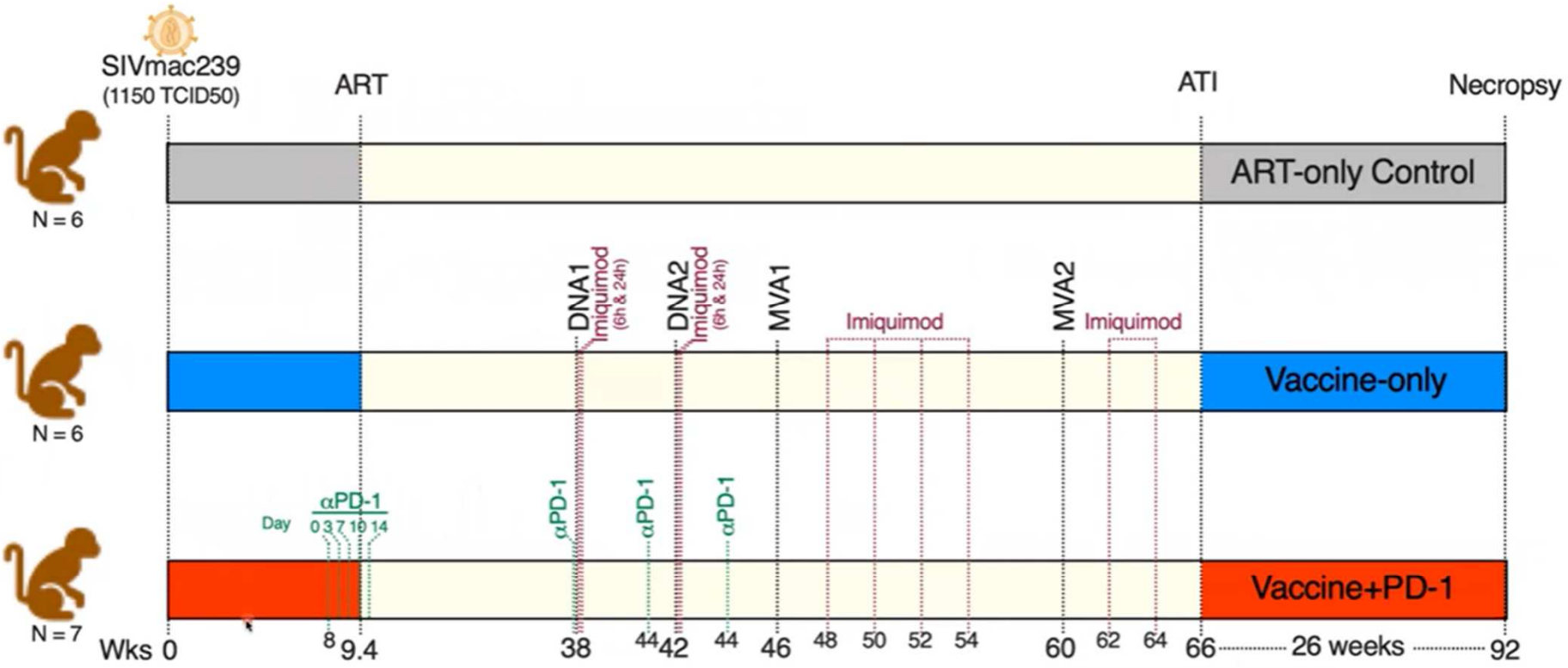
Sheikh Abdul Rahman

Yerkes National Primate Research Center – Emory University
Atlanta, GA / USA

Disclosure: None

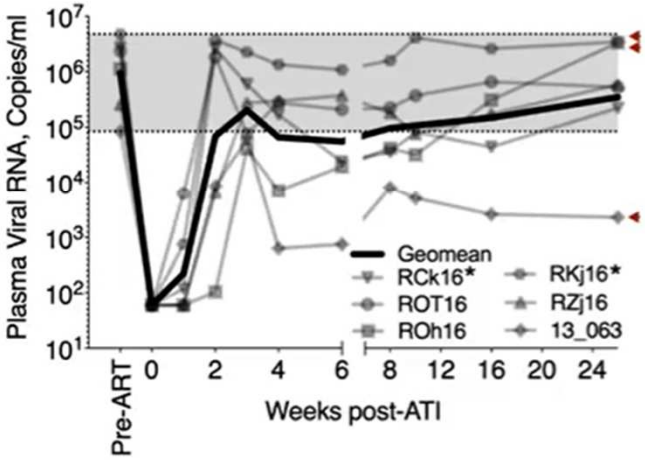
CROI 2021

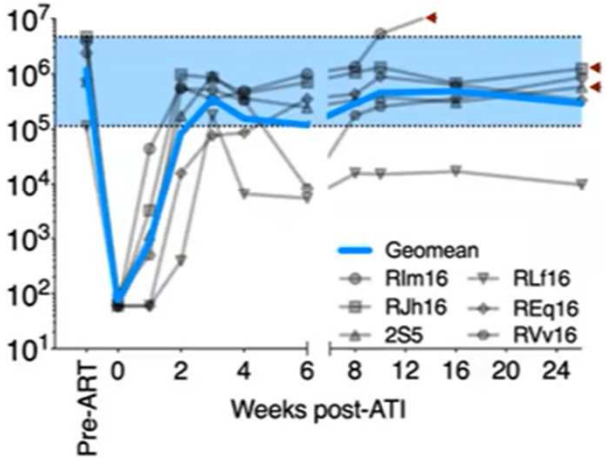
Study Design

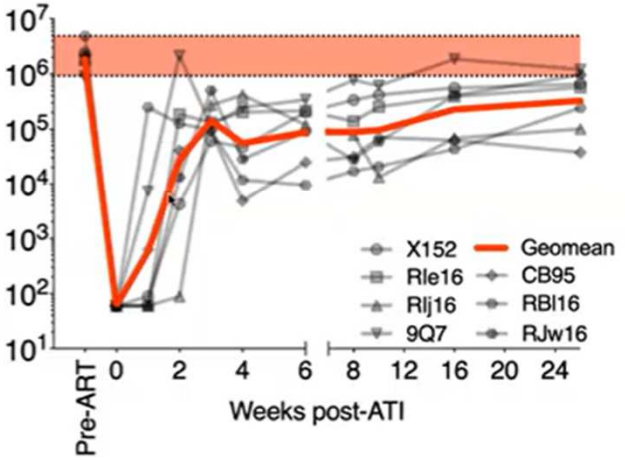


SIV Rebounded in All Three Groups

Vaccine combined with PD-1 blockade showed better control

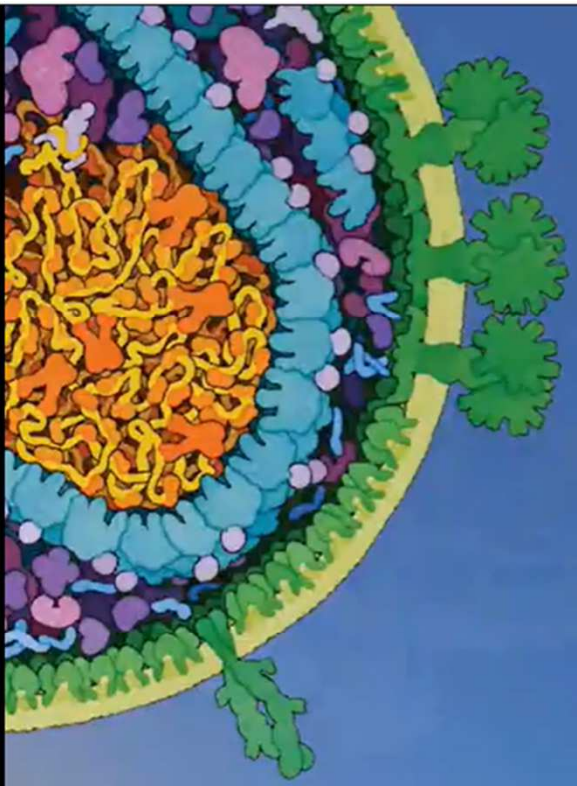






Conclusion

- CD40L+TLR7 agonist adjuvated DNA/MVA vaccine induced broad and potent anti-viral CD8 T cells under ART with enhanced their localization to lymphoid tissue.
- Combining therapeutic vaccine with PD-1 blockade significantly preserved these responses after ART interruption.
- Vaccination with PD-1 blockade significantly reduced SIV reservoirs in lymph node.
- There was no delay in viral rebound post ART interruption. However, Vaccine+PD-1 combination showed significantly better and persistent control of rebounding viremia overtime in these chronically infected macaques.
- Viral suppression strongly associated with several CD8 T cell functional quality indicating viral control was mediated by potent and broad anti-viral CD8 T cells.



ORAL ABSTRACT

An Env-Gag mRNA vaccine protects macaques from heterologous tier-2 SHIV infection

Peng ZHANG Ph.D.

Laboratory of Immunoregulation,
National Institute of Allergy and Infectious Diseases, National Institutes of Health
Bethesda, Maryland , USA

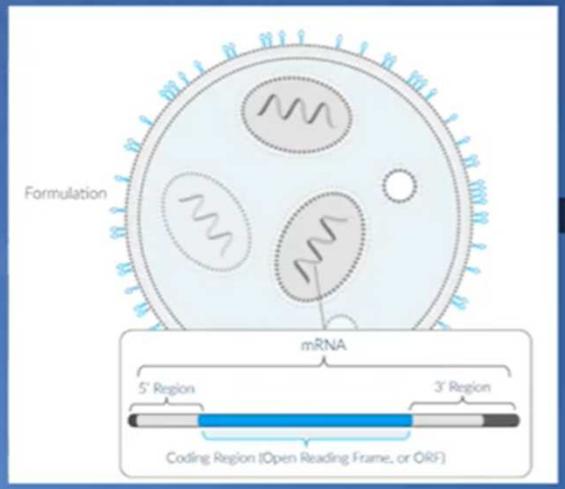
Disclosure: None

CROI 2021

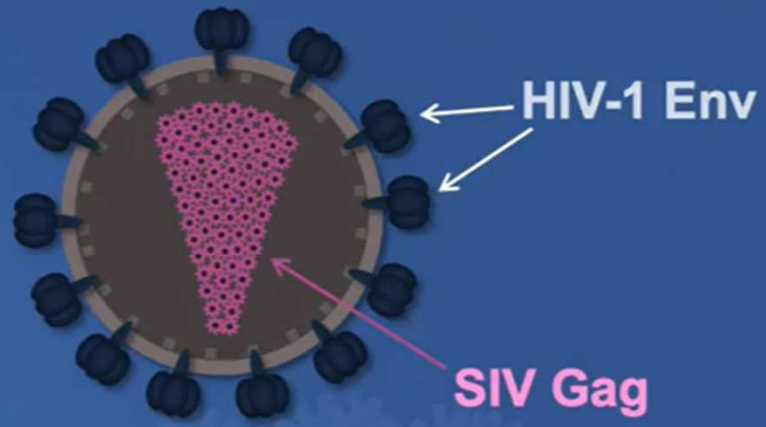
Coformulation of Gag + Env mRNA Induces the Production of Extracellular Virus-like Particles (VLP)

Gag+Env mRNA

Lipid nanoparticles



Virus-like particle (VLP)



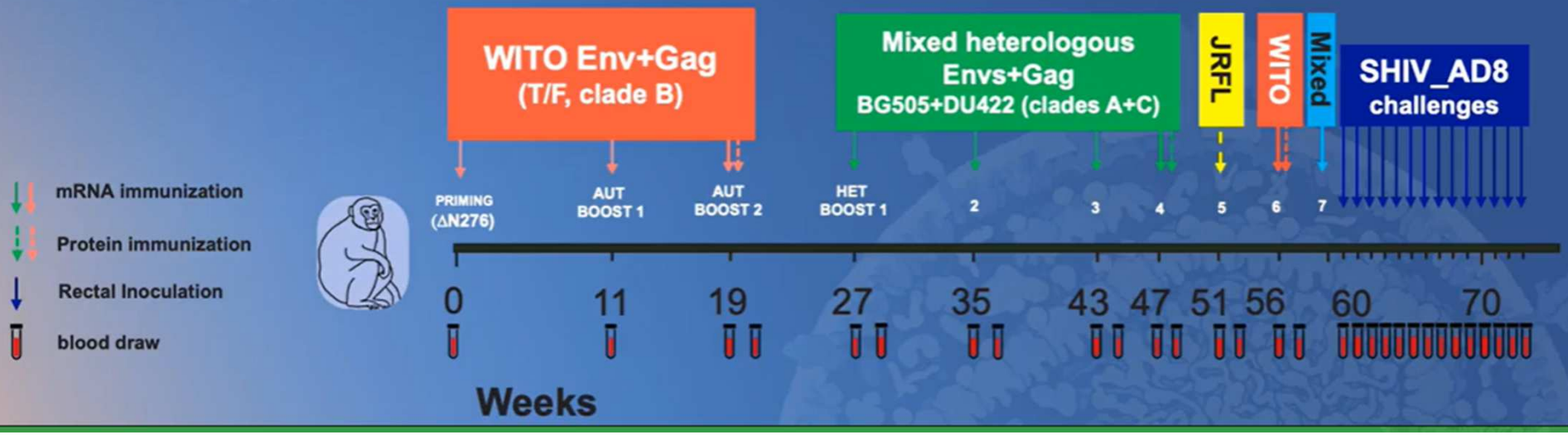
Design of the Study

Animals: Rhesus macaques (*M. mulatta*), juvenile males

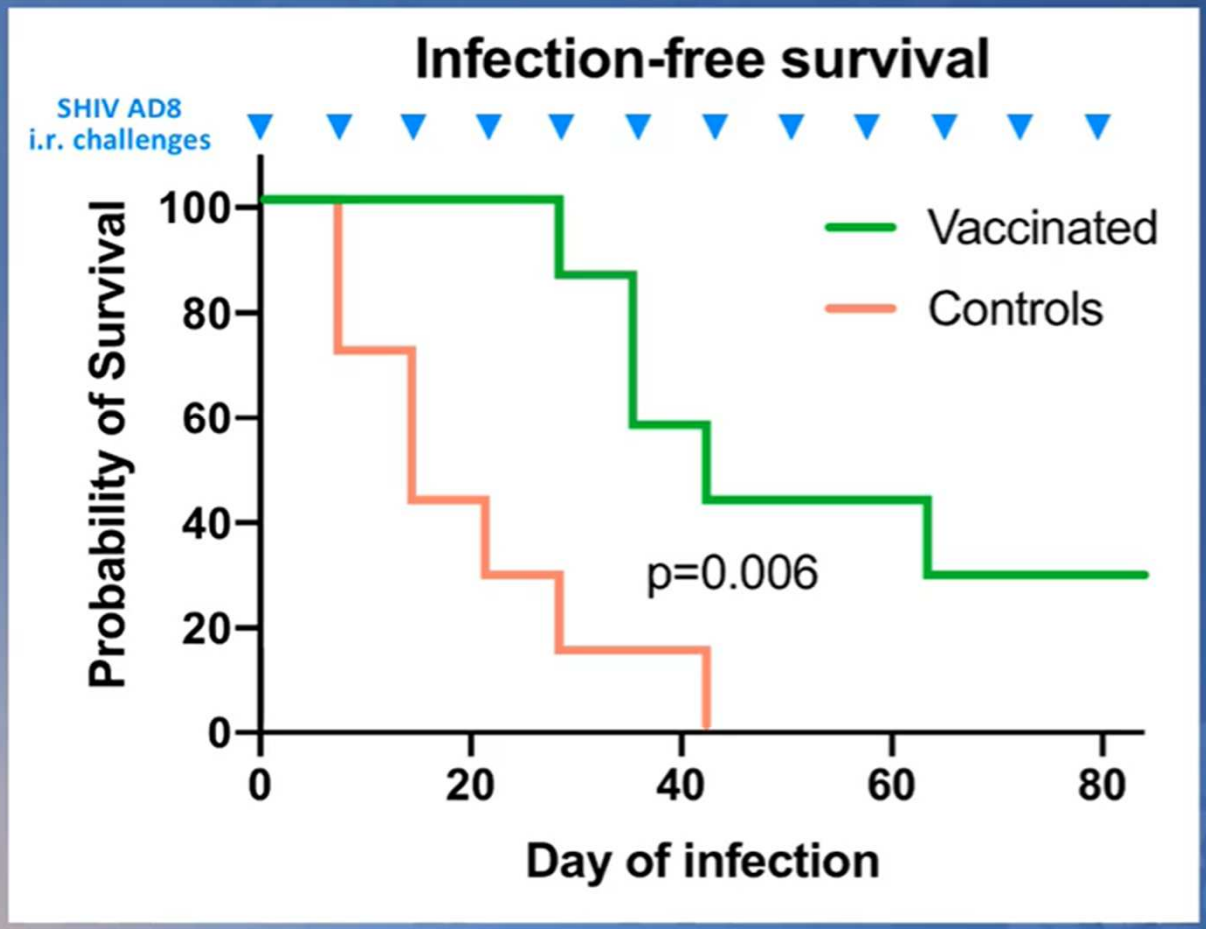
Immunogens: mRNA (HIV-1 Env, SIV Gag), 200-400 μg/animal by IM injection

Study groups:
- **Arm 1 (n=3):** Clade-B priming (WITO Env+Gag), clades A+C boosts (BG505+DU422+Gag) + final protein boosts (SOSIP.664 trimers)
- **Arm 2 (n=4):** Clade-B priming (WITO+Gag), clades A+C boosts (BG505+DU422+Gag)
- **Arm 3 (n=7):** Naïve controls (added at challenge phase)

Challenge: *In vivo*-titrated SHIV-AD8, 13 weekly low-dose 10 $TCID_{50}$ by rectal inoculation



Protection from Tier-2 SHIV (AD8) 10 TCID50 repeated Challenges in mRNA-Immunized Macaques

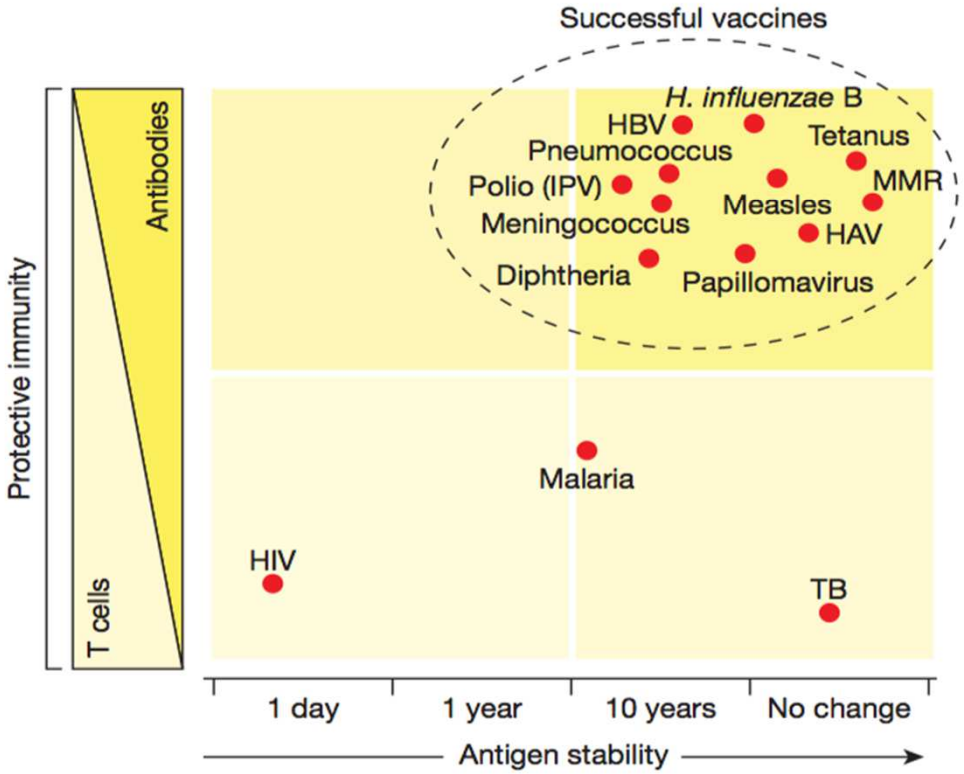


	Hazard ratio	HR 95% CI		Per-exposure risk reduction	PERR 95% CI	
		lower	upper		lower	upper
All vaccinated vs. Control	0.15	0.03	0.78	85%	22%	97%
mRNA+ Protein vs. Controls	0.12	0.01	1.07	88%	1%	99%
mRNA only vs. Controls	0.24	0.04	1.31	76%	1%	96%

Zhang *et al., in preparation*

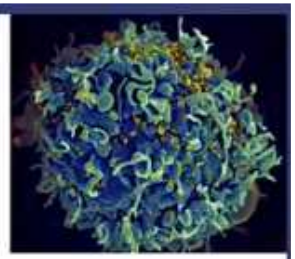
Challenging infectious diseases

Historically successful vaccines have been developed mostly against those pathogens that can be treated by antibodies and have a stable antigen repertoire (Box 1 Figure). HIV, malaria and tuberculosis vaccines do not fall within the cluster of successful vaccines in the graph, because of antigenic variability and the requirement of T-cell immunity for protection. Developing vaccines against these pathogens requires novel approaches.



Rappuoli R, Nature 2011

Why has HIV vaccine development been so challenging?



Genetic diversity of virus greater than any other pathogen

- Envelope less immunogenic than other viruses (perhaps due to glycan shield)[1]
- The gp160 envelope trimeric structure is unique, hard to simulate and has fewer trimers on the surface[2]

No natural immunity to HIV infection and no human challenge model[3,4] (latency, no cure)

Imperfect animal model – different virus (SIV/SHIV)[4]

- Expensive, non-predictive of vaccine efficacy

Limited return on investment to develop vaccines[5]

- Innovation comes from the public sector, less so from private sector
- Reluctance to do expensive efficacy trials of candidate vaccines
- Need for expanded capacity to manufacture complicated vaccine products

Vaccine development is slow[6]

SIV, Simian immunodeficiency virus; SHIV, simian-human immunodeficiency virus

1. Klasse PJ, et al. Cell Host Microbe. 2020;27:507-518.
2. Ward AB and Wilson IA. Trends Biochem Sci. 2015; 40: 101–107.
3. Elsheikh MM, et al. EBioMedicine. 2019; 45: 624–629.
4. Sui Y, et al. Curr Protoc Immunol. 2013; 102: 12.14.1–12.14.30.
5. Serdobova I and Kieny M. Am J Public Health. 2006 September; 96(9): 1554–1559.
6. Struck MM. Nat Biotechnol. 1996;14:591–593.

VRC01 Efficacy in Preventing HIV Infection:
AMP Study Design

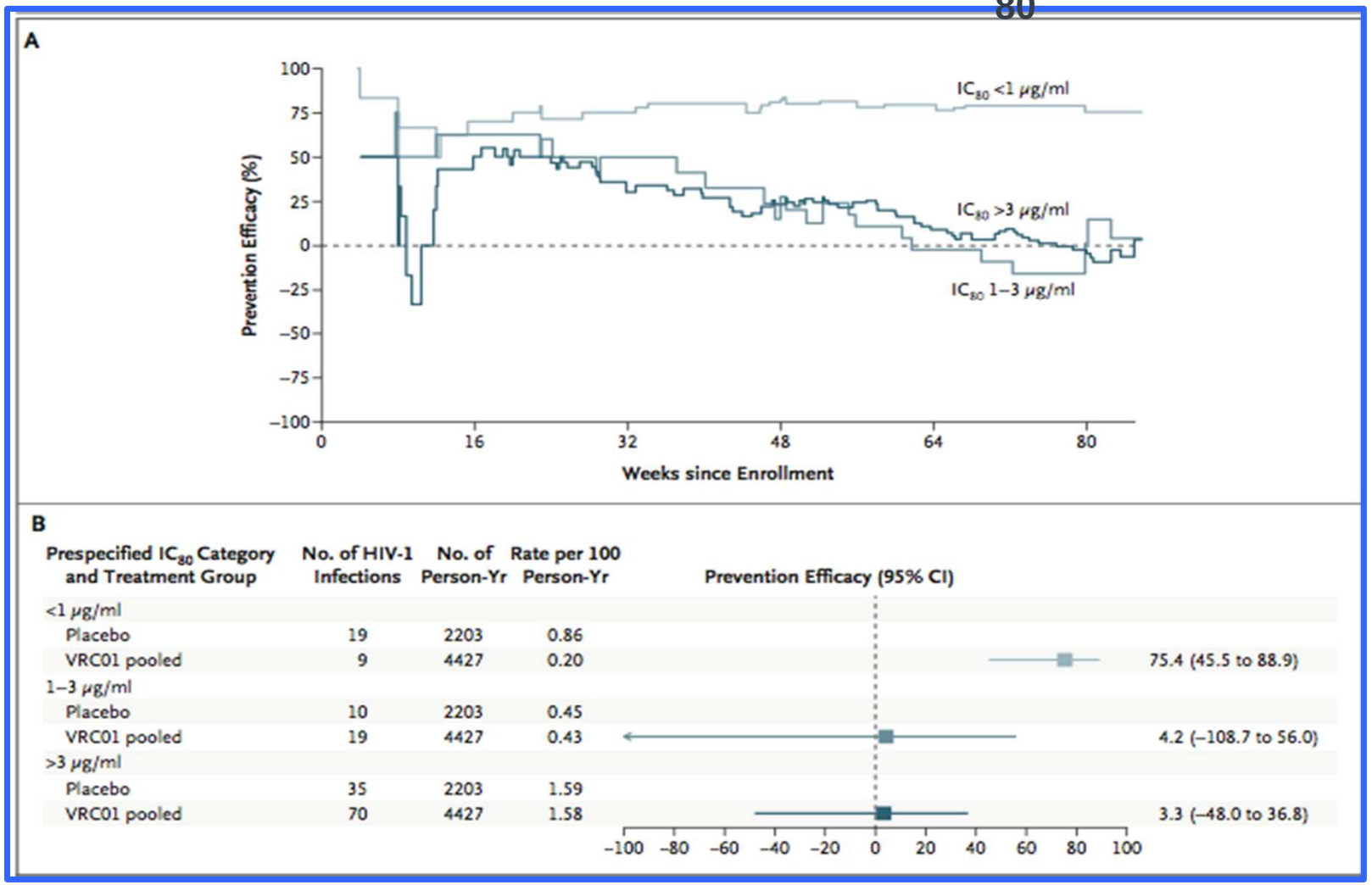
- 2 double-blind, placebo-controlled, proof-of-concept phase IIb trials of broadly neutralizing antibody VRC01 in preventing HIV infection
  - HVTN 703/HPTN 081: N = 1924 cisgender women in sub-Saharan Africa
  - HVTN 704/HPTN 085: N = 2699 MSM and TG persons who have sex with men in Americas/Europe
- Patients randomized to VRC01 10 mg/kg vs 30 mg/kg vs placebo control Q8W for 10 infusions
  - Efficacy tracked through Wk 80
  - Safety/tolerability tracked through Wk 104

Participants, n	VRC01 10 mg/kg	VRC01 30 mg/kg	Control	Total
HVTN 703/HPTN 081	642	645	637	1924
HVTN 704/HPTN 085	899	897	903	2699

Corey. HIVR4P 2021. Abstr HY01.01LB. NCT02568215. NCT02716675.

HVTN 704/ HPTN 085 and HVTN 703/HPTN 081

Prevention Efficacy of VRC01 against HIV-1 of Different in Vitro Sensitivities (IC_{80}) to VRC01



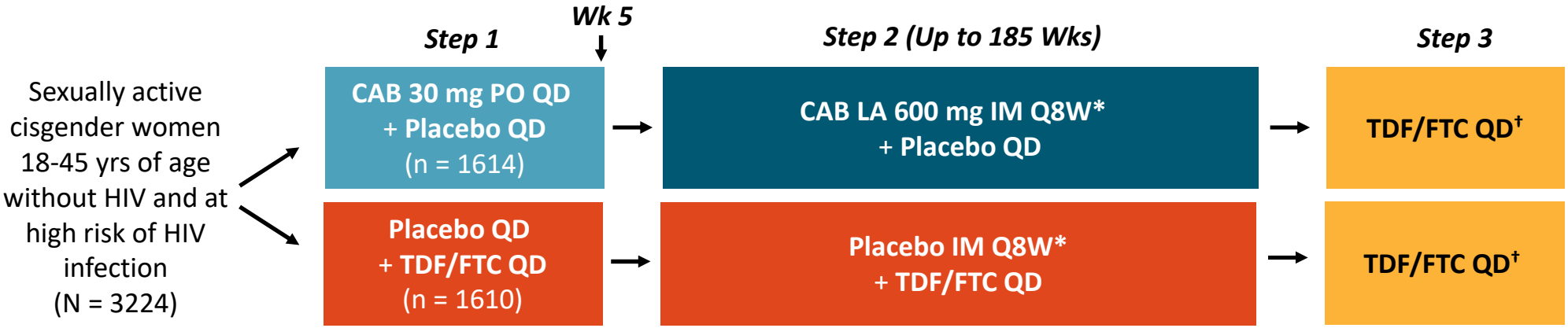
B

Prespecified IC_{80} Category and Treatment Group	No. of HIV-1 Infections	No. of Person-Yr	Rate per 100 Person-Yr	Prevention Efficacy (95% CI)
<1 μg/ml				
Placebo	19	2203	0.86	
VRC01 pooled	9	4427	0.20	75.4 (45.5 to 88.9)
1–3 μg/ml				
Placebo	10	2203	0.45	
VRC01 pooled	19	4427	0.43	4.2 (−108.7 to 56.0)
>3 μg/ml				
Placebo	35	2203	1.59	
VRC01 pooled	70	4427	1.58	3.3 (−48.0 to 36.8)

L Corey, NEJM 2021

HPTN 084 Interim Analysis: Long-Acting CAB vs TDF/FTC as HIV PrEP in Cisgender Women

- Double-blind, placebo-controlled phase IIb/III trial comparing efficacy, safety of LA injectable CAB vs daily oral TDF/FTC in cisgender women in sub-Saharan Africa



*First 2 doses given 4 wks apart, then every 8 wks thereafter.
†Open-label TDF/FTC initiated maximum 8 wks after last injection for up to 48 wks.

- Primary endpoint: superiority analysis of HIV incidence during steps 1 and 2
  - Prespecified stopping boundary crossed (planned interim review: November 5, 2020)

Delany-Moretlwe. HIVR4P 2021. Abstr HY01-02. NCT02720094.

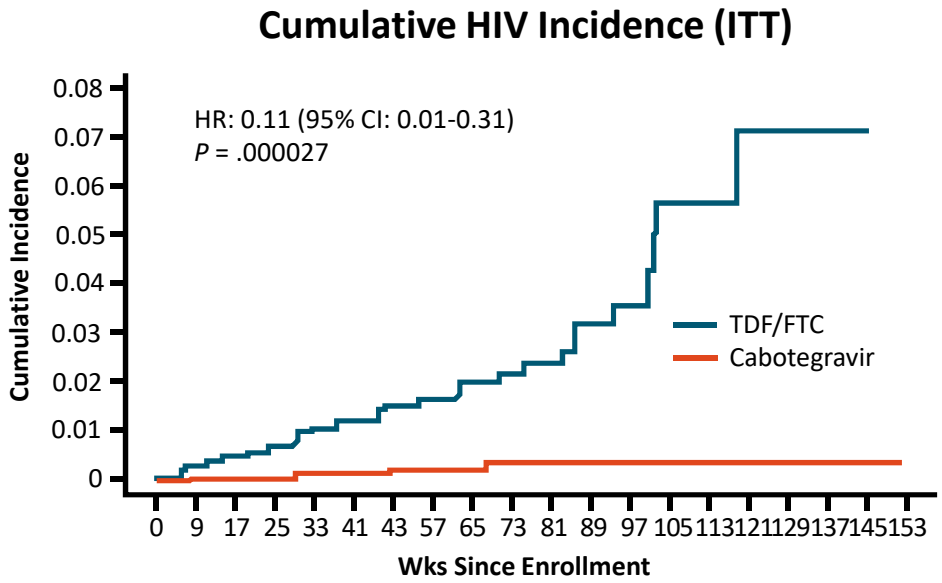
Slide credit: clinicaloptions.com

HPTN 084 Interim Analysis: HIV Incidence

- Pooled HIV incidence of 1.03 (95% CI: 0.73-1.40) per 100 PY suggests both agents highly effective in reducing HIV acquisition in study population
  - No differences in treatment effects between prespecified subgroups, including age, BMI, contraceptive use

Incidence	Cabotegravir (n = 1953 PY)	TDF/FTC (n = 1939 PY)
HIV infections, n	4	36
HIV incidence per 100 PY (95%)	0.2 (0.06-0.52)	1.86 (1.30-2.57)

- Women in cabotegravir arm had 89% lower risk of HIV infection vs TDF/FTC



Delany-Moretlwe. HIVR4P 2021. Abstr HY01.02.

Slide credit: clinicaloptions.com

TAB. **1** Studi clinici vaccinali di efficacia contro HIV-1

Nome dello studio	Immunogeno	Anni	Coorte vaccinata	Paesi coinvolti	Commenti
VAX 003	gp120 bivalente	1999-2003	Tossicodipendenti	Tailandia	No protezione No riduzione della carica virale
VAX 004	gp120 bivalente (AIDSVAX® B/E)	1998-2003	Coppie discordanti	USA	No protezione No riduzione della carica virale
HVTN 502/504 (STEP)	Vettore Ad5+proteine (Gag, Pol e Nef)	2004-2007	Uomini omosessuali Uomini e donne eterosessuali ad alto rischio	USA	Interrotto nel 2007. Il rischio di infezione appariva più elevato nei maschi Ad5 sieropositivi o non circoncisi
HVTN 503 (Phambili)	Vettore Ad5+proteine (Gag, Pol e Nef)	2007	Uomini e donne eterosessuali	Sud Africa	Interrotto a settembre 2007 a seguito dei risultati dello STEP. No protezione No riduzione della carica virale
RV144	1ª dose: vettore canarypox (ALVAC-HIV vCP1521) 2ª dose: gp120 bivalente (AIDSVAX® gp120 B/E)	2003-2009	Uomini e donne HIV negativi	Tailandia	31,2% protezione
HVTN 505	1ª dose: DNA codificante Gag, Pol, Nef e Env 2ª dose: Ad5 codificante Gag-Pol+Env	2009-2017	Uomini omosessuali Transessuali che fanno sesso con uomini	USA	No protezione No riduzione della carica virale
HVTN 702 (Uhambo)	1ª dose: vettore canaripox (ALVAC-HIV vCP2438) 2ª dose: gp120 bivalente (gp120 C/MF59)	2016-2020	Uomini e donne	Sud Africa	Interrotto a febbraio 2020 No protezione

HPX2008 /HVTN 705 (Imbokodo)	1-4ª dose: Ad26.Mos4.HIV 5-6ª dose: gp140 trimerica	2017-2022	Donne	Sud Africa	In corso
HVTN 706/HPX3002 (Mosaico)	1-2ª dose: Ad26.Mos4.HIV 3-4ª dose: Ad26.Mos4.HIV+ Mosaico e gp140 C	2019-2023	Uomini omosessuali Transessuali che fanno sesso con uomini	Argentina, Brasile, Italia, Messico, Perù, Polonia, Spagna e USA	In corso
PrEPVacc	*Prima randomizzazione* Gruppo A: DNA-HIV-PT123+ AIDSVAX®/BE Gruppo B: DNA-HIV-PT123+ CN54gp140/MPLA + MVA-CMDR+ CN54gp140/MPLA *Seconda randomizzazione* TAF/FTC oppure TDF/FTC	2020 (ritardato al 2021) -2023	Uomini e donne	Est e Sud Africa	In corso

A Combination Efficacy Study in Africa of Two DNA-MVA-Env Protein or DNA-Env Protein HIV-1 Vaccine Regimens With PrEP (PrEPVacc)

Condition or disease	Intervention/treatment	Phase
HIV Infections	Biological: Vaccine Group A: DNA-HIV-PT123 and AIDSVAX® B/E (weeks 0,4,24,48) Biological: Vaccine Group B: DNA-HIV-PT123 and CN54gp140+MPLA-L (weeks 0,4), then MVA and CN54gp140+MPLA-L (weeks 24,48) Biological: Vaccine Group C: Saline placebo (weeks 0,4,24,48) Drug: Control PrEP:TDF/FTC once daily (weeks 0-26) Drug: Experimental PrEP:TAF/FTC once daily (weeks 0-26)	Phase 2

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 DECEMBER 3, 2009 VOL. 361 NO. 23

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

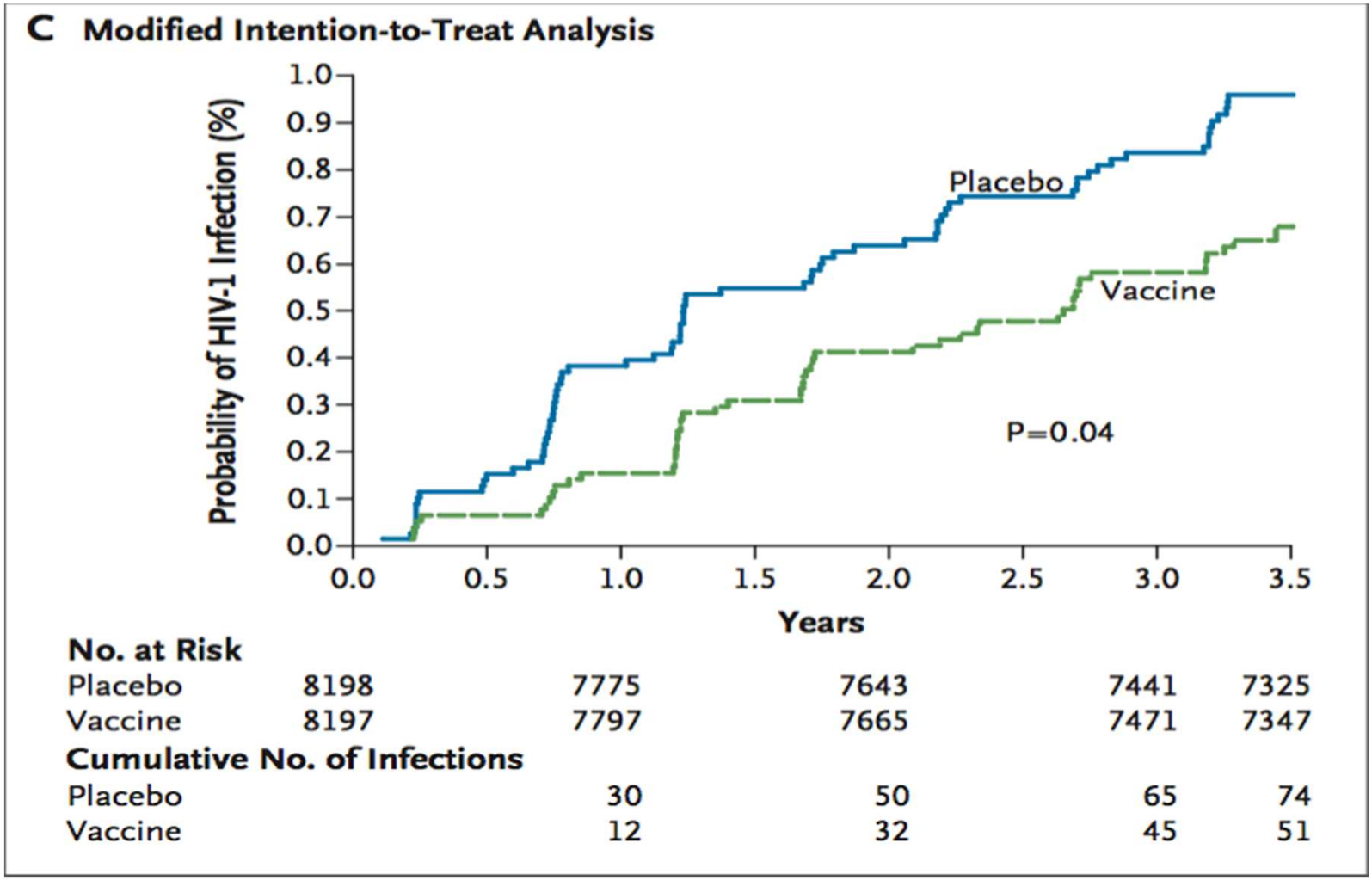
RV 144

METHODS

In a community-based, randomized, multicenter, double-blind, placebo-controlled efficacy trial, we evaluated four priming injections of a recombinant canarypox vector vaccine (ALVAC-HIV [vCP1521]) plus two booster injections of a recombinant glycoprotein 120 subunit vaccine (AIDSVAX B/E). The vaccine and placebo injections were administered to 16,402 healthy men and women between the ages of 18 and 30 years in Rayong and Chon Buri provinces in Thailand. The volunteers, primarily at heterosexual risk for HIV infection, were monitored for the coprimary end points: HIV-1 infection and early HIV-1 viremia, at the end of the 6-month vaccination series and every 6 months thereafter for 3 years.

S. Rerks-Ngarm, NEJM 2009

RV 144 trial



S. Rerks-Ngarm, NEJM 2009

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 NOVEMBER 28, 2013 VOL. 369 NO. 22

Efficacy Trial of a DNA/rAd5 HIV-1 Preventive Vaccine

HVTN 505

We randomly assigned 2504 men or transgender women who have sex with men to receive the DNA/rAd5 vaccine or placebo.

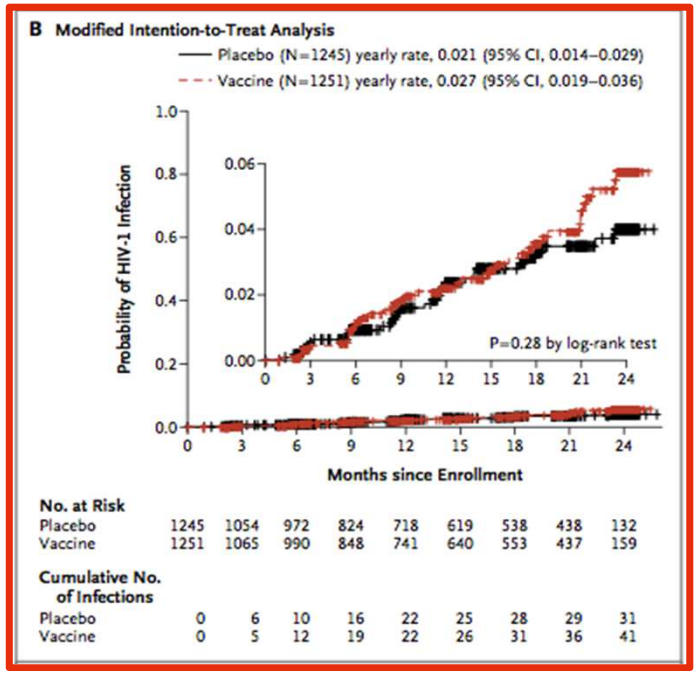
The 6-plasmid DNA vaccine (expressing clade B Gag, Pol, and Nef and Env proteins from clades A, B, and C) was administered at weeks 0, 4, and 8. The rAd5 vector boost (expressing clade B Gag-Pol fusion protein and Env glycoproteins from clades A, B, and C) was administered at week 24

We assessed HIV-1 acquisition from week 28 through month 24 (termed week 28+ infection), viral-load set point (mean plasma HIV-1 RNA level 10 to 20 weeks after diagnosis), and safety

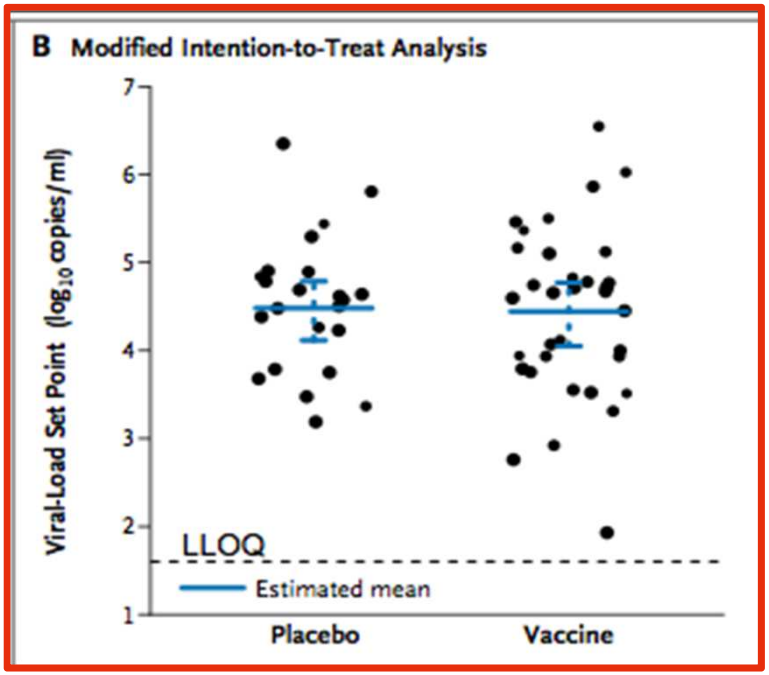
S. Hammer, NEJM 2013

HVTN 505

Cumulative incidence



Viral-load set points



SM Hammer, NEJM 2013

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 MARCH 25, 2021 VOL. 384 NO. 12

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

HVTN 702

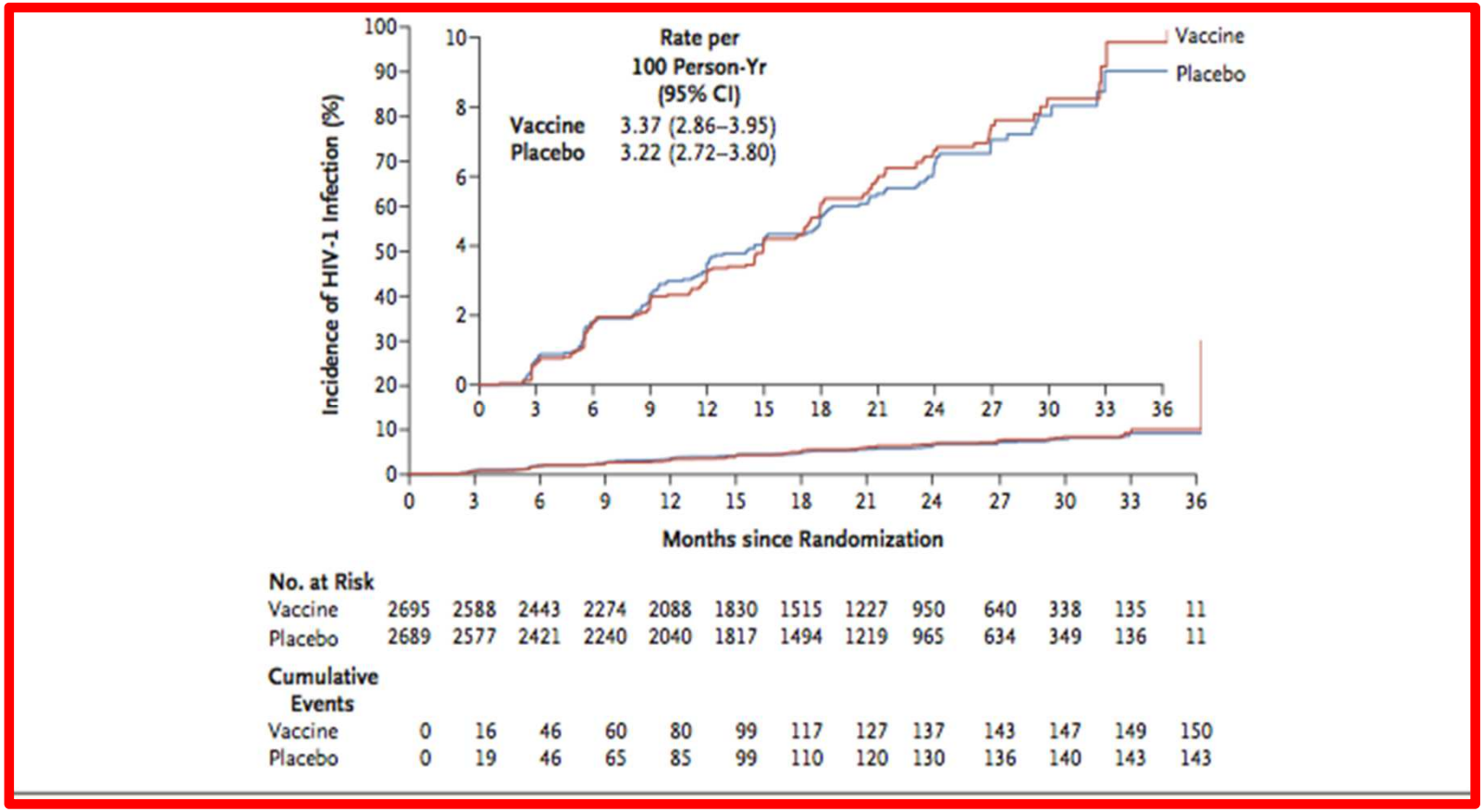
In this phase 2b–3 trial, we randomly assigned 5404 adults without HIV-1 infection to receive the vaccine or placebo

The vaccine regimen consisted of injections of ALVAC-HIV at months 0 and 1, followed by four booster injections of ALVAC-HIV plus bivalent subtype C gp120–MF59 adjuvant at months 3, 6, 12, and 18

The primary efficacy outcome was the occurrence of HIV-1 infection from randomization to 24 months

GE Gray, NEJM 2021

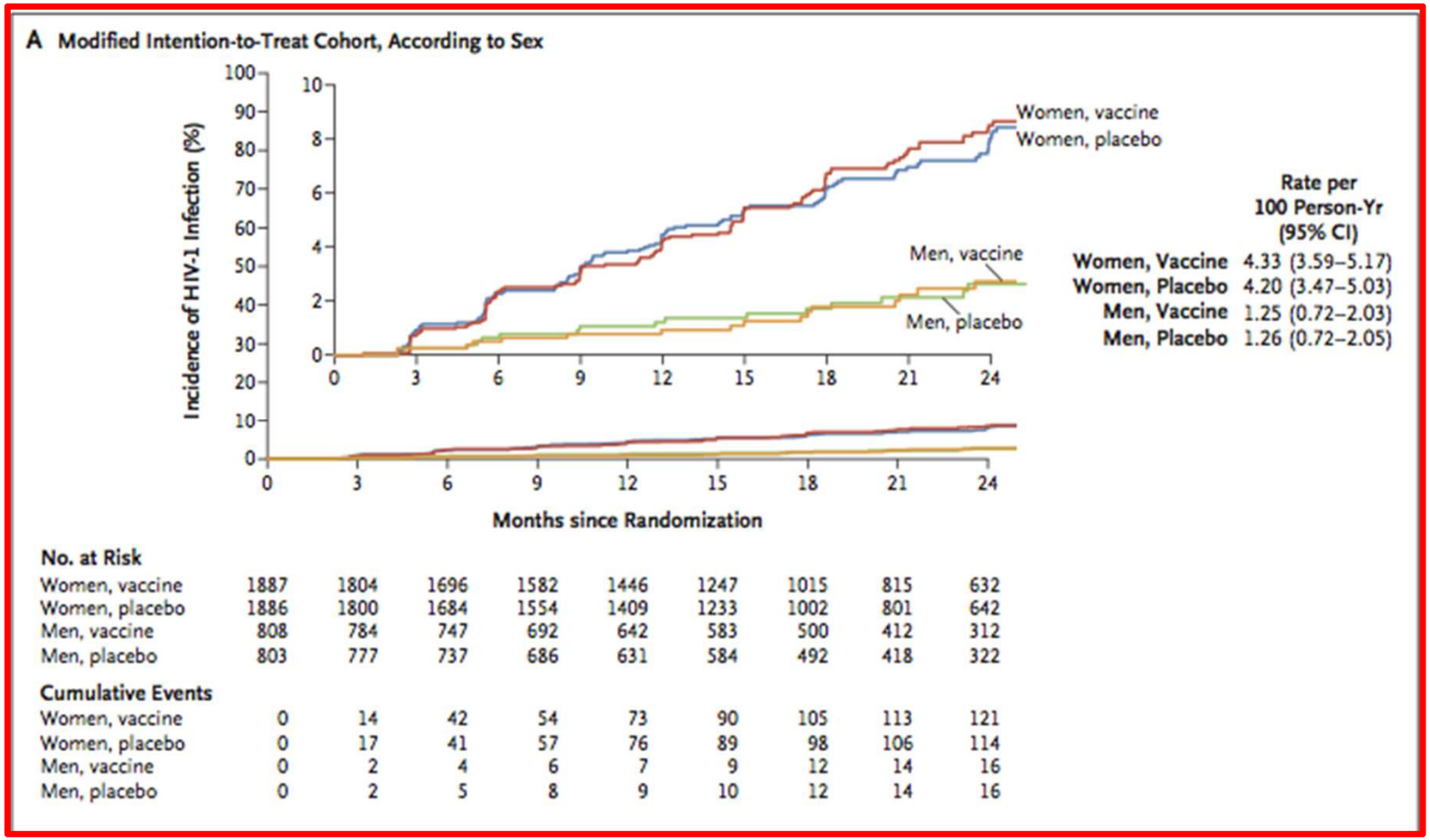
HVTN 702 Cumulative incidence of HIV-1 infection (0-36 months)



No. at Risk													
Vaccine	2695	2588	2443	2274	2088	1830	1515	1227	950	640	338	135	11
Placebo	2689	2577	2421	2240	2040	1817	1494	1219	965	634	349	136	11
Cumulative Events													
Vaccine	0	16	46	60	80	99	117	127	137	143	147	149	150
Placebo	0	19	46	65	85	99	110	120	130	136	140	143	143

Ge Gray, NEJM 2021

HVTN 702 Cumulative incidence of HIV-1 infection according to sex



No. at Risk									
Women, vaccine	1887	1804	1696	1582	1446	1247	1015	815	632
Women, placebo	1886	1800	1684	1554	1409	1233	1002	801	642
Men, vaccine	808	784	747	692	642	583	500	412	312
Men, placebo	803	777	737	686	631	584	492	418	322
Cumulative Events									
Women, vaccine	0	14	42	54	73	90	105	113	121
Women, placebo	0	17	41	57	76	89	98	106	114
Men, vaccine	0	2	4	6	7	9	12	14	16
Men, placebo	0	2	5	8	9	10	12	14	16

GE Gray, NEJM 2021

IMBOKODO
Ph2b

Southern Africa

Predominantly Clade C

Heterosexual Women

Intra-vaginal transmission

Limited PrEP use

MOSAICO
Ph3

Americas, Europe

Predominantly Clade B

MSM + TG

Intra-rectal transmission

Increased PrEP use

Janssen Infectious Diseases & Vaccines
PHARMACEUTICAL COMPANIES OF Johnson & Johnson

Recombinant vector-based vaccines

= non-pathogenic infectious viruses expressing antigenic protein genes of a pathogen

- Potent immunogenicity in animal and human diseases
- Need to select the proper antigen that will trigger protective immunity
- Activation of innate immunity
- Ability to induce cellular immunity and humoral immunity
- Relative ease of production for many viral and non viral vectors
- Generally favorable safety profile and lack of persistence in vivo

Replicating viral vectors

Advantages

Persistent, potentially life-long immunity

Limitations

Vector-induced disease induction in vaccinated individuals
Spread of the vector virus in the population
Risk of genetic instability

Non-replicating viral vectors

Advantages

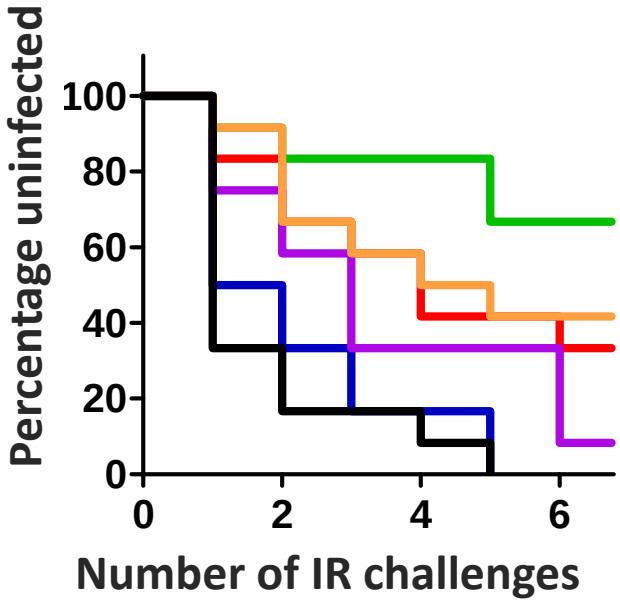
Possibility to delete replication gene to create replication incompetent vector
Quickly cleared from body → Safety profile
Same vector can be used for multiple vaccine

Limitations

Generally less robust and/or less persistent immune response
High dose or repeated administration needed/possible for some vectors

1. Volker Understanding modern day vaccines what you need to know 2017
2. Francis Recent Advances in VaccineTechnologies 2017
3. Strugnell R, et al. Chapter 3 in: Garçon N, et al. Understanding Modern Vaccines, Perspectives in Vaccinology, Vol 1, Amsterdam, Elsevier, 2011, pp. 60–88
4. Weiner and Nabel in Plotkin chapter 67 dvpl gene based vectors 2017
5. Rollier Viral vectors as vaccine platforms: deployment in sight 2011
6. Ewer Viral vectors as vaccine platforms: from immunogenicity to impact 2016
7. https://www.ema.europa.eu/en
8. https://www.tga.gov.au/

The Ad26/Ad26+gp140 HIV vaccine regimen provided significant protection in NHP



(virus SHIV-SF162P3, expressing clade B Env)

Vaccinations *Mo 0, 3*	*Mo 6, 12*	Risk reduction *per exposure*	Full protection *6 challenges*
Ad26,	**Ad26+Clade C gp140**	**94%**	**67%**
Ad26,	MVA+Clade C gp140	87%	42%
Ad26,	Clade C gp140	84%	33%
Ad26,	MVA	71%	8%
Ad26,	Ad26	35%	0%
Sham		0%	0%

- Binding **antibodies** to HIV Env together with Env specific **T cells** post 3rd and post 4th vaccination correlated with protection
- **Functional antibodies, not broad neutralization** were found to correlate with protection
  - Antibody dependent cellular phagocytosis (ADCP)

Barouch, Tomaka, Wegmann, et al., The Lancet, 2018

Safety and immunogenicity of two heterologous HIV vaccine regimens in healthy, HIV-uninfected adults (TRAVERSE): a randomised, parallel-group, placebo-controlled, double-blind, phase 1/2a study

On day 0, participants received a first injection of tetravalent vaccine (Ad26.Mos4.HIV or placebo) or trivalent vaccine (Ad26.Mos.HIV or placebo), and those injections were repeated 12 weeks later. At week 24, vaccine groups received a third dose of tetravalent or trivalent together with clade C gp140, and this was repeated at week 48, with placebos again administered to the placebo group.

The tetravalent vaccine regimen was generally safe, well-tolerated, and found to elicit higher immune responses than the trivalent regimen. Regimens that use this tetravalent vaccine component are being advanced into field trials to assess efficacy against HIV-1 infection.

LR Baden, Lancet HIV 2020

31 October 2017

START of

Proof of Concept study

Imbokodo

Imbokodo, *Zulu for "rock"*
The Zulu phrase "To strike a woman, is to strike a rock" refers to the strength and importance of women in their community

Aim: To evaluate the efficacy of the vaccine regimen in reducing the incidence of HIV infection

Imbokodo/HPX2008/HVTN 705:

a phase 2b multicenter, randomized, parallel group, placebo-controlled, double-blind clinical trial

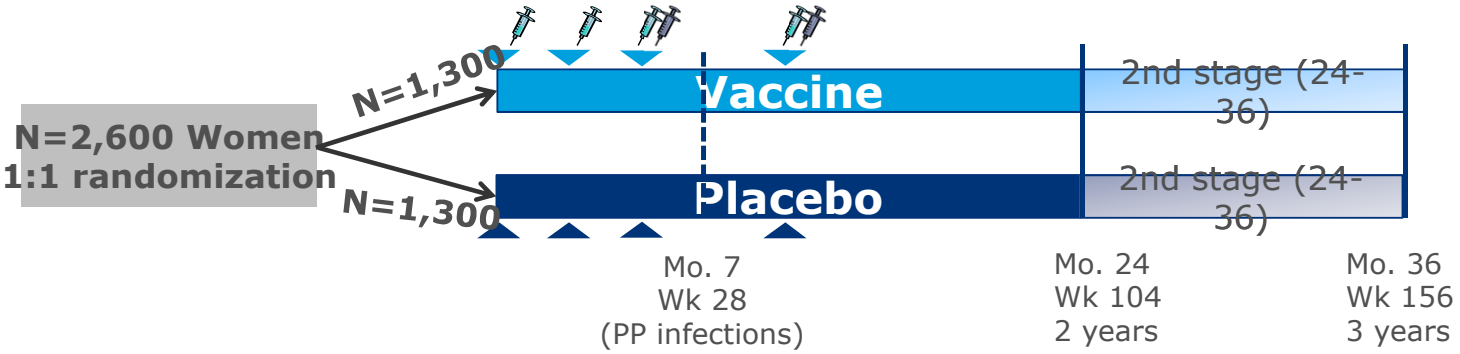
Population: Sexually active HIV-1 uninfected women (born female), age 18-35 years

Vaccine regimen: 2x Ad26.Mos4.HIV (week 0,12), 2x Ad26.Mos4.HIV+ Clade C gp140 (week 24, 48)

Objective: to evaluate the efficacy of the vaccine regimen in reducing the incidence of HIV infection in women

Protective Efficacy hypothesis: 50% (lower bound >0%) reduction in HIV-1 acquisition

Status: fully enrolled May 2019



MOSAICO

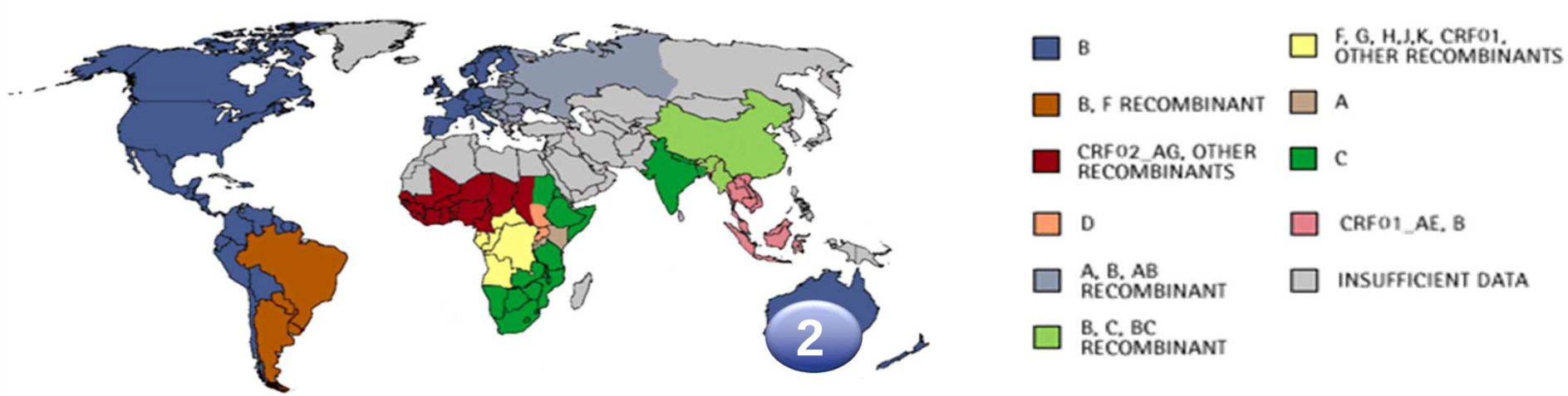
HPX3002/HVTN706

A Multi-center, Randomized, Double-blind, Placebo-controlled Phase 3 Efficacy Study of a Heterologous Vaccine Regimen of Ad26.Mos4.HIV and Adjuvanted Clade C gp140 and Mosaic gp140 to Prevent HIV-1 Infection Among Cis-gender Men and Transgender Individuals who Have Sex with Cis-gender Men and/or Transgender Individuals.

Janssen Infectious Diseases & Vaccines

PHARMACEUTICAL COMPANIES OF Johnson & Johnson

The Future: HIV Preventive Vaccine
Prophylactic Vaccine Aiming at Protection Against the globally predominant clades of HIV-1



1

Vectors that elicit optimal immune responses

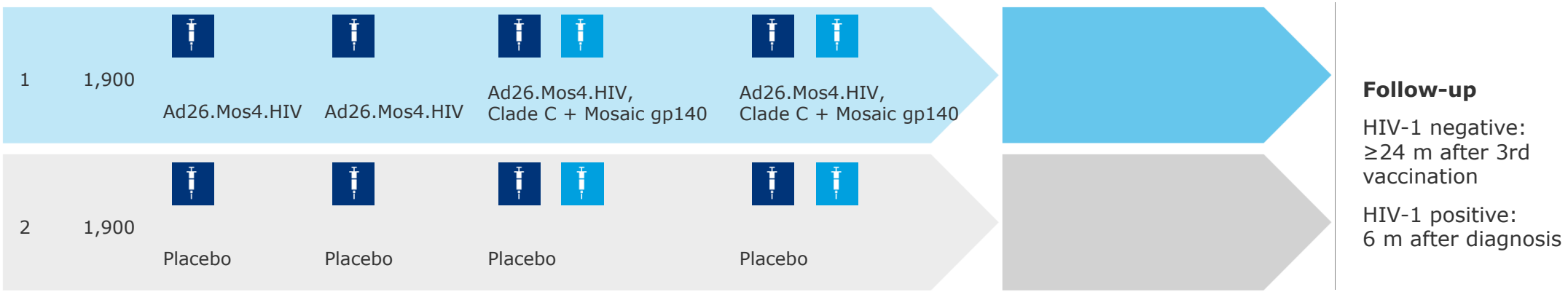
Mosaic inserts for global coverage (Gag-Pol-Env)

3

Trimeric env proteins for improved humoral immunity

MOSAICO - Study design

3,800 participants; 1:1 randomization (stratified by site)



Primary Objective and Endpoint

Primary Objective

To evaluate the vaccine efficacy (VE) for the prevention of HIV-1 infection in HIV-1 seronegative cis-gender men and transgender individuals having sex with cis-gender men and/or transgender individuals.

Primary Endpoint

Confirmed HIV-1 infections diagnosed between Month 7 and Month x (with 24≤x≤30 months) visits in the per-protocol (PP) population.

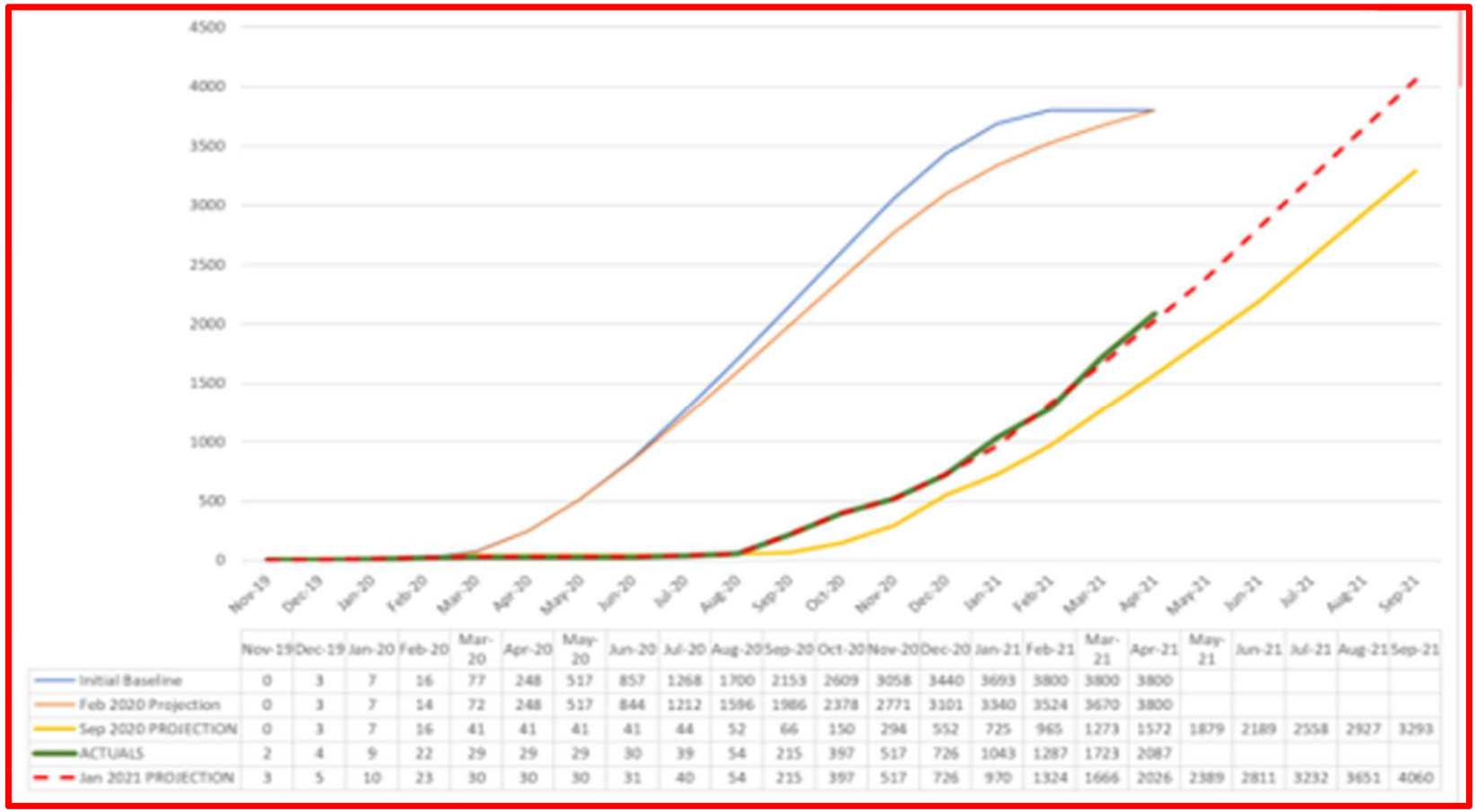
Main inclusion criteria

HIV-uninfected cis-gender men and transgender individuals having sex with cis-gender men and/or transgender individuals who are considered to be **at increased risk for HIV infection**. Participants must in the last 6 months have had:

- **Any condomless receptive anal or vaginal sex (not included is condomless anal sex within a mutually monogamous relationship ≥12 months if the partner is HIV negative or living with HIV and virally suppressed), OR**
- **Rectal or urethral gonorrhea or chlamydia or incident syphilis, OR**
- **Any stimulant use (eg, cocaine, amphetamine), OR**
- **5 or more sex partners**

Potential participant is negative for HIV-1 and HIV-2 infection <28 days prior to first vaccination.

MOSAICO



	Nov-19	Dec-19	Jan-20	Feb-20	Mar-20	Apr-20	May-20	Jun-20	Jul-20	Aug-20	Sep-20	Oct-20	Nov-20	Dec-20	Jan-21	Feb-21	Mar-21	Apr-21	May-21	Jun-21	Jul-21	Aug-21	Sep-21
Initial Baseline	0	3	7	16	77	248	517	857	1268	1700	2153	2609	3058	3440	3693	3800	3800	3800					
Feb 2020 Projection	0	3	7	14	72	248	517	844	1212	1596	1986	2378	2771	3101	3340	3524	3670	3800					
Sep 2020 PROJECTION	0	3	7	16	41	41	41	41	44	52	66	150	294	552	725	965	1273	1572	1879	2189	2558	2927	3293
ACTUALS	2	4	9	22	29	29	29	30	39	54	215	397	517	726	1043	1287	1723	2087					
Jan 2021 PROJECTION	3	5	10	23	30	30	30	31	40	54	215	397	517	726	970	1324	1666	2026	2389	2811	3232	3651	4060

In Italy 74 patients screened