19ª edición

POSTCROI

Una actualización de la "29th Conference on Retroviruses and Opportunistic Infections"

Vacunas

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Servei Malalties Infeccioses

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HUGTIP, Badalona

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HIV

General

Sunday February 13th
Opening Session

3 – Vaccine Strategies for HIV-1 & COVID-19
Dan H. Barouch

Wednesday February 16th
Plenary Session 3

117 – Past & Future of HIV Vaccines
Mark Feinberg

Preventive:

Active Immunization

Wednesday February 16th
Oral Abstract Session 10

121 Phase IIIb Efficacy trial of MOSAIC HIV-1 vaccine regimen in African women: IMBOKODO
Glenda E. Gray

Passive Immunization

Thursday February 24th
Symposium 7

149 Lessons learned from the AMP:
Carolyn Williamson

Tuesday February 15th
Oral Abstract Session 7

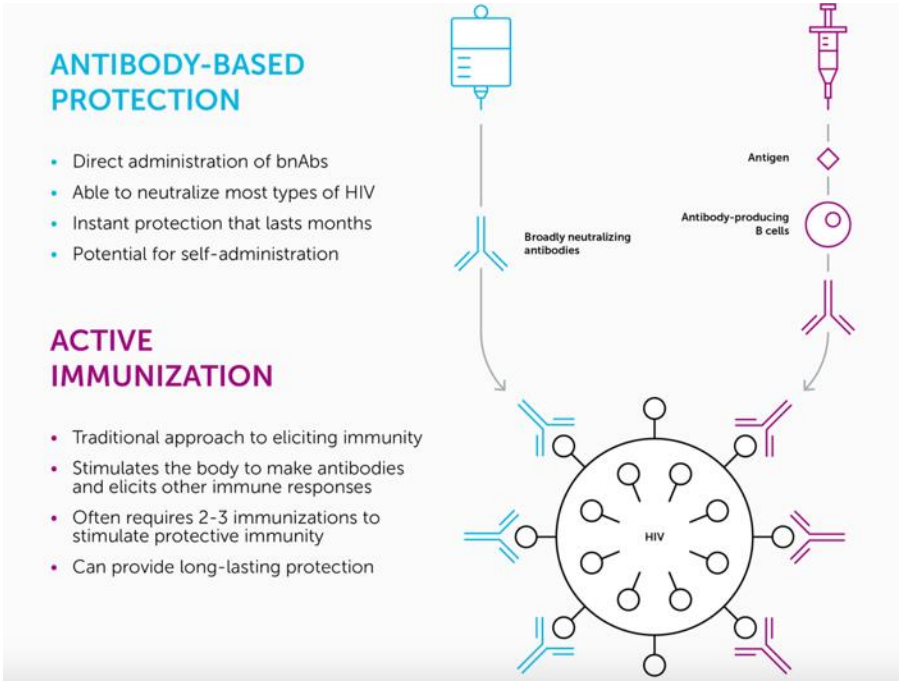
81 Phase I study of combinaton Ab
Magdalena E. Sobieszczyk

Therapeutic:

Combinations

Tuesday February 15th
Oral Abstract Session 5

63 Therapeutic efficacy of combined active and passive immunization in SHIV+ macaques
Victoria E. Walker-Sperling



COV

COV vaccines

Monday February 14th
Oral Abstract Session -4

47 – Safety & Effectiveness of Ad26.CoV2.S in SA : Sisonke
Glenda E. Gray

48 – COVID-19 Booster in IS
Jung Sun

Breakthrough infections

Monday February 14th
Oral Abstract Session -4

49- Infectiousness of breakthrough infections after vaccination and natural infection (Qatar)
Laith Abu-Raddad

Wednesday February 16th
Interactive Session -8

Viral load kinetics in partially or fully vaccinated individuals infected with SARS-CoV-2
Annelies Wilder-Smith

Monday February 14th
Interactive Session 1

COVID-19 – *John P. Moore*
HPV - *Margaret A. Stanley*
Flu – *Florian Krammer*
Herpes – *Betsy Herold*
HIV-1 – *Alexandra Trkola*

Mandates / Hesitancy

Monday February 14th
Interactive Session 3
History - *Ruth Macklin*
Minorities - *Matifadza H. Davis*

CT design

Sunday February 13th
Workshop 4
Correlates - *Peter Gilbert*
Effectiveness - *Sheena G. Sullivan*

General

Sunday February 13th

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Plenary Session 3

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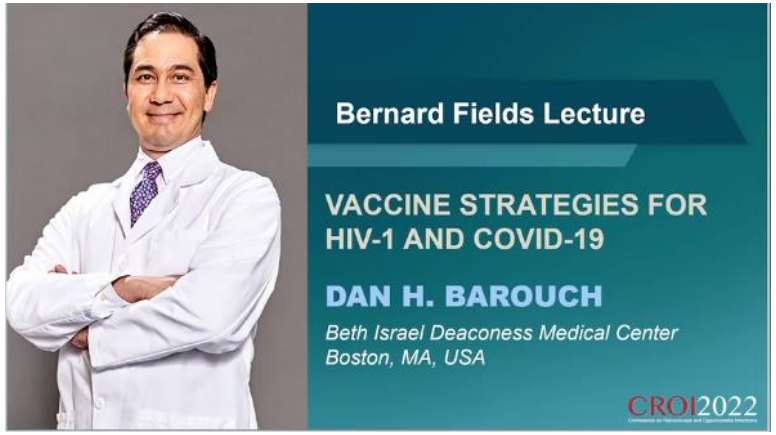
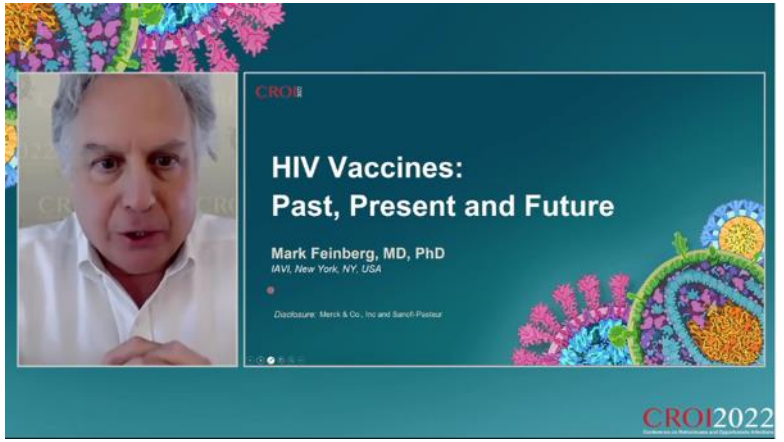




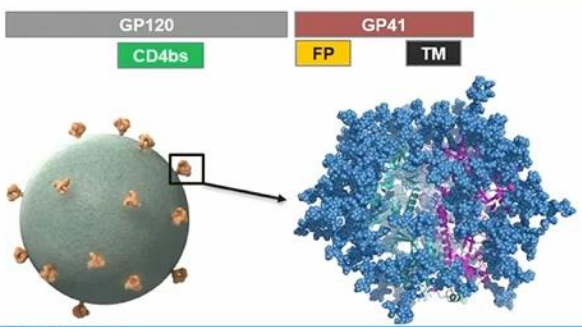
Two Contrasting Global Pandemics

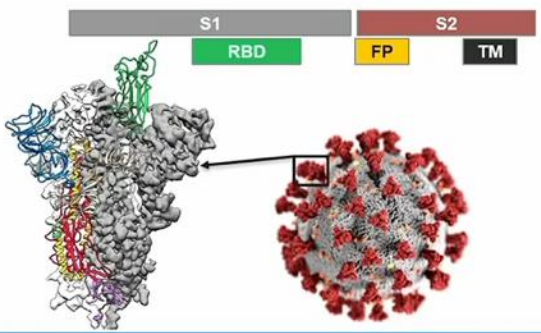
HIV-1
- 40 Years
- Retrovirus
- Chronic persistent infection
- Immunodeficiency (AIDS)
- 79 million infections
- 36 million deaths
- Enormous viral diversity
- Env difficult to neutralize
- No vaccine available

SARS-CoV-2
- 2 Years
- Coronavirus
- Acute infection
- Respiratory illness (COVID-19)
- 408 million infections
- 5.8 million deaths
- Limited viral diversity
- Spike easy to neutralize
- Multiple vaccines available

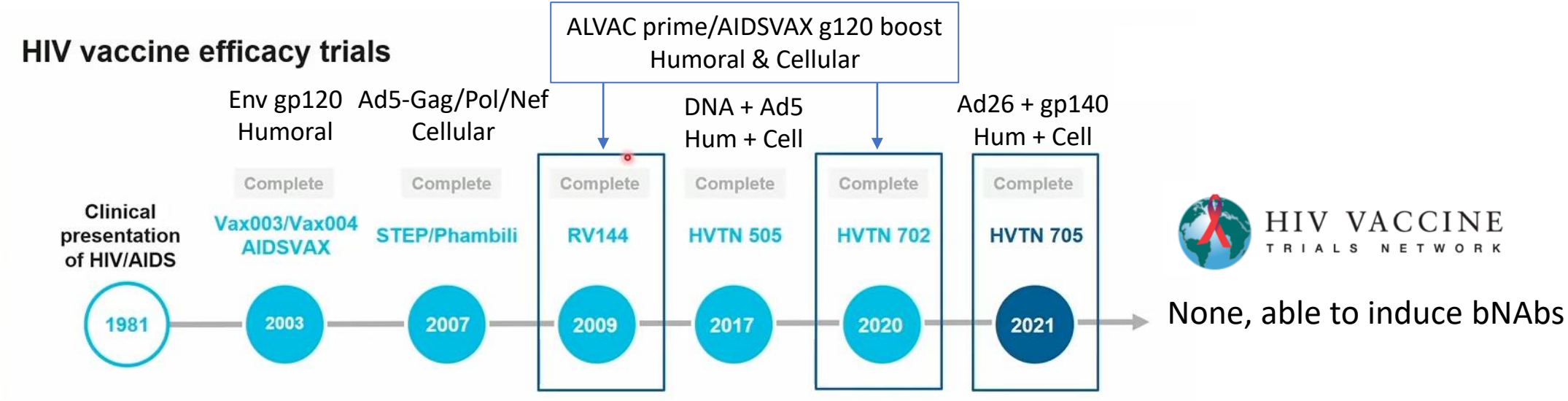
SARS-CoV-2 and HIV: Similarities and differences

HIV-1	SARS-CoV-2
Target cell/disease = **CD4+ T cells…..AIDS**	Target cell/disease = **Epithelial cells lungs….COVID-19**
Host receptor = **CD4 and CCR5**	Host receptor = **ACE2**
Entry = **Env, 2 subunits (GP120 & GP41)**	Entry = **Spike, 2 subunits (S1 & S2)**
→ **trimeric glycoprotein**	→ **trimeric glycoprotein**
• Enormous diversity, persistent infection	• More limited diversity, acute infection
• High level glycosylation of Env	• More limited glycosylation of S
• Neutralizing epitopes structurally shielded	• Neutralizing epitopes readily accessible to Abs
• Neutralizing antibodies not readily elicited in natural infection, and to date, not by vaccination	• Neutralizing antibodies readily elicited by infection and vaccination

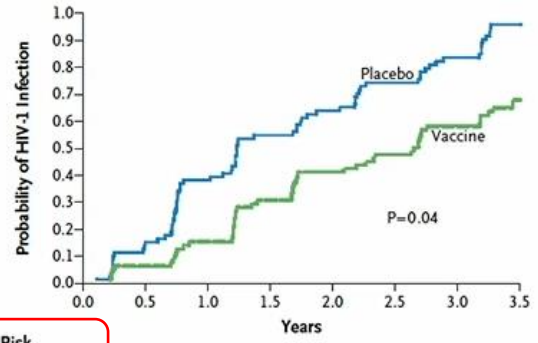




HIV vaccine efficacy trials



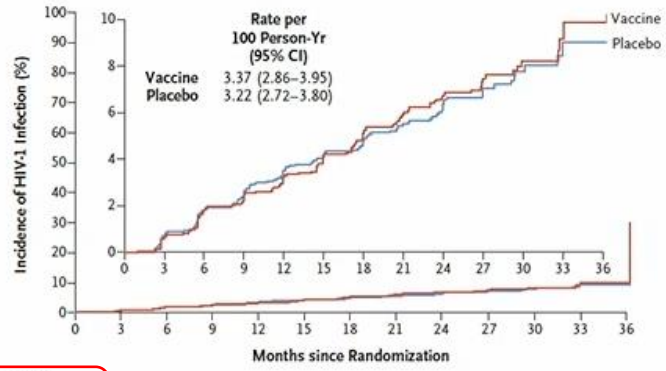
RV144 – Thailand (2009) VE=31%



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	

		RV144	HVTN 702
		Complete	Complete
Viral	Viral Subtype	AE	C
	Viral Diversity	Relatively Homogenous	Highly diverse
Population	HIV Risk/Incidence	0.28%	~4%
	Host Genetics	Thai	African
	Mucosal Inflammation	TBD	TBD
Vaccine	Adjuvant	Aluminum hydroxide	MF59
	ALVAC Inserts	Subtype AE vCP1521	Subtype C vCP2438
	Protein Boost	Bivalent AE/B (A244/MN)	Bivalent C (TV1.C/1086.C)
	Protein Dose	Higher (300 mg of each protein)	Lower (100 mg of each protein)
	Dosing Schedule	M 0/1/3/6	M 0/1/3/6/12 (18)

HVTN702 – South Africa (2020) VE=0%



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	

Rerks-Ngarm, NEJM 2009

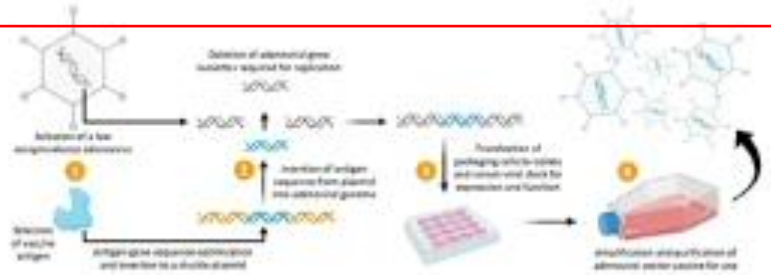
Gray, NEJM 2021

Barouch

Novel Vaccine Platforms: Gene-Based Vaccines

Nucleic Acid Vaccines
(DNA, mRNA)

Viral Vector Vaccines
(Adenovirus, Poxvirus)

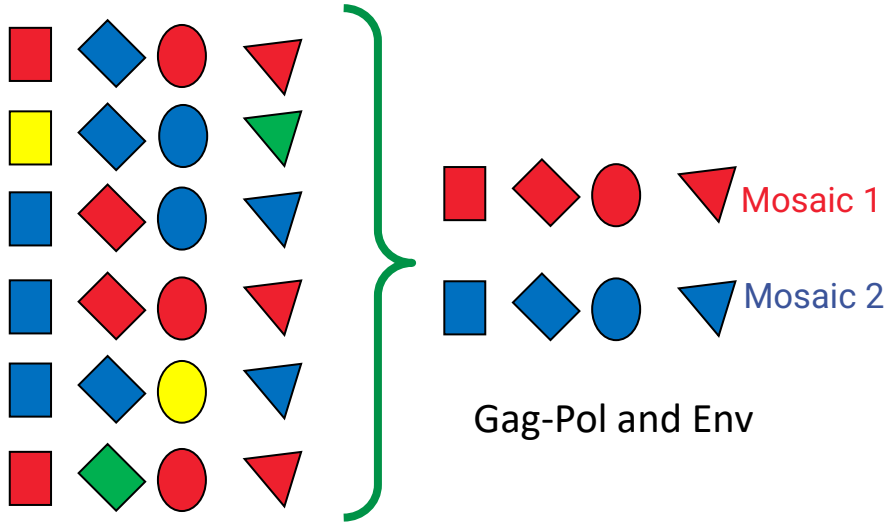


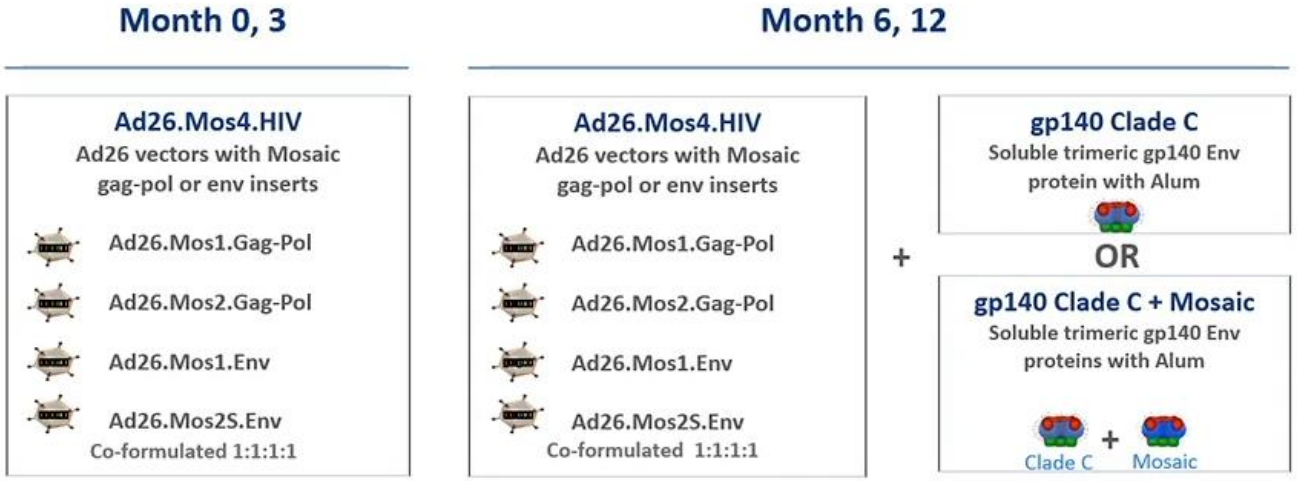
Gebre et al. Cell 2021; 184:1589-1603

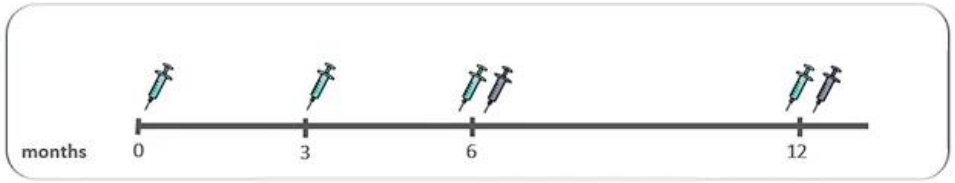
Ad26-vectored vaccines (JnJ):

- Ad26-HIV
- Ad26-ZIKV
- Ad26-Ebola
- Ad26-RSV
- → Ad26-COV

Ad26-HIV







→ Two Complementary Phase 2b/3 Efficacy Studies

IMBOKODO

Phase: 2b

Enrollment: 2,637

Participants: Young Women (aged 18-35)

Location: 5 Southern African Countries

Timeline: Began Nov 2017, Vaccinations completed in July 2020

IMBOKODO

MOSAICO

Phase: 3

Target Enrollment: 3,800

Participants: MSM and TGI (aged 18-60)

Location: 8 Countries in the Americas and Europe

Timeline: Began end 2019, enrollment ongoing

MOSAICO

Delayed because of COVID-19 PrEP implementation

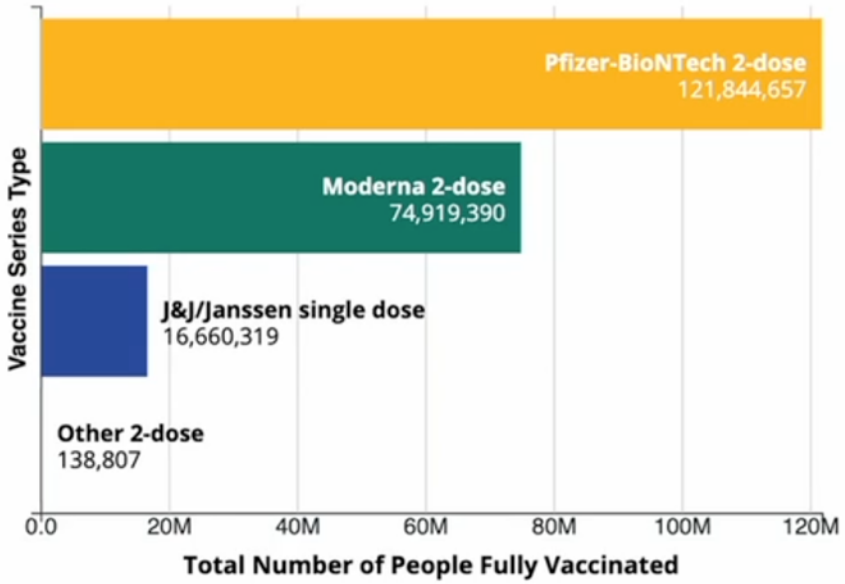
Fisher W, et al. Nat Med 2007
Barouch Nat Med 2010
Barouch, Cell 2013

<u>Differences:</u> HIV-1 clade, gender, route, protein boost

Ad26.COV2.S (JnJ)

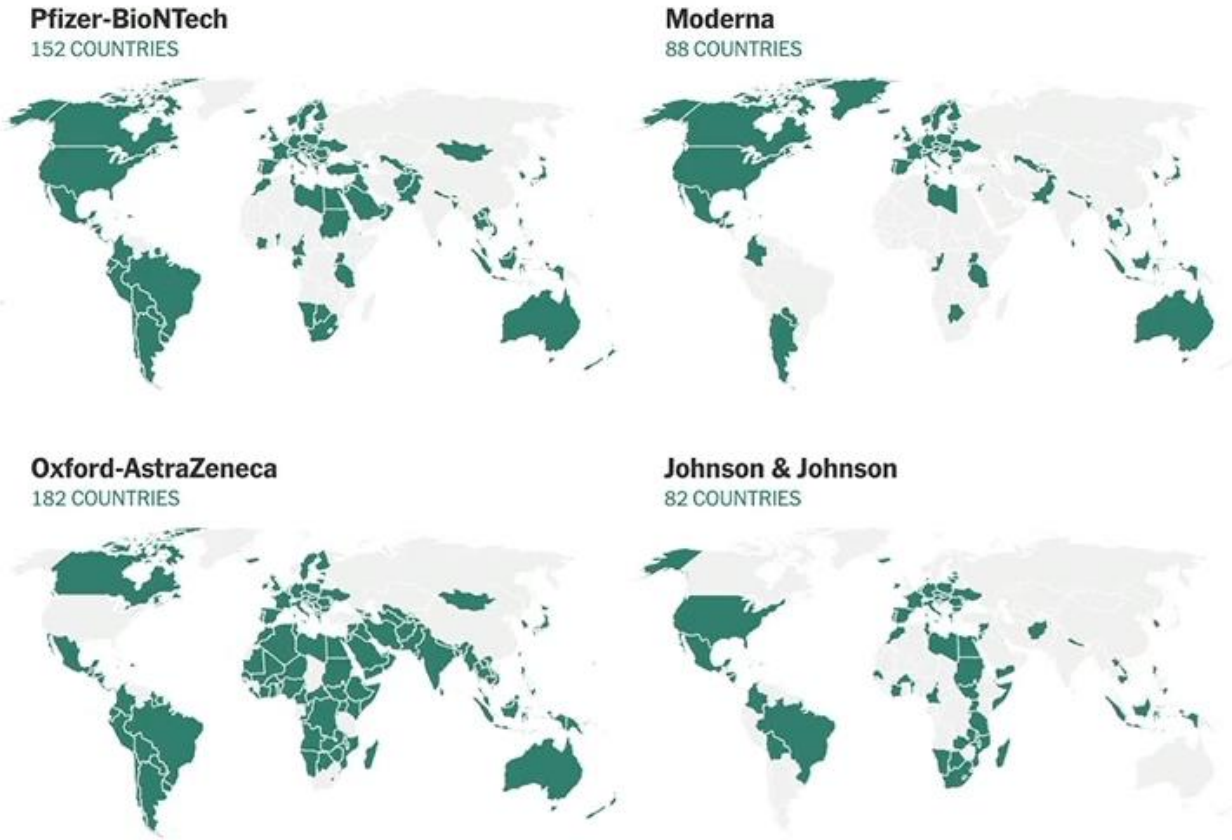
1 shot – ENSEMBLE (Shaddof, NEJm 2021) 72% VE , pre-Omicron
2 shots (wk 0,8) – ENSEMBLE 2 (Hardt, medRxiv 2022) 94% VE , pre-Omicron
Implementation (SouthAfrica) – Sisonke (OA47)

Fully Vaccinated Individuals in the US



CDC F

Limited Use of mRNA Vaccines in Africa



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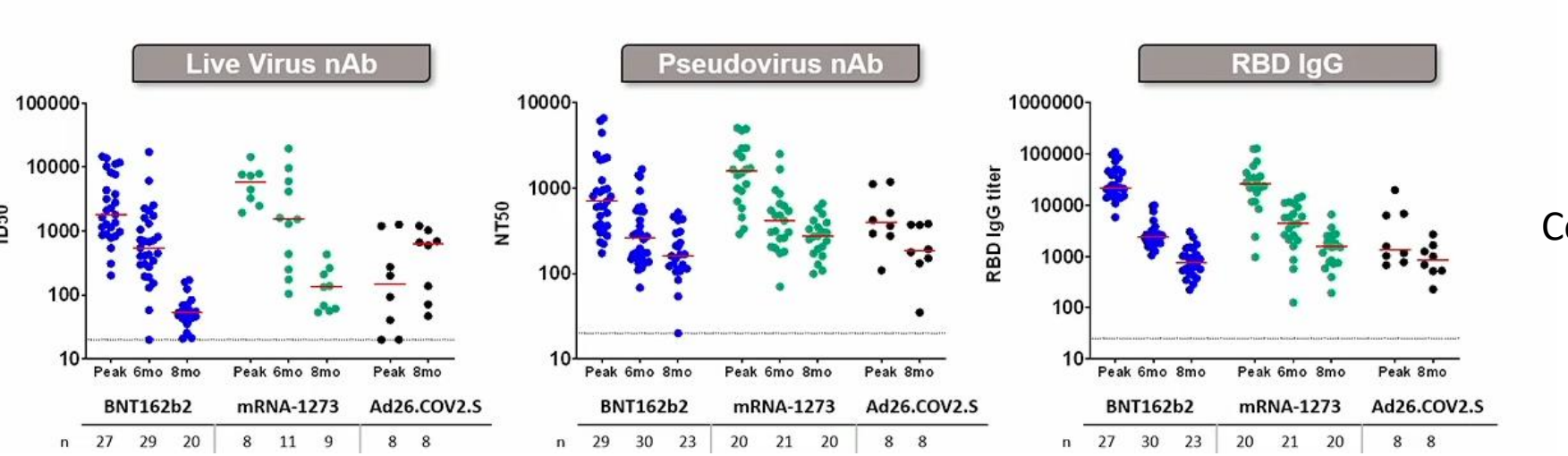
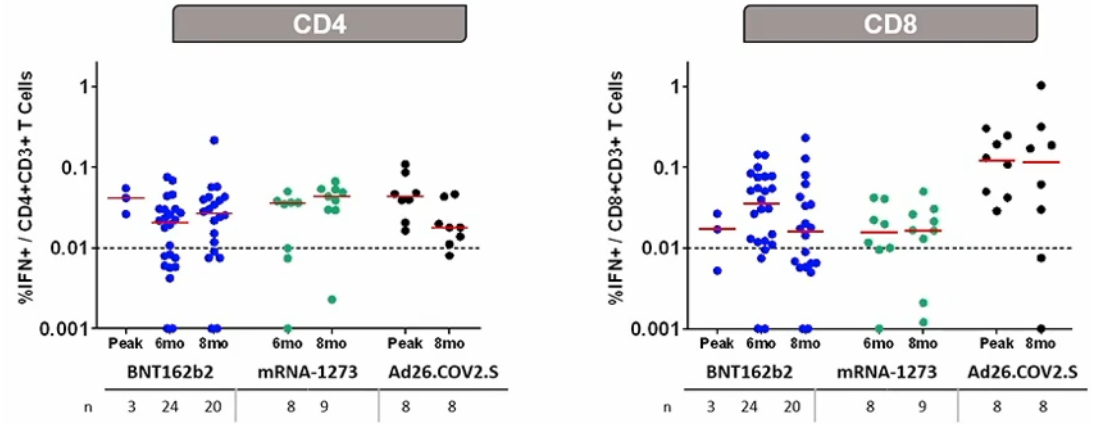
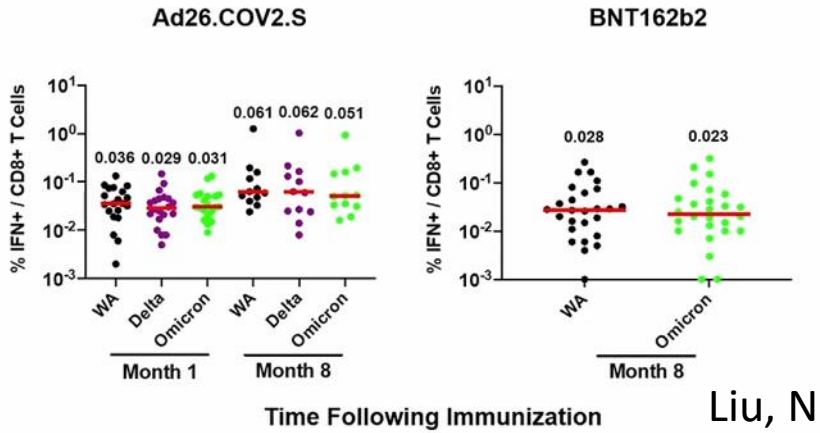


Collier, NEJM 2021

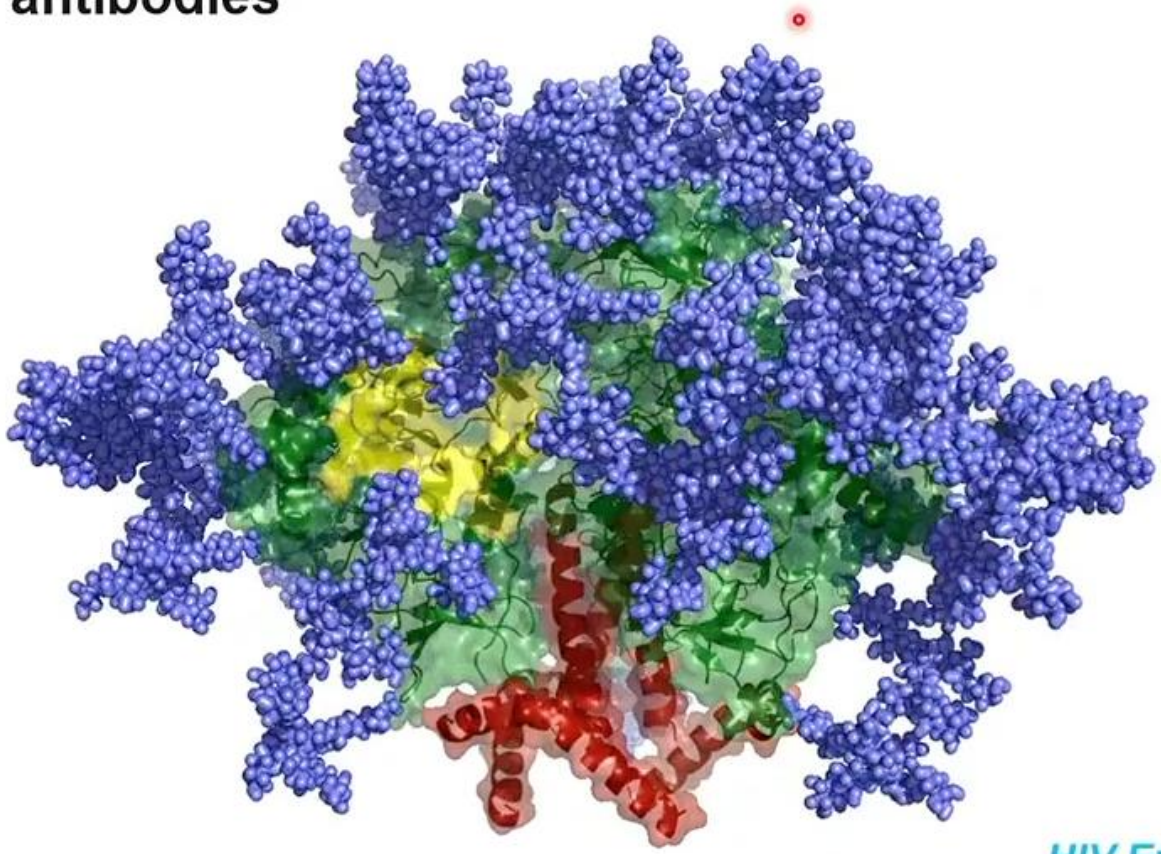


Vaccine-Elicited CD8 T Cell Responses are Highly Cross-Reactive to Omicron



Liu, Nature 2022

The HIV Env glycoprotein is a vexing immunologic target whose structure shields conserved protein epitopes and limits access of neutralizing antibodies

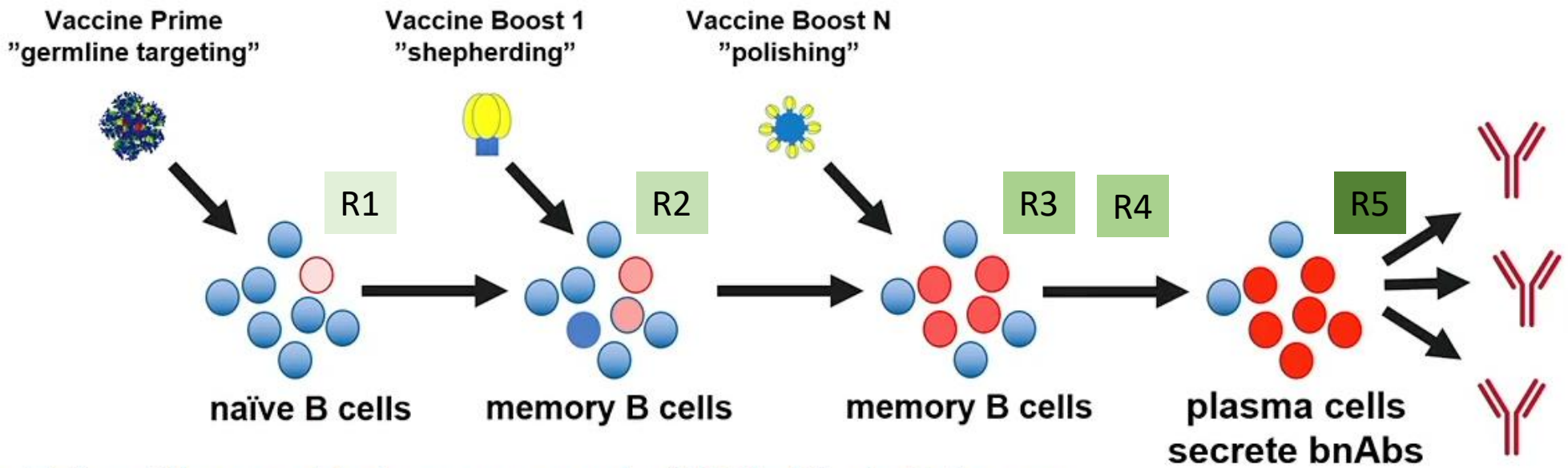


- HIV Env consists of ~50% glycans by mass, complicating Ab access to neutralization epitopes.
- HIV Env has 5 variable loops that can vary in length and glycosylation.
- In order to access recessed neutralization epitopes, long Ab heavy chain complementarity determining regions (HCDR3s) are often required, and these are present at low frequency in the human naïve B-cell repertoire and may also be subject to immune tolerance deletion.
- Most of the native glycoprotein is not highly immunogenic.

HIV Env trimers alone do not induce bnAbs; extensive Ab affinity maturation is required for neutralization

Strategy to induce bnAbs:
Germline targeting approach

Germline targeting is an approach where the immune system is manipulated to elicit a very specific antibody response by finding the shortest **pathway from germline to affinity mature antibodies with strategically designed priming and boosting immunogens.***

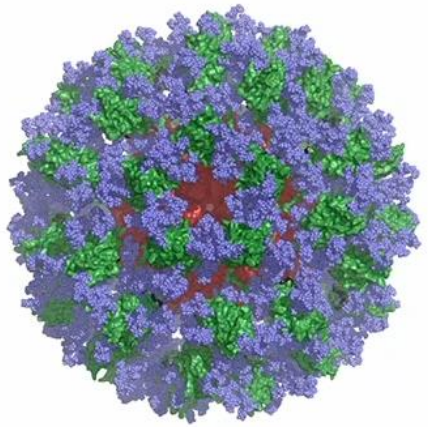


*Elucidation of the unmutated common ancestor (UCA) of the bnAb lineage is paired with definition of the optimal Env immunogen to trigger appropriate B cell precursor

Somatic hypermutation

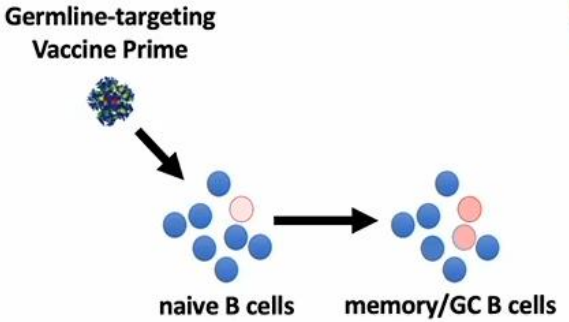
Feinberg - IAVI

IAVI G001 Phase I Trial: eOD-GT8 60mer/AS01$_B$



- First-in-human test of germline targeting
- Self-assembling nanoparticle + strong adjuvant
- First vaccination: Sept 2018; last vaccination March 2020
- Conducted at FHCRC (Seattle) and GWU (Washington, DC)
- Primary endpoint is safety
- Major immunological endpoint is to determine if the vaccine induces VRC01-class IgG+ B cells
- Critical readout by B-cell sorting/sequencing at VRC and FHCRC
  - ❖ first-in-human use of this assay as the bottom-line endpoint
  - ❖ credit to McDermott/Koup (VRC), Cohen/McElrath (FHCRC) and their teams

Study Group	N	eOD-GT8 60mer dose	Week 0	Week 8
1 (low dose)	18	**20 µg**	eOD-GT8 60mer/ AS01$_B$	eOD-GT8 60mer/ AS01$_B$
	6	-	buffer	buffer
2 (high dose)	18	**100 µg**	eOD-GT8 60mer/ AS01$_B$	eOD-GT8 60mer/ AS01$_B$
	6	-	buffer	buffer
Total	48			



- **eOD-GT8 60mer/AS01$_B$ was safe and well tolerated**
- **Strong CD4bs responses**

  After 1-2 shots, **0.06-0.42%** of IgG memory B cells in PBMCs were CD4bs-specific
- **High positivity VRC01-class responses (VH1-2 + 5 amino acid LCDR3)**

  After 1-2 shots, **94-97%** vaccinees produced VRC01-class responses

See upcoming session by **Bill Schief**:
February 24, 8:30AM – 10AM MT
Jump-Started Immune Response: Now, how to teach breadth?

- **High frequency VRC01-class responses**

  After 1-2 shots, **0.014-0.10%** of IgG memory B cells in PBMCs were VRC01-class
- **Autologous boost increased mutation levels and affinities**

  Key support for sequential vaccination in humans
- **Post-vaccination antibodies can be used to help select boost candidate**

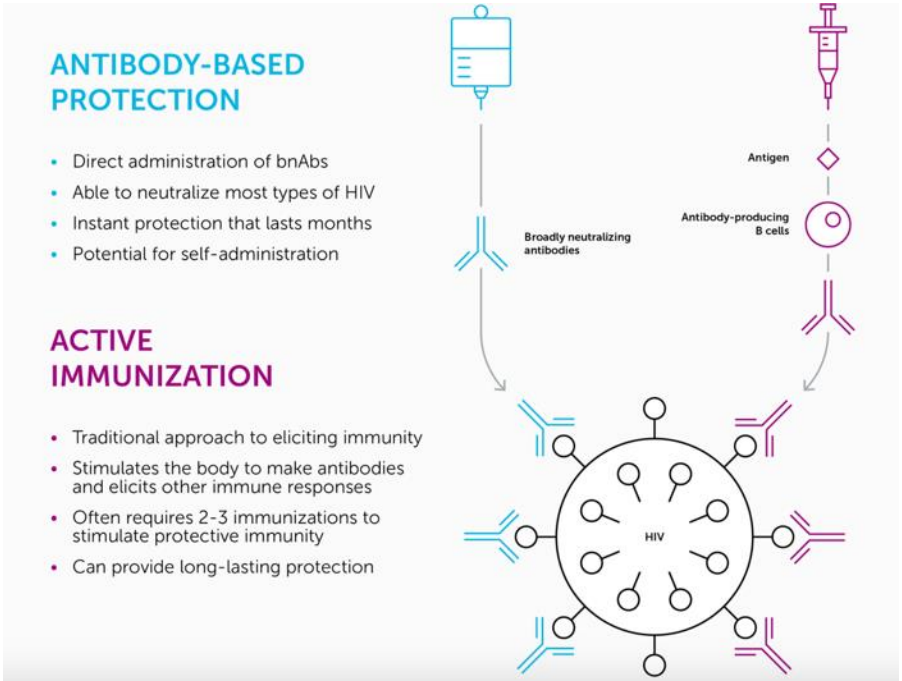
iavi Scripps Research
BILL & MELINDA GATES foundation

Preventive:

Active Immunization

Wednesday February 16th
Oral Abstract Session 10

121 Phase IIIb Efficacy trial of MOSAIC HIV-1 vaccine regimen in African women: IMBOKODO
Glenda E. Gray



OA121 Phase IIIb Efficacy trial of MOSAIC HIV-1 vaccine regimen in African women: IMBOKODO

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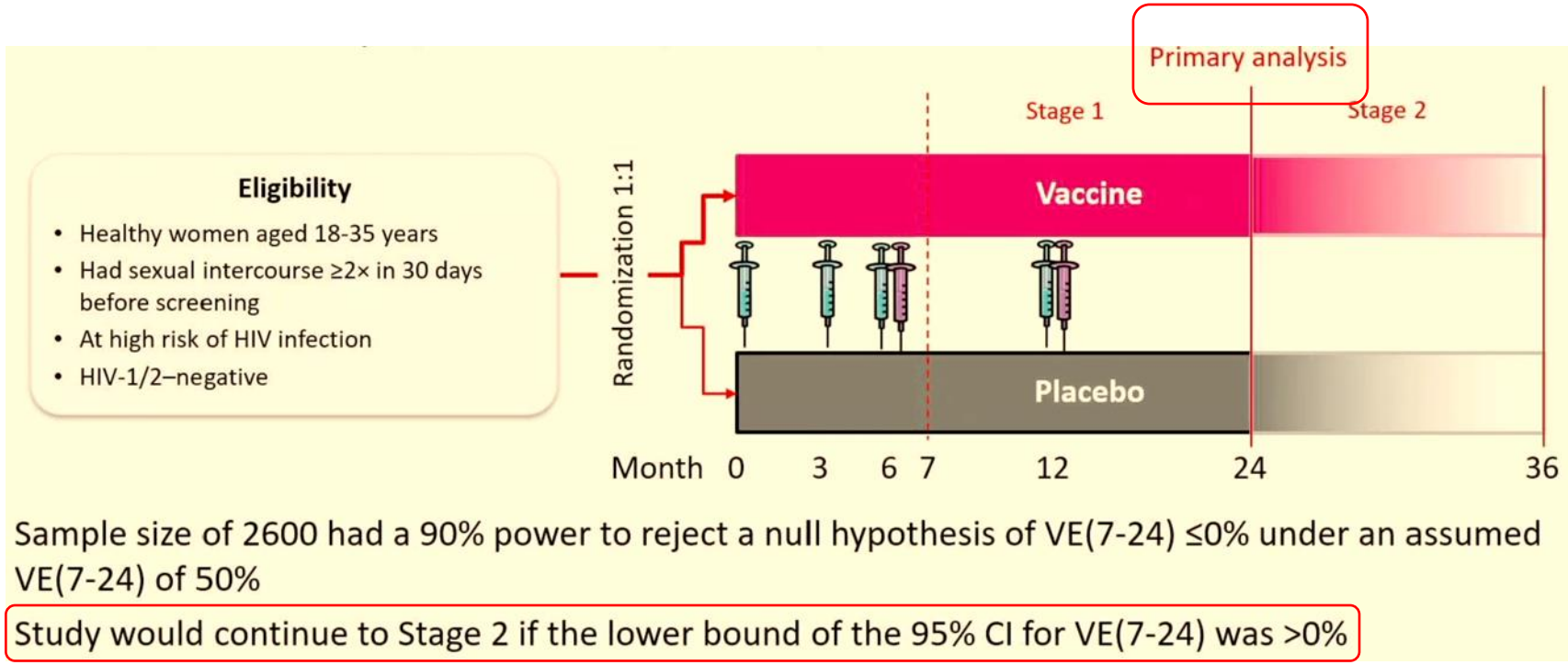
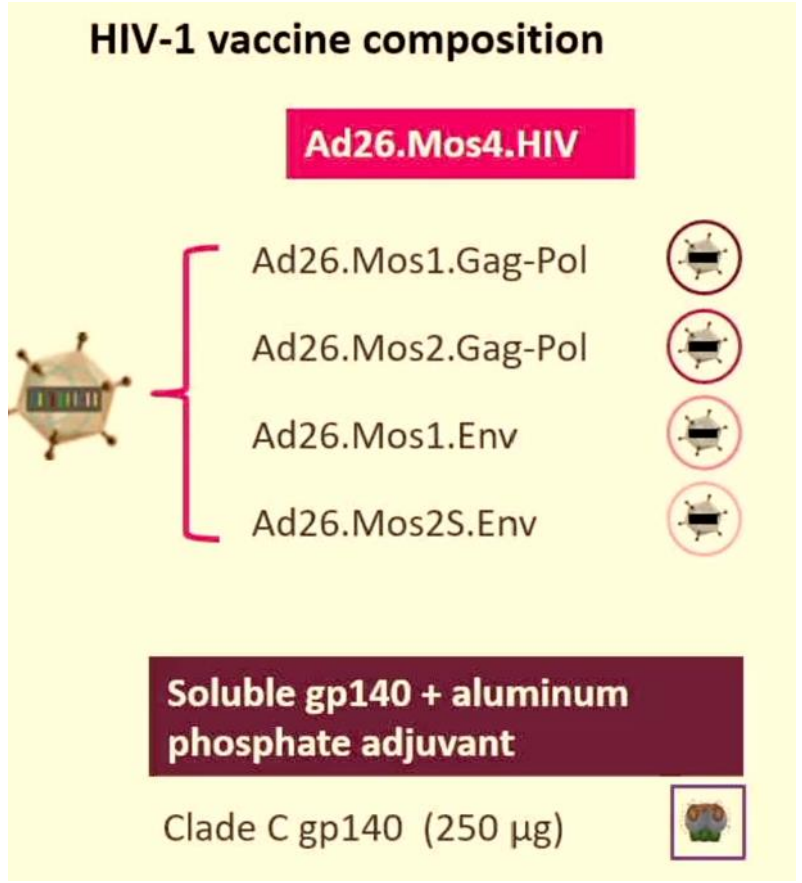
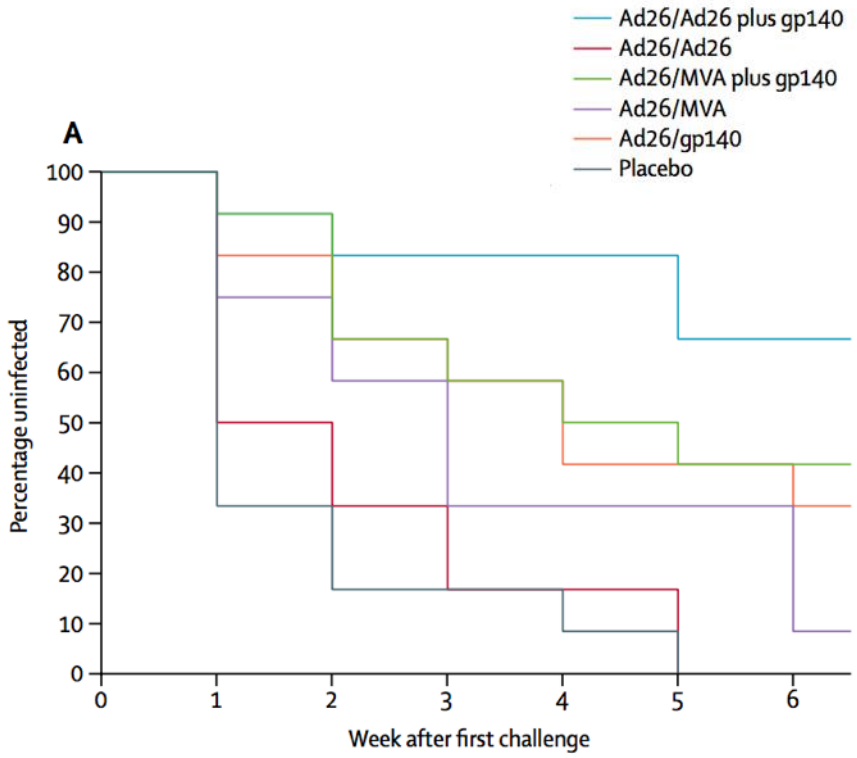


Sample size of 2600 had a 90% power to reject a null hypothesis of VE(7-24) ≤0% under an assumed VE(7-24) of 50%

Study would continue to Stage 2 if the lower bound of the 95% CI for VE(7-24) was >0%

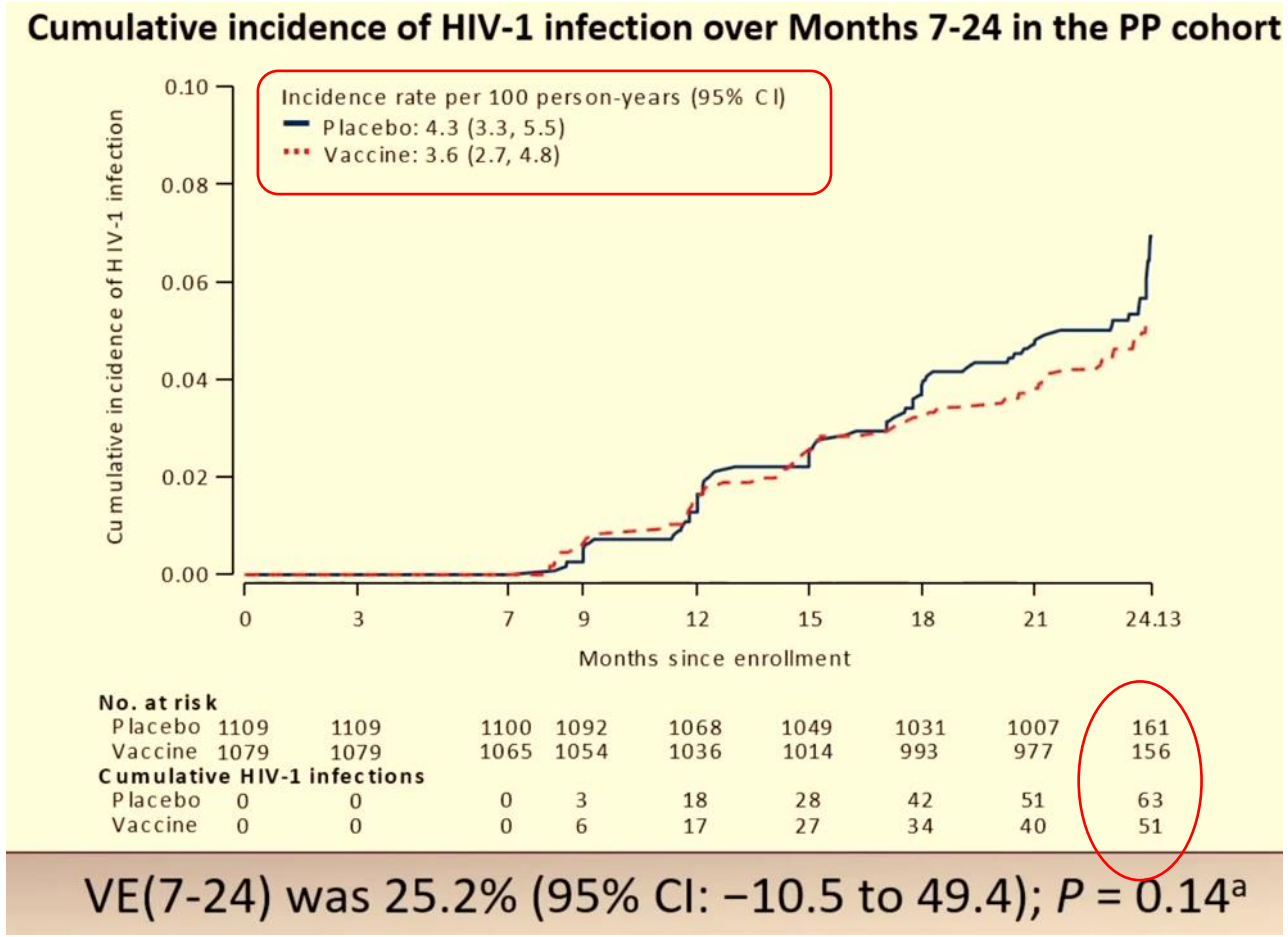


NHP



Barouch, Lancet 2018

Human CT….



Subtype B, MSM, anal intercourse, protein boost gp140 Clade C + mosaic. Ongoing….

Preventive:

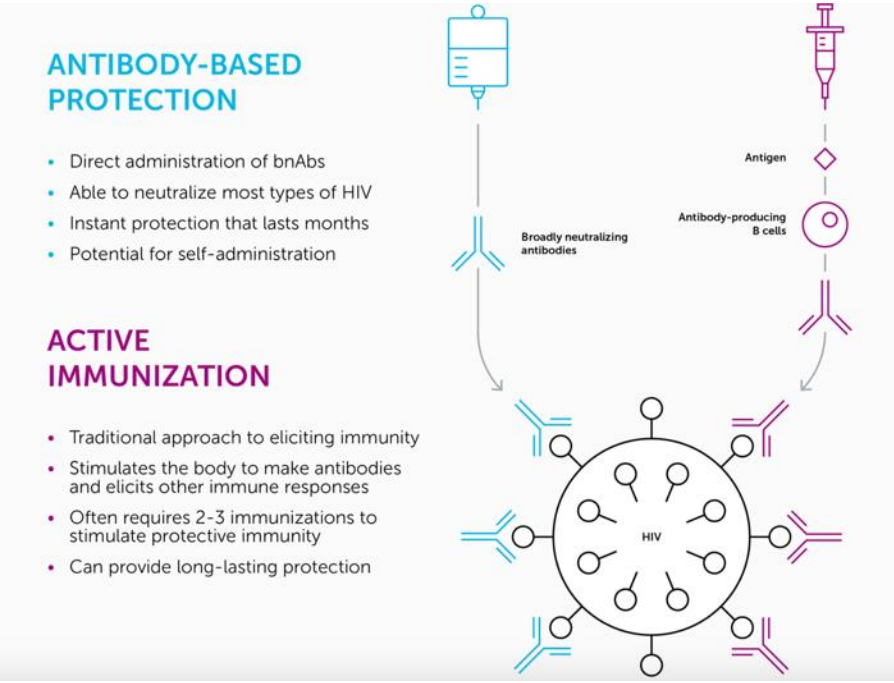
Passive Immunization

Thursday February 24th
Symposium 7

149 Lessons learned from the AMP:
Carolyn Williamson

Tuesday February 15th
Oral Abstract Session 7

81 Phase I study of combinaton Ab
Magdalena E. Sobieszczyk



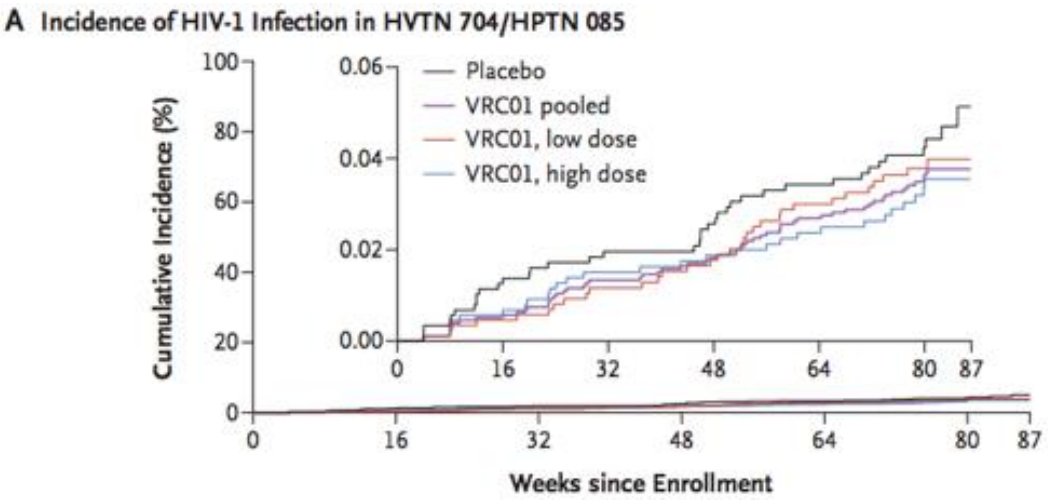
OA149 Lessons learned from the AMP (Antibody mediated protection)

Carolyn Williamson

Proof of concept in Humans that bNAb can protect from HIV acquisition
VRC01 (CD4 binding site)
10mg/kg and 30 mg/kg

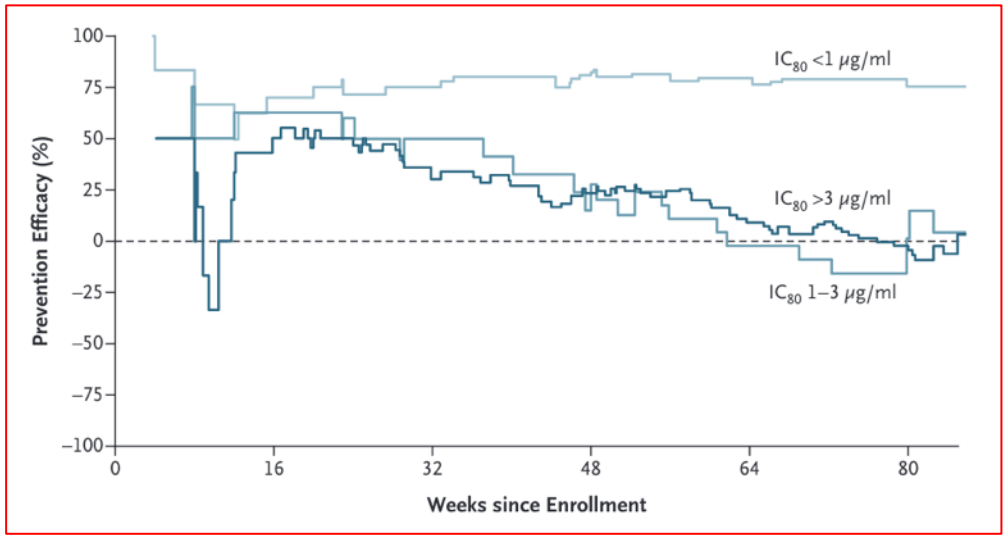
Every 2 months (total 10 infusions)

High risk women (Africa)
MSM and TGI (Americas)
Total 4.600



Corey, NEJM 2021

PE 75% (45-89) against MOST SENSITIVE viruses (<1ug/ml) after 2 doses

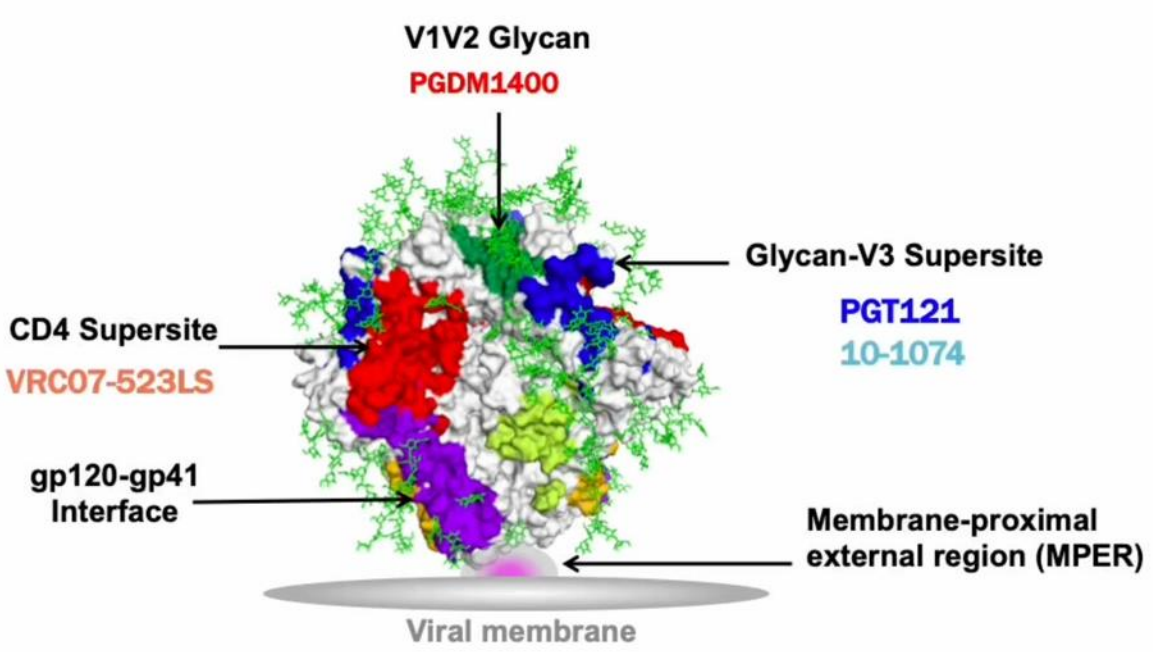


→ Need 2-3 different targets (combination of bNAbs)
→ Titer biomarker for prevention :
90% protection requires serum **neutralization ID_{80} titer of 200**

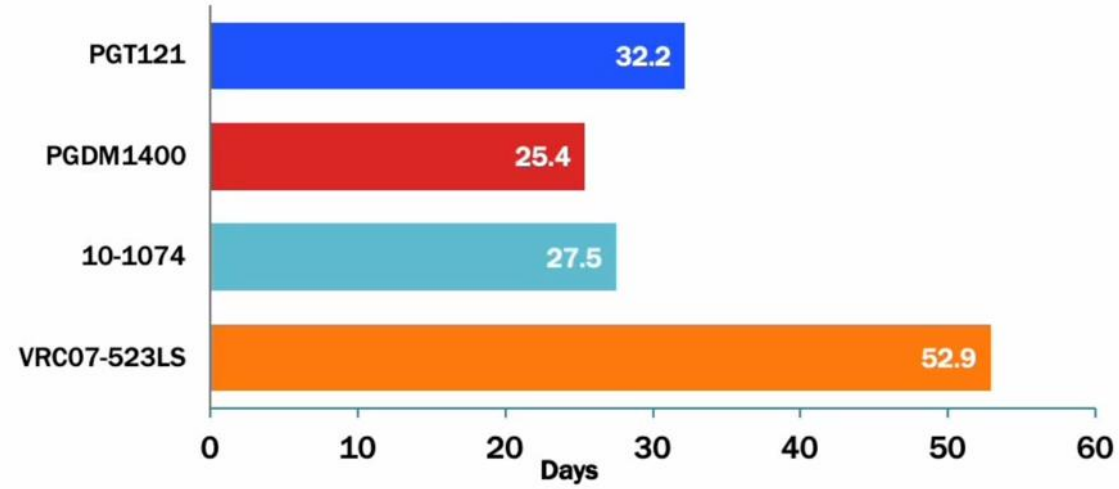
Gilbert, submitted

OA81 Phase I study of combinaton anti-HIV neutralizing antibodies in HIV-negative adults

Magdalena E. Sobieszczyk



Study arm	N	Dose	Month 0	Month 4
Treatment 1 T1	6	20+20 mg/kg	PGT121 VRC07-523LS	–
Treatment 2 T2	6	20+20 mg/kg	PGDM1400 VRC07-523LS	–
Treatment 3 T3	6	20+20 mg/kg	10-1074 VRC07-523LS	–
Treatment 4 T4 T4	9	20+20+20 mg/kg	PGDM1400 PGT121 VRC07-523LS	PGDM1400 PGT121 VRC07-523LS



- PK patterns were consistent for each bnAb between the dual or triple combinations (and consistent with prior data)
- Neutralization function was maintained as predicted by PK data
- Complementary neutralization magnitude and breadth of infused bnAbs were maintained in this ‘first in human’ study

Therapeutic:

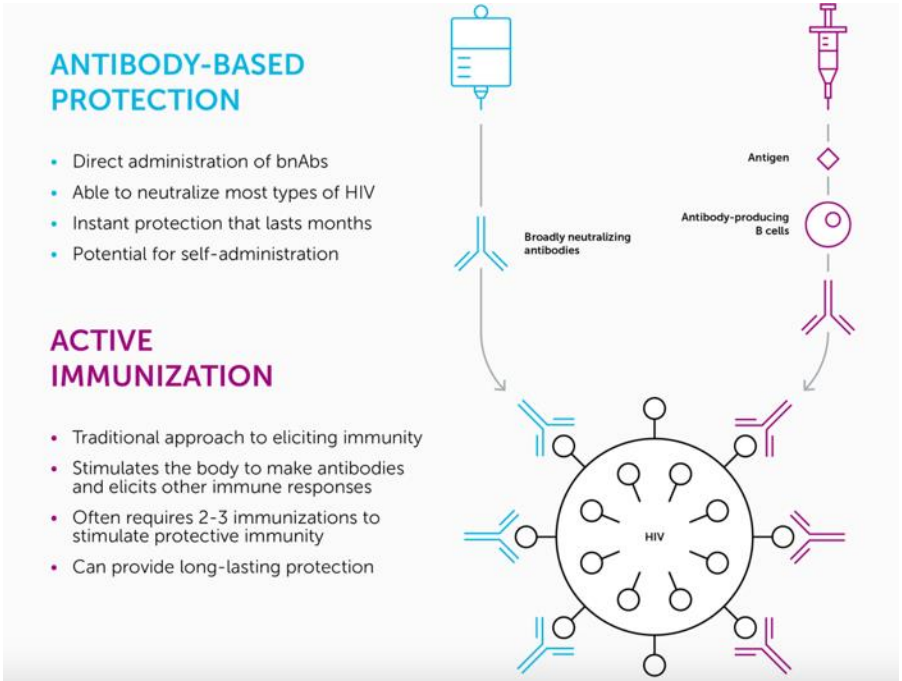
Combinations

Tuesday February 15th

Oral Abstract Session 5

63 Therapeutic efficacy of combined active and passive immunization in SHIV+ macaques

Victoria E. Walker-Sperling

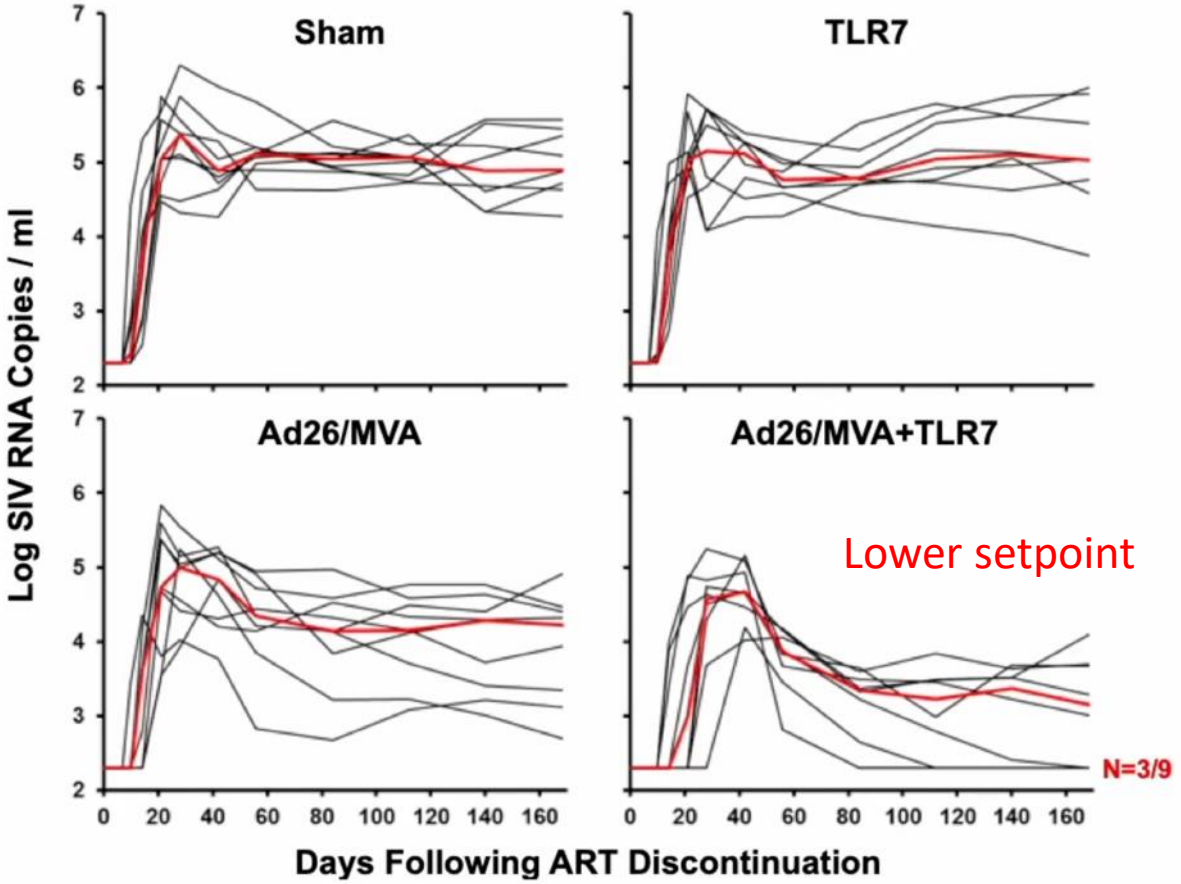


OA63 Therapeutic efficacy of combined active and passive immunization in SHIV+ macaques

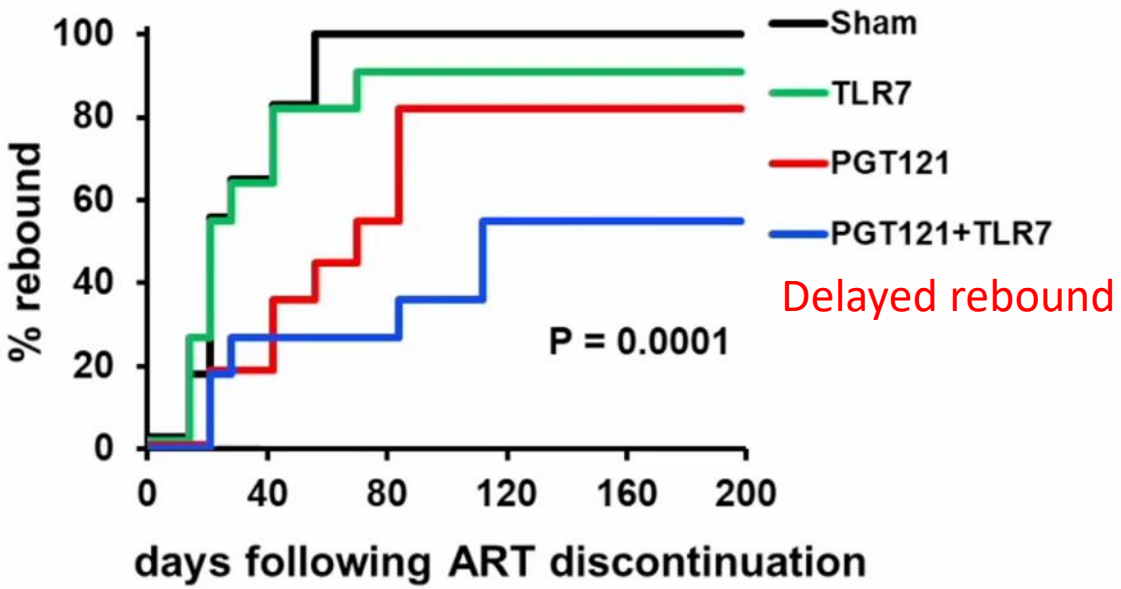
Victoria E. Walker-Sperling

SHIV model of acute infection – ART started at day 9

- Ad26/MVA - vaccine
- TRL7 agonist (Vesatolimod) – latency reversing agent +/- immunemodulator
- PGT121 – bNAb against glycan V3 supersite



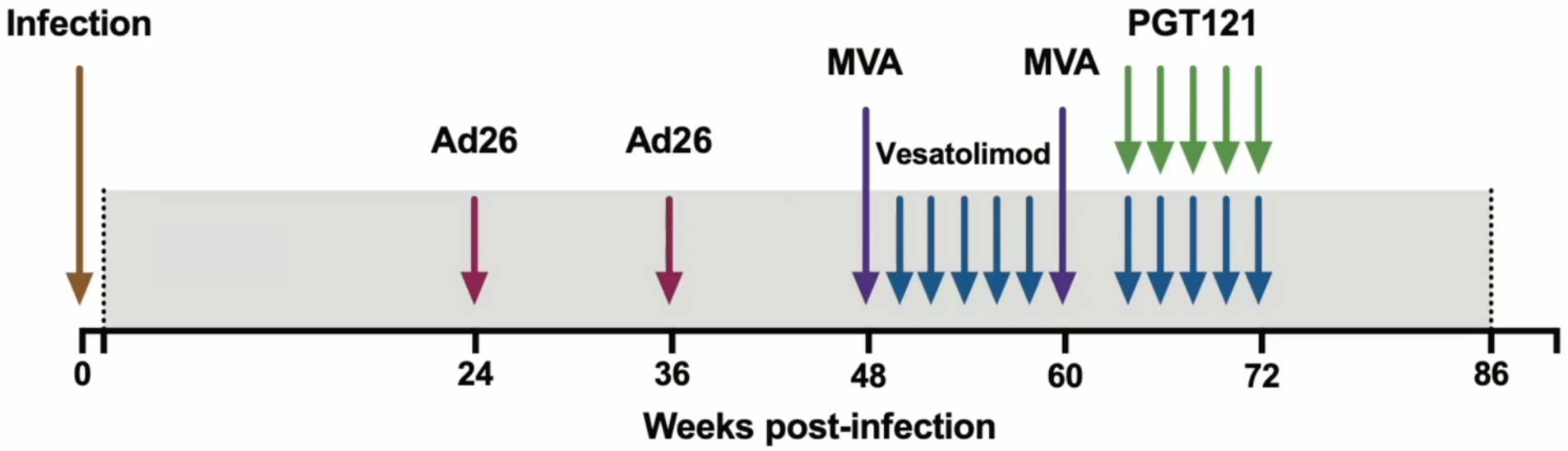
Borducchi, Nature 2016

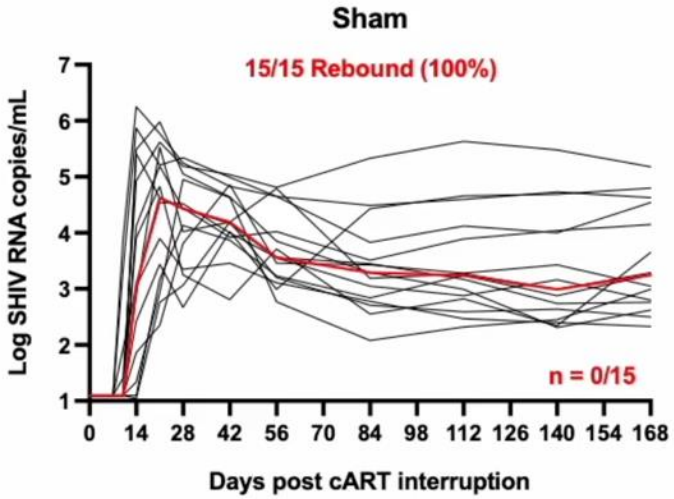


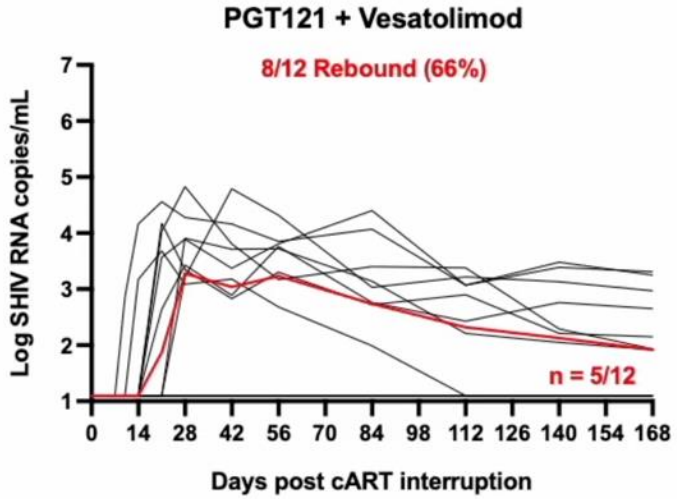
Borducchi, Nature 2018

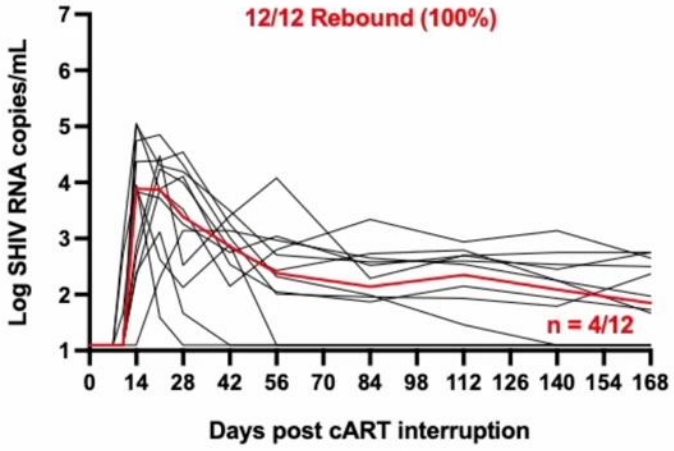
- 51 Rhesus macaques infected intrarectally with SHIV-SF162P3 and treated from D9 onward with preformulated, daily ART (TDF, FTC, DTG).
  - Group 1: Ad26/MVA + PGT121 + Vesatolimod (N=12)
  - Group 2: Ad26/MVA + Vesatolimod (N=12)
  - Group 3: PGT121 + Vesatolimod (N=12)
  - Group 4: Sham (N=15)

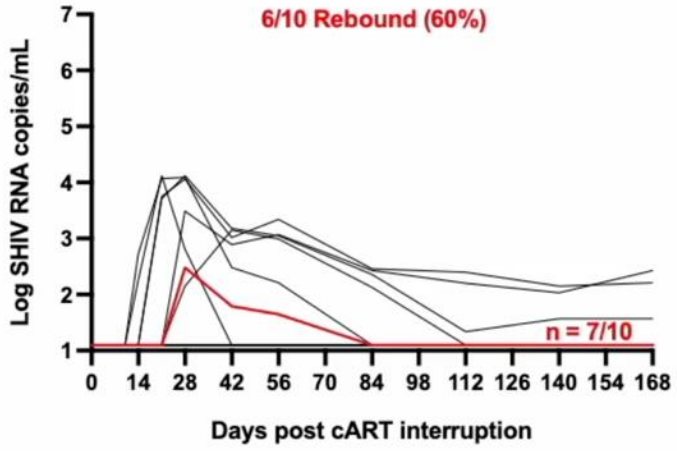
→ Equivalent to AELIX003 CT w/HTI vaccines

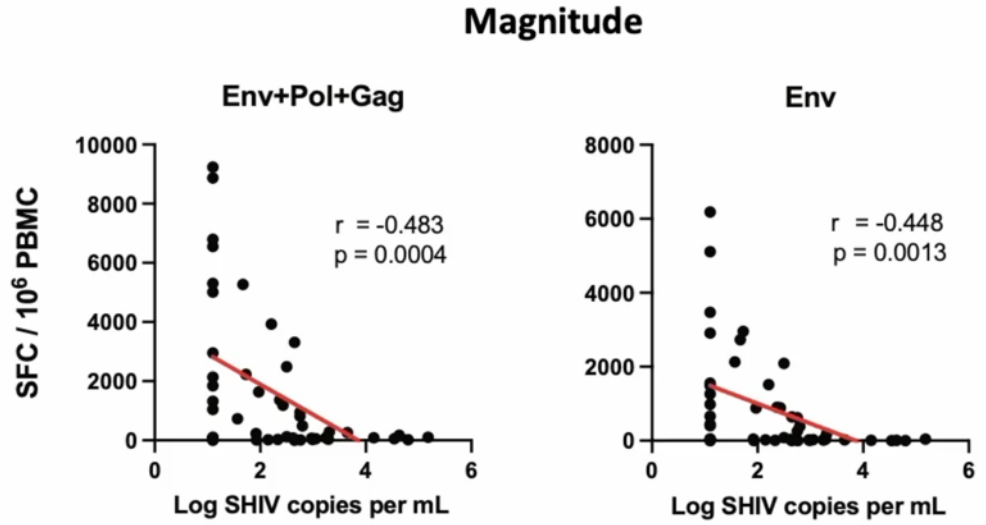


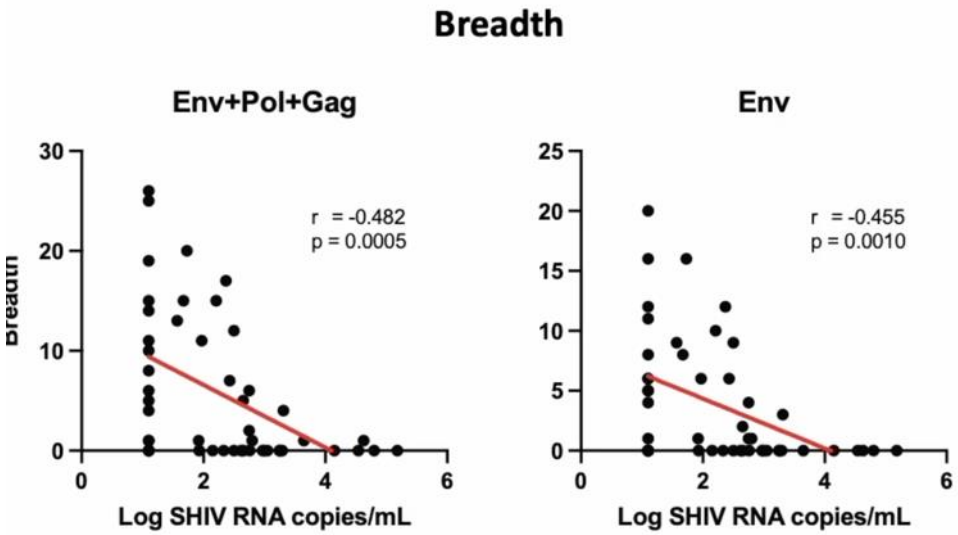












Delayed Rebound, Lower setpoint, higher PTC

COV

COV vaccines

Monday February 14th
Oral Abstract Session -4

47 – Safety & Effectiveness of Ad26.CoV2.S in SA : Sisonke
Glenda E. Gray

48 – COVID-19 Booster in IS
Jung Sun

Breakthrough infections

Monday February 14th
Oral Abstract Session -4

49- Infectiousness of breakthrough infections after vaccination and natural infection (Qatar)
Laith Abu-Raddad

Wednesday February 16th
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Viral load kinetics in partially or fully vaccinated individuals infected with SARS-CoV-2
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Monday February 14th
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HPV - *Margaret A. Stanley*
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Mandates / Hesitancy

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Effectiveness - *Sheena G. Sullivan*

COV vaccines

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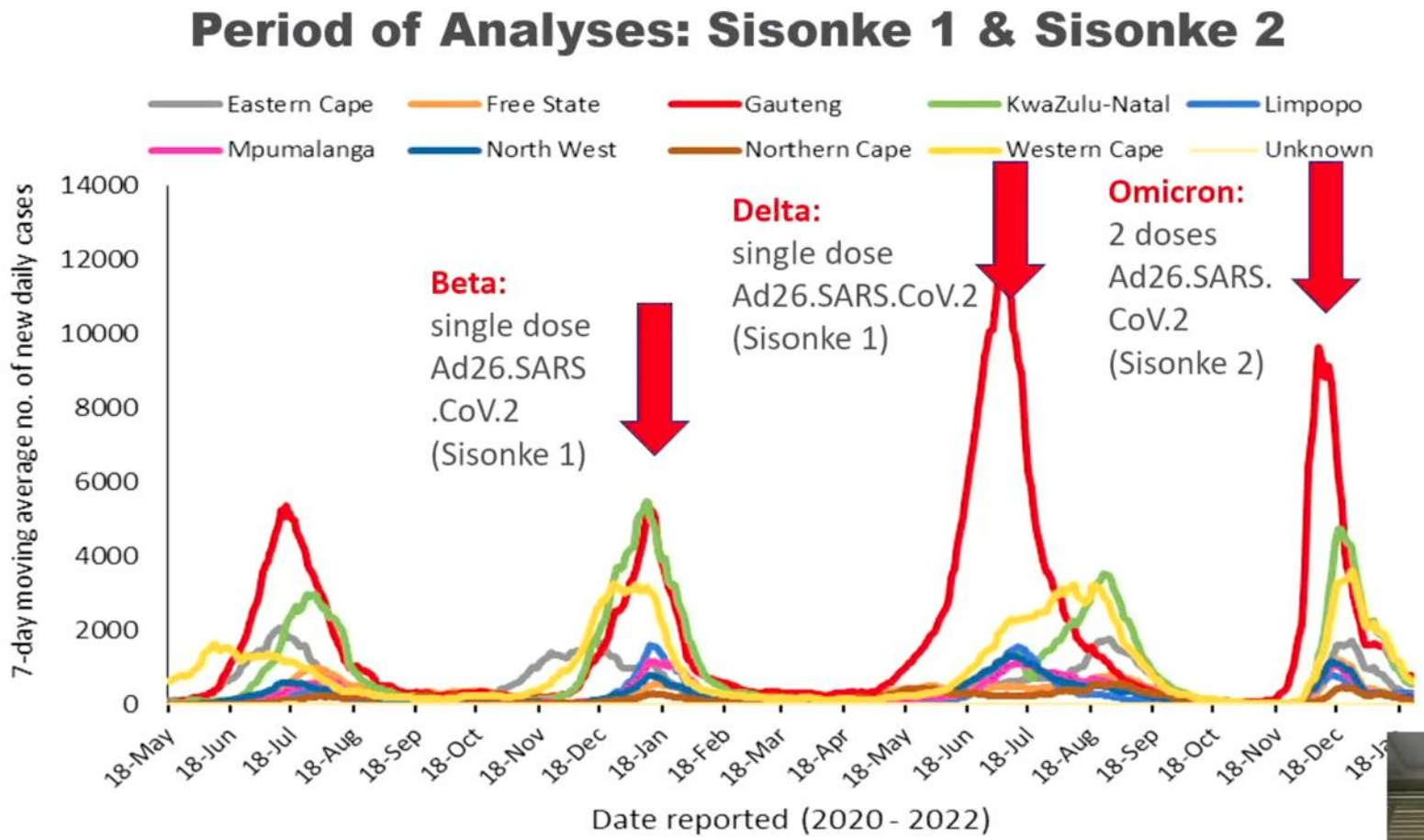
OA47. Implementation Ad26.COV2.S (1 or 2 shots in health-care workers in SouthAfrica) – Sisonke

Glenda Gray

EFFECTIVENESS vs EFFICACY (ENSEMBLE 1 & 2 Clinical Trials)

496,434 HCW 237,981HCW



7-day moving average number of new cases by province and date of reporting, 18 May 2020 to date, S
(source NICD)

HTA: 74,381 (16%)
DM : 28,063 (6%)
VIH: 39,386 (8%)

Safety:

TTS : 2 cases → Observed/Expected ratio (95% CI): **2.40 (0.29-8.66**)
Guillaim Barré : 4 cases → O/E ratio : **5.09 (1.39 – 13.02)**

Effectiveness : Test Negative Case Control

Sub-population	Sub-cohort	Covid -19 hospital admissions			Covid -19 hospital admission requiring critical or intensive care			Covid-19 related death		
		Vaccinated Events/ P-Y	Unvaccinated Events/ P-Y	VE (95% CI) %	Vaccinated Events/ P-Y	Unvaccinated Events/ P-Y	VE (95% CI) %	Vaccinated Events/ P-Y	Unvaccinated Events/ P-Y	VE (95% CI) %
One or more co-existing risk factors for severe Covid-19	Scheme A	91/6 446	265/6 378	66 (57,73)	11/6 455	77/6 394	86 (76,94)	6/6 456	58/6 398	89 (78,98)
	Scheme B	90/8 359	247/8 351	63 (54,72)	24/8 363	85/8 366	71 (57,83)	12/8 367	56/8 374	78 (60,89)
HIV	Scheme A	12/997	14/705	-	-	-	-	-	-	-
	Scheme B	18/3 802	66/3 731	73 (58,85)	4/3 802	19/3 736	79 (51,96)	5/3 803	15/3 738	65 (13,93)

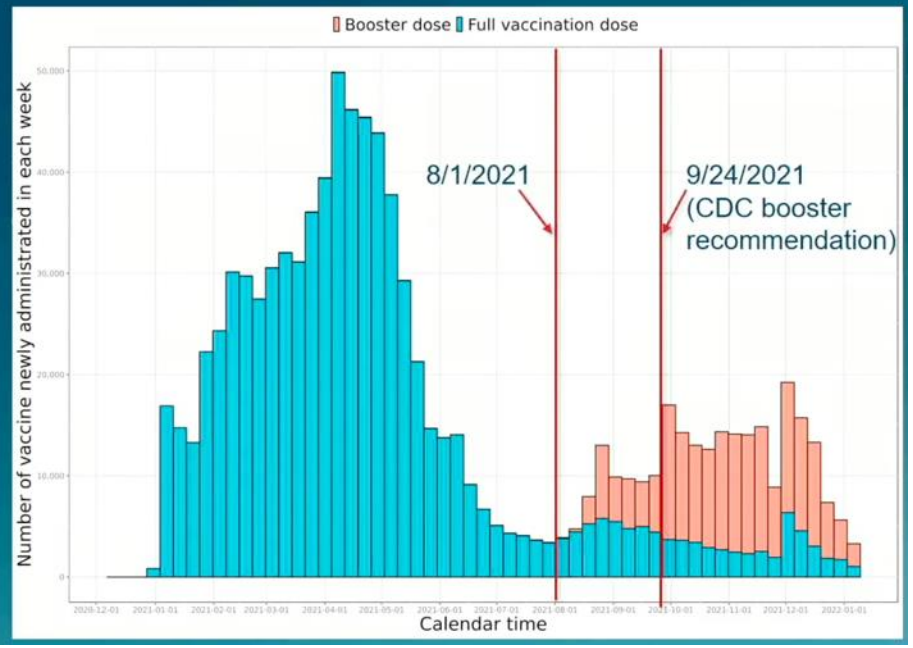
Sisonke 2 , data from **15 nov- 20 Dec 21 (Omicron)** : Effectiveness against admission 84% 14 days post boost and 85% at 1-2 m

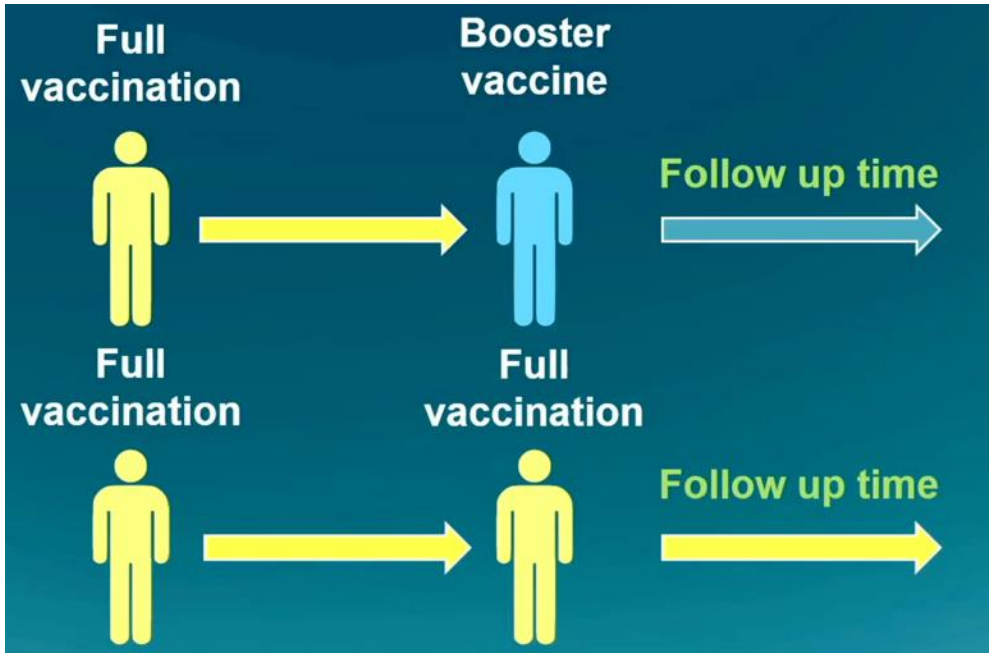
OA48. COVID-19 booster vaccine effectiveness in people with and without immune disfunction

Jing Sun

National COVID Cohort Collaborative

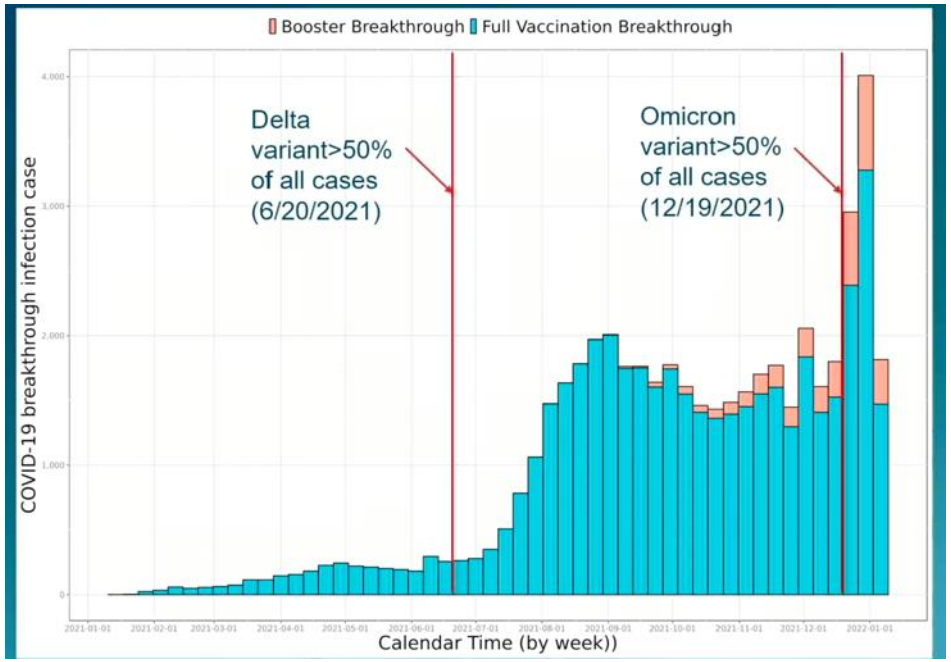
- N3C: NIH funded, rapidly developing open science community
- N3C Enclave includes patient-level data from over 60 clinical centers across the U.S.
- Total COVID-19+ vaccination
  - Full vaccine: 784,555
  - Booster Vaccine: 174,042





- **Analytical approach**
  - **Propensity score matched Cox regression models for hazard of breakthrough infection**
  - **Multivariable logistic regression models for risk of hospitalization, invasive ventilation, and death**

Without ISC



Months since full vaccination	Breakthrough events during follow-up		Sample size in boosted or non-boosted group*	Hazard Ratio (95% CI)	P-value	Booster vaccine efficacy
	Boosted group	Non-boosted group				
≤5	26	88	2006	0.33 (0.22, 0.52)	<0.001	70.5%
6	34	129	3166	0.27 (0.19, 0.40)	<0.001	73.6%
7	184	815	27148	0.23 (0.19, 0.27)	<0.001	77.4%
8	413	1102	40383	0.36 (0.32, 0.41)	<0.001	62.5%
9	389	812	28952	0.45 (0.40, 0.51)	<0.001	52.1%

With ISC

Months since full vaccination	Breakthrough events during follow-up		Sample size in boosted or non-boosted group*	Hazard Ratio (95% CI)	P-value	Booster vaccine efficacy
	Boosted group	Non-boosted group				
≤5	141	201	4418	0.84 (0.67, 1.04)	0.11	29.9%
6	110	185	4587	0.60 (0.47, 0.75)	<0.001	40.5%
7	157	394	12210	0.39 (0.32, 0.47)	<0.001	60.2%
8	150	376	14600	0.38 (0.31, 0.46)	<0.001	60.1%
9	75	124	8423	0.56 (0.42, 0.75)	<0.001	39.5%

	Patients without immune dysfunction		Patients with immune dysfunction	
	Odds Ratio (95% CI)	P-value	Odds Ratio (95% CI)	P-value
Hospitalization	0.13 (0.12, 0.15)	<0.001	0.21 (0.19, 0.23)	<0.001
Invasive ventilation	0.09 (0.05, 0.19)	<0.001	0.25 (0.18, 0.34)	<0.001
Death	0.13 (0.06, 0.30)	<0.001	0.17 (0.11, 0.27)	<0.001

→ **Booster vaccine effectiveness against breakthrough infection is lower in IS, but still significant after 6 months of vax**
→**Reduced risk of hospitalization, invasive ventilation and death even in IS**

Breakthrough infections

Monday February 14th

Oral Abstract Session -4

49- Infectiousness of breakthrough infections after vaccination and natural infection (Qatar)

Laith Abu-Raddad

Wednesday February 16th

Interactive Session -8

Viral load kinetics in partially or fully vaccinated individuals infected with SARS-CoV-2

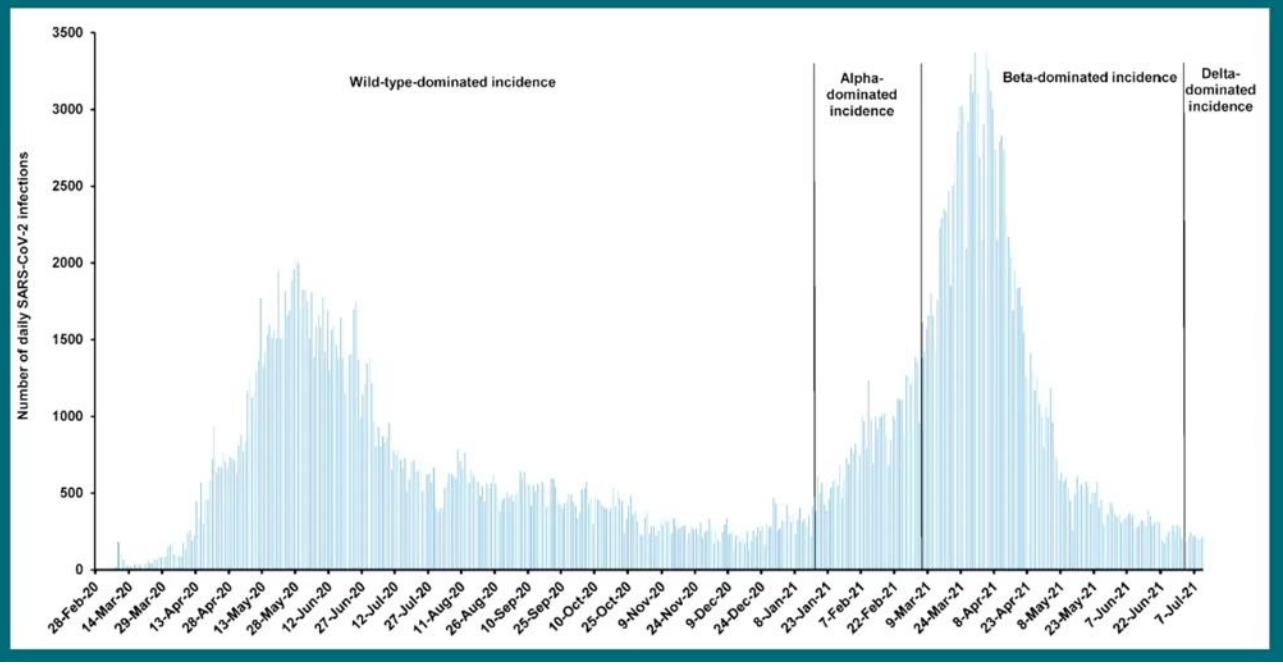
Annelies Wilder-Smith

OA49- Infectiousness of breakthrough infections after vaccination and natural infection (Qatar)

Laith Abu-Raddad

- Leveraging Qatar's national databases, effects of vaccination and of prior infection on SARS-CoV-2 infectiousness were investigated, between February 28, 2020 and July 11, 2021, through pairwise comparison of the RT-qPCR Ct values in matched cohorts of:
  1. Primary infections in unvaccinated individuals
  2. Reinfections in unvaccinated individuals
  3. BNT162b2 (Pfizer-BioNTech) breakthrough infections
  4. mRNA-1273 (Moderna) breakthrough infections

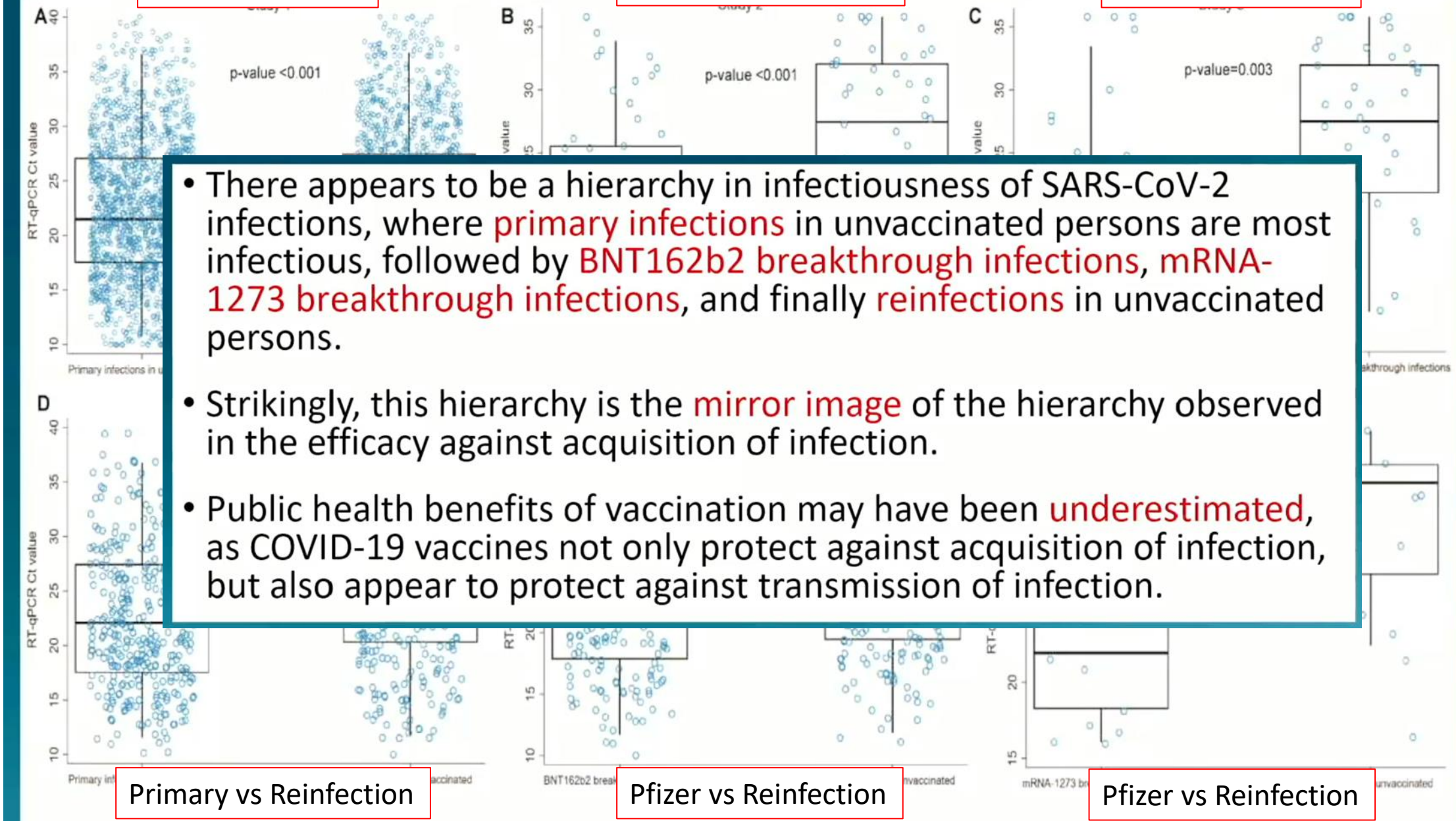
Pre-Delta & Pre-Omicron



Primary vs Pfizer

Primary vs Moderna

Pfizer vs Moderna



- There appears to be a hierarchy in infectiousness of SARS-CoV-2 infections, where primary infections in unvaccinated persons are most infectious, followed by BNT162b2 breakthrough infections, mRNA-1273 breakthrough infections, and finally reinfections in unvaccinated persons.
- Strikingly, this hierarchy is the mirror image of the hierarchy observed in the efficacy against acquisition of infection.
- Public health benefits of vaccination may have been underestimated, as COVID-19 vaccines not only protect against acquisition of infection, but also appear to protect against transmission of infection.

Primary vs Reinfection

Pfizer vs Reinfection

Pfizer vs Reinfection

Abbreviations: RT-qPCR, real time reverse transcription polymerase chain reaction

Symptom.

&

Asympt.

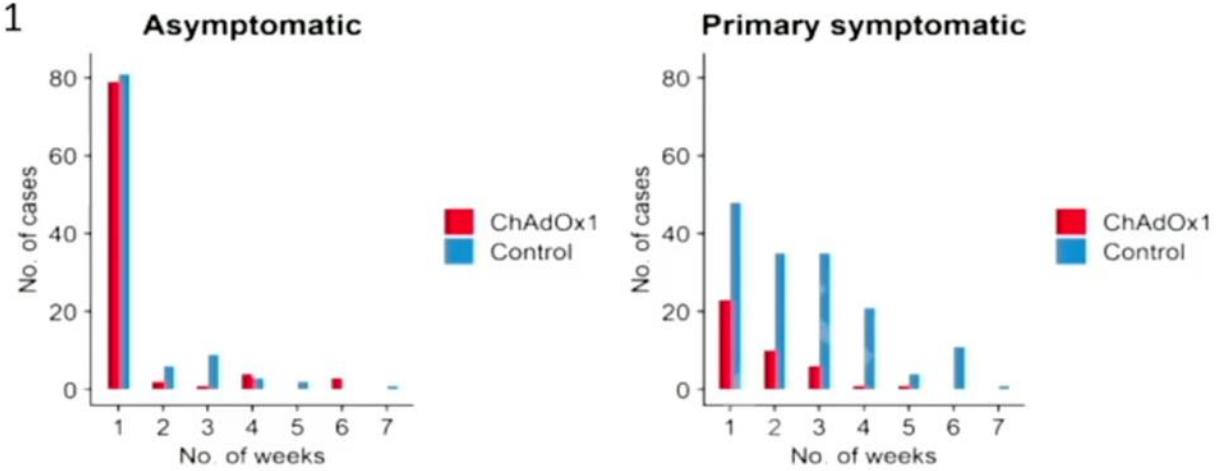
Viral load kinetics in partially or fully vaccinated individuals infected with SARS-CoV-2

Annelies Wilder-Smith

Ancestral strain/Alpha:

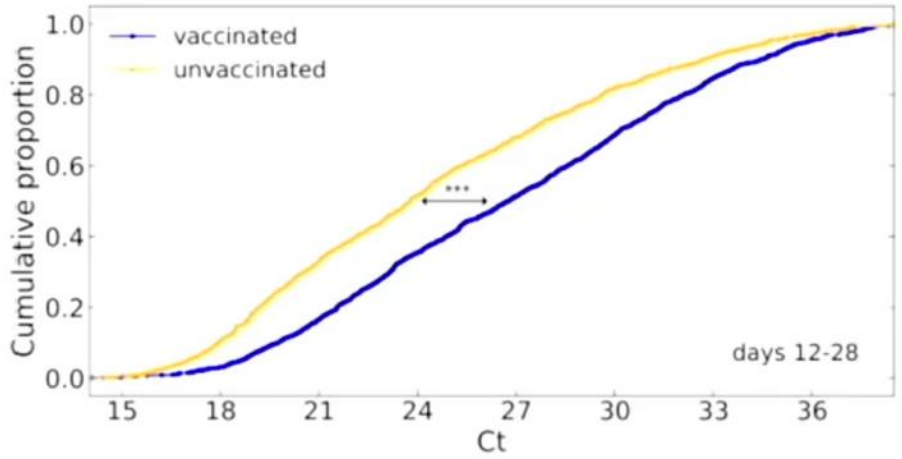
Evidence on COVID-19 vaccines and risk of SARS-CoV-2 transmission using viral load and duration of protection:

1



- AZ - ChAdOx1 vaccine
- Using duration of NAAT testing positivity as a proxy measure transmissibility:
- Vaccinated group shed virus for shorter duration of time

2

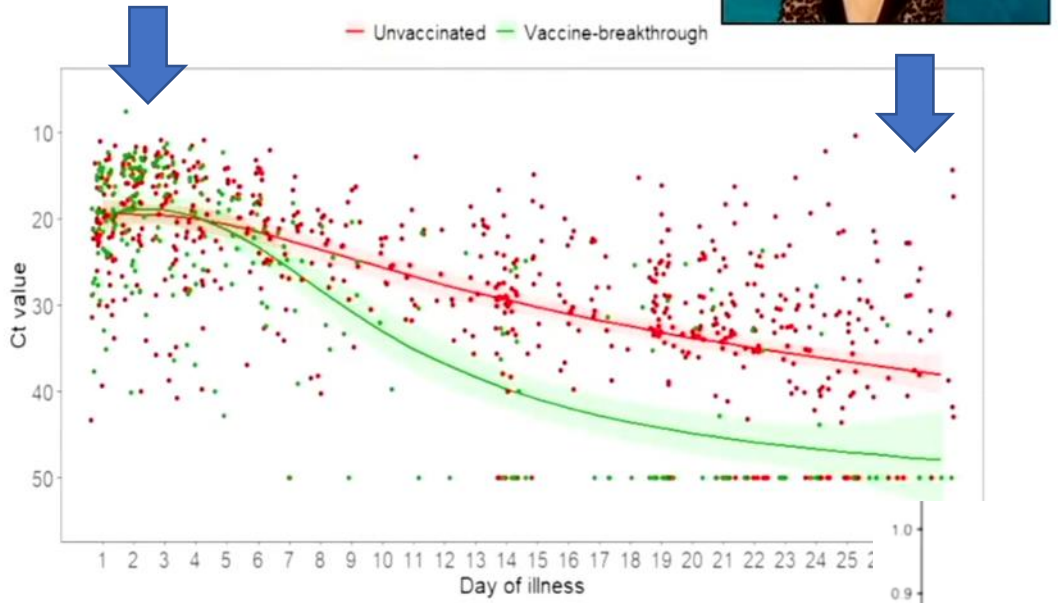


- Pfizer BNT162b2 COVID-19 mRNA vaccine
- Using viral load as a proxy measure of transmissibility
- Vaccinated group had a lower viral load

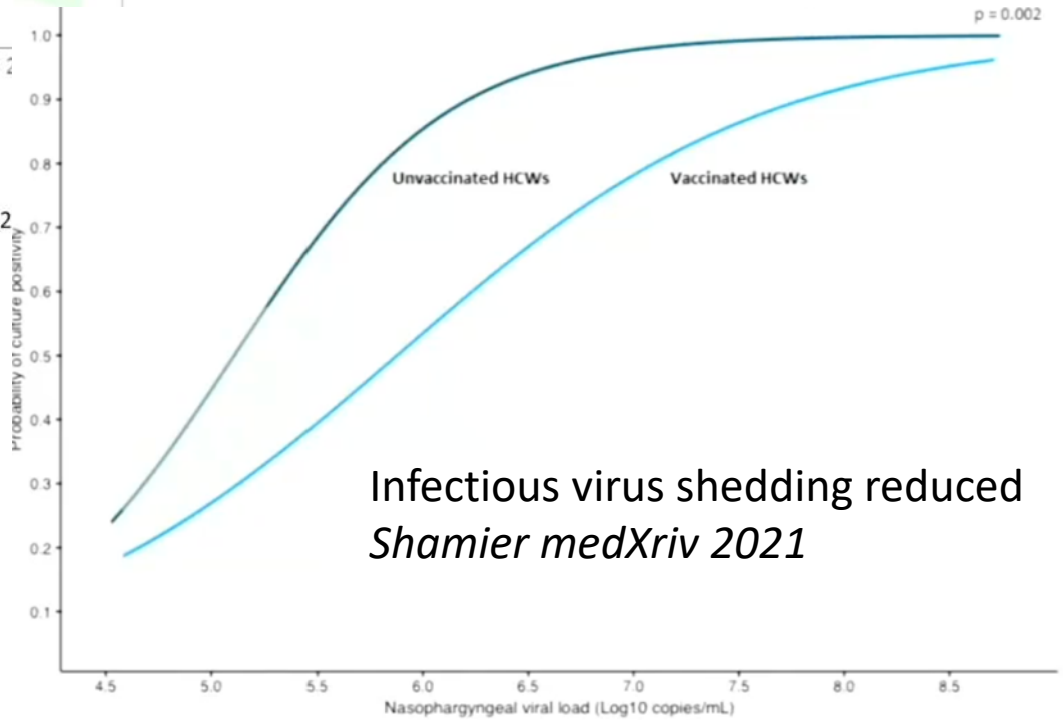
1. Emary KRW, Golubchik T, Aley PK, Ariani CV, Angus BJ, Bibi S, et al. Efficacy of ChAdOx1 nCoV-19 (AZD1222) Vaccine Against SARS-CoV-2 VOC 202012/01 (B.1.1.7).
2. Levine-Tiefenbrun M, Yelin I, Katz R, Herzel E, Golan Z, Schreiber L, et al. Decreased SARS-CoV-2 viral load following vaccination.

Delta: Virological kinetics of SARS-CoV-2 De variant vaccine-breakthrough infections

- Of 218 individuals with Delta infection, 84 had received a mRNA vaccine of which 71 were fully vaccinated, 130 were unvaccinated and 4 received a non-mRNA
- PCR cycle threshold (Ct) values were similar between both vaccinated and unvaccinated groups at diagnosis.
- Significantly older age in the vaccine breakthrough group
- Vaccination is associated with faster decline in viral RNA load

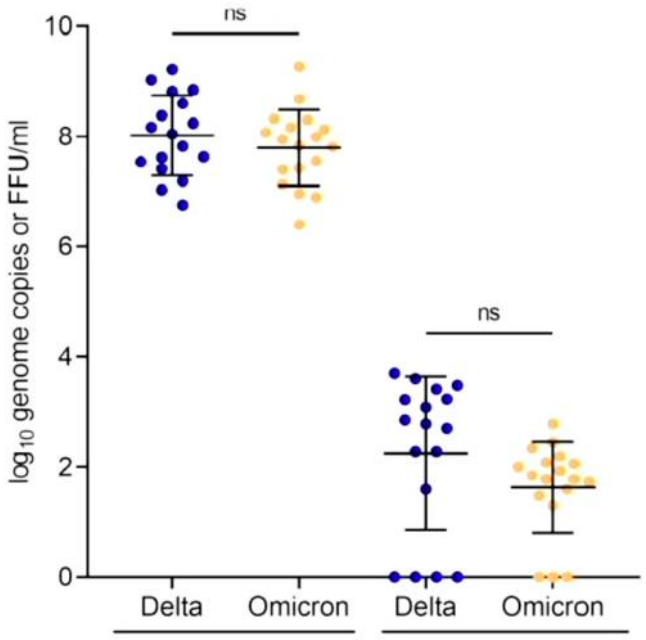


- Chia et al 2021, Singapore 10.1101/2021.07.28.212



Infectious virus shedding reduced
Shamier medXriv 2021

Omicron



SARS-CoV-2 RNA genome copies

Infectious viral titers

Puhach medXriv 2022

Impact of vaccination on transmission in relation to variant

Outcome	Wild-type and non-Delta	Delta	Omicron
Transmission	↓	↔	↔
Transmission over time	↔	↑	↑
Ct values	↑	↔	↔
Time to viral clearance		↓	↓
Infectivity	↓	↔	↔

Monday February 14th

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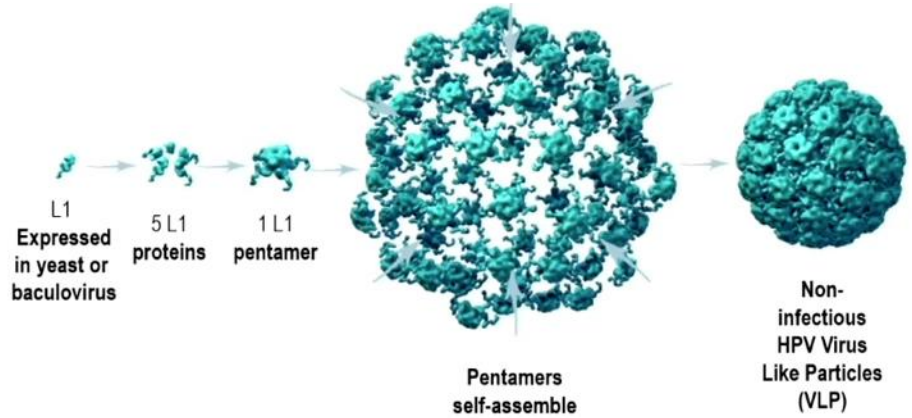
HPV - *Margaret A. Stanley*
Flu – *Florian Krammer*
Herpes – *Betsy Herold*
HIV-1 – *Alexandra Trkola*

John P. Moore: COVID-19 vax: 'It helps if it prevents infection, it matters if it prevents death'



Margaret A. Stanley:

HPV as success of vaccine for a strictly mucosal infection,
L1 protein assembled as VLP,
Ongoing work as a cancer vaccine in already infected individuals

Natural infection

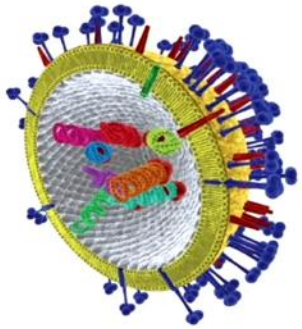
- 70-80% women 20-30% men sero-convert
- Antibody response to HPV infection is typically slow and weak
- Neutralising antibody responses are to L1
- Cross neutralising antibodies not detected
- Antibody generated in natural infections in women is partially protective against subsequent incident infection but not in men
- Avidity index very variable

HPV L1 VLP vaccination

- In clinical trials 100% women and men sero-conver
- Peak antibody titres are 2-3 logs greater than in natural infections
- Neutralising antibody persists for >16 years post immunisation
- Both type specific and cross neutralising antibodie detected
- No breakthrough disease caused by vaccine HPV types detected after 16 years follow up in RCTs
- Avidity index consistently high
- No antibody threshold level for the protection provided by HPV vaccines has been identified
- No immune correlate

Florian Krammer: Universal Flu vaccines

Target Overview for Universal Influenza Virus Vaccines



- **Internal proteins**
- **M2e**
- **Neuraminidase (NA)**
- **Stalk domain of the hemagglutinin (HA)**

Alexandra Trkola : HIV

How Sterilizing immunity may be achieved? Getting bNAb vaccines to work:

Options:

1. **High bnAb titer** fully blocking incoming virus
2. **Multi-specific bnAb activity**
   - Additive effect of bnAb combinations directed to different sites
   - Goal: efficacy at overall lower bnAb titer
3. **Multi-component vaccines (bnAb+CD8⁺ T cells)**
   - First line defense against incoming virus by bnAbs
   - Second line defense against early infected cells by antibody effector functions (ADCC etc.) and cellular immune responses (CD8+ T cells)

Can mRNA vaccines solve the HIV-1 vaccine problem?

Partially - Yes

- **Game changer in immunogen production and delivery** (easy to manufacture and upscale)
- Will greatly speed up vaccine development.
- Multi-specific vaccines become more achievable
- Improved immunogen exposure: mRNA present for several days

Partially - No

- The mRNA platform itself does not solve the HIV-1 immunogen problem – we need immunogens that reliably induce bnAb activity
- Current SARS-CoV-2 mRNA vaccines do not sustain high level titers for extended time

New difficulties through SARS-CoV-2 vaccines

- Increasing vaccine hesitancy in many countries
- May impact also HIV-1 vaccine acceptance

Mandates / Hesitancy

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19ª edición

POSTCROI

Una actualización de la "29th Conference on Retroviruses and Opportunistic Infections"

¡MUCHAS GRACIAS!

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