



THERAPEUTIC VACCINES (TV) & OTHER IMMUNE INTERVENTIONS (IBT) IN HIV INFECTION: 2013

**Hospital Clínic – Facultad de Medicina (U.B.)
Barcelona (España)**



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Global Advocacy for HIV Prevention





Treatment Action Group

Therapeutic vaccines against HIV infection

Felipe García,* Agathe León, Josep M Gatell, Montserrat Plana and Teresa Gallart

Hospital Clinic-HIVACAT; IDIBAPS; University of Barcelona; Barcelona, Spain

Keywords: therapeutic vaccine, dendritic cell, HIV, functional cure, recombinant virus, DNA

Immunological Reviews 2013

Guislaine Carcelain
Brigitte Autran

Immune interventions in HIV
infection

REVIEW



Vaccine and immunotherapeutic interventions

Giuseppe Pantaleo^a and Yves Lévy^b

2013



THERAPEUTIC VACCINES (TV) & OTHER IMMUNE INTERVENTIONS (IBT) IN HIV INFECTION: 2013

1. Where are we with ART
2. Untreated patients. TV/IBT to control productive HIV replication or restore CD4's
3. TV/IBT in virologically suppressed patients with chronic HIV infection
4. TV to reduce the size of the reservoirs and/or to control already depleted reservoirs
5. Final considerations

Hospital Clinic. Barcelona, June 2013. N=4500

Fig

Indetectabilidad por año sobre pacientes activos con al menos 1 año de TARGA (cv<400)
Sobre la última carga viral disponible en cada año de cada paciente

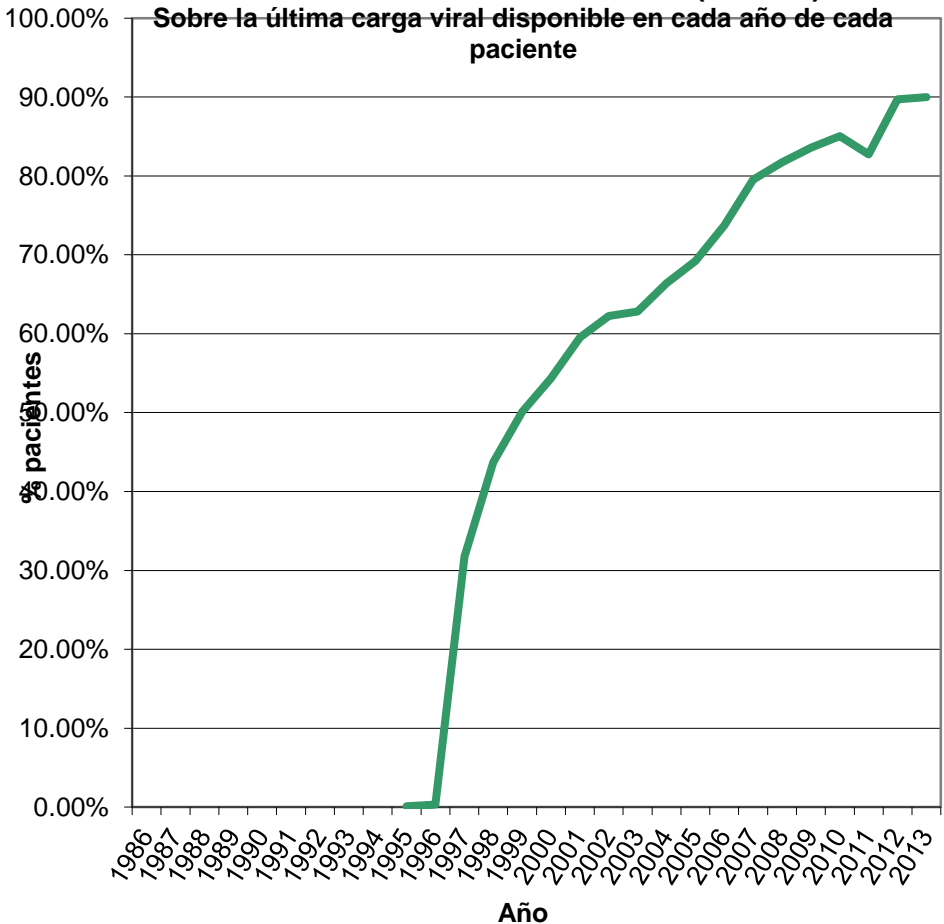
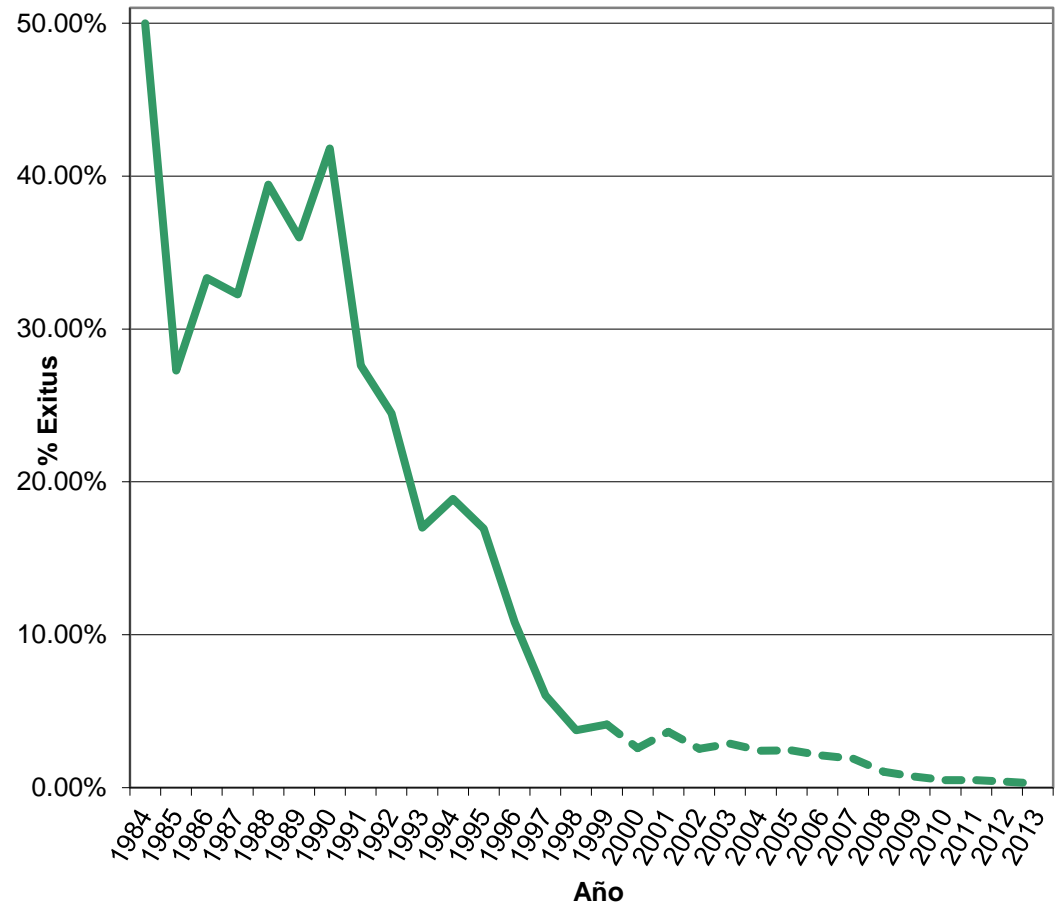
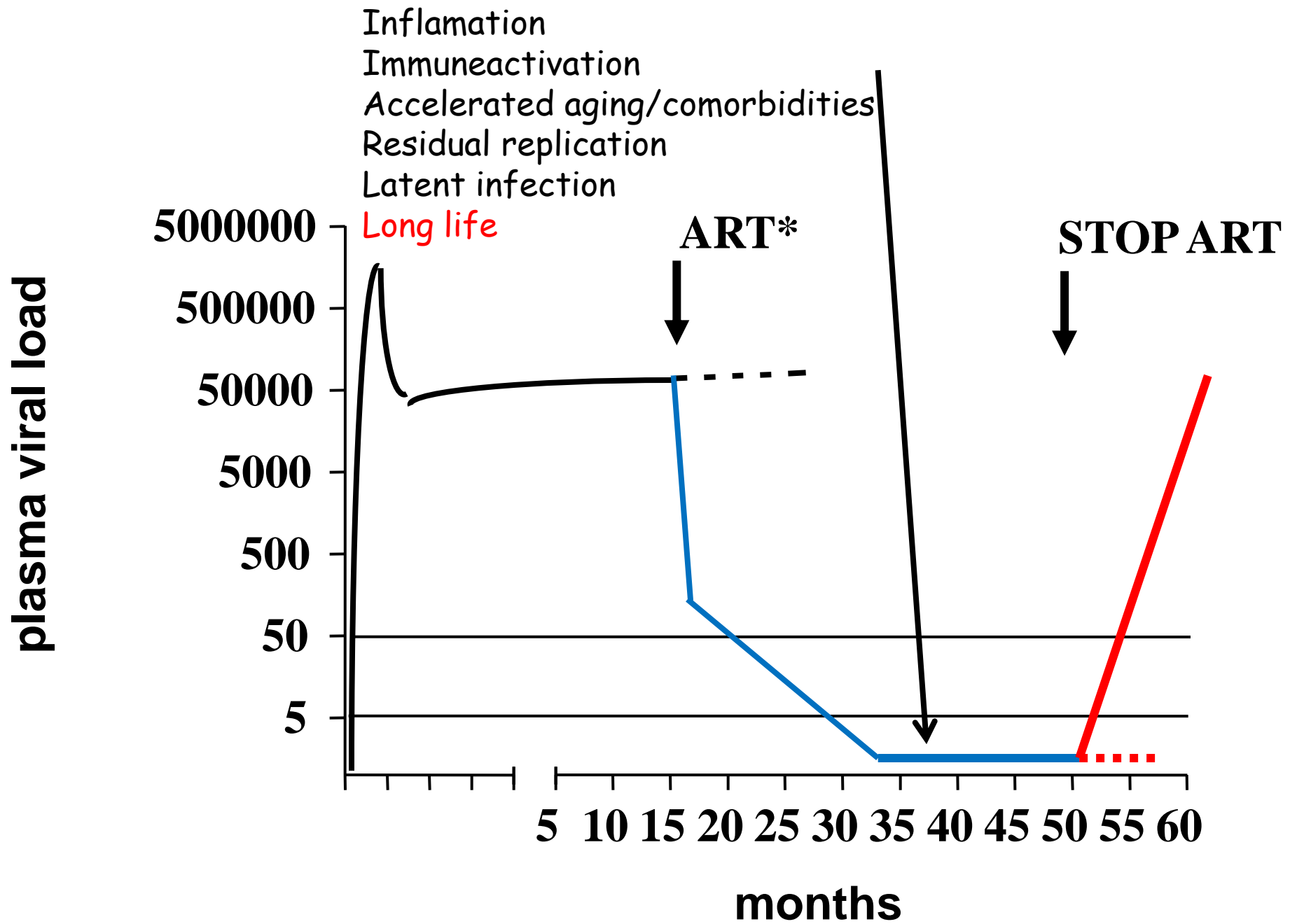


Fig.

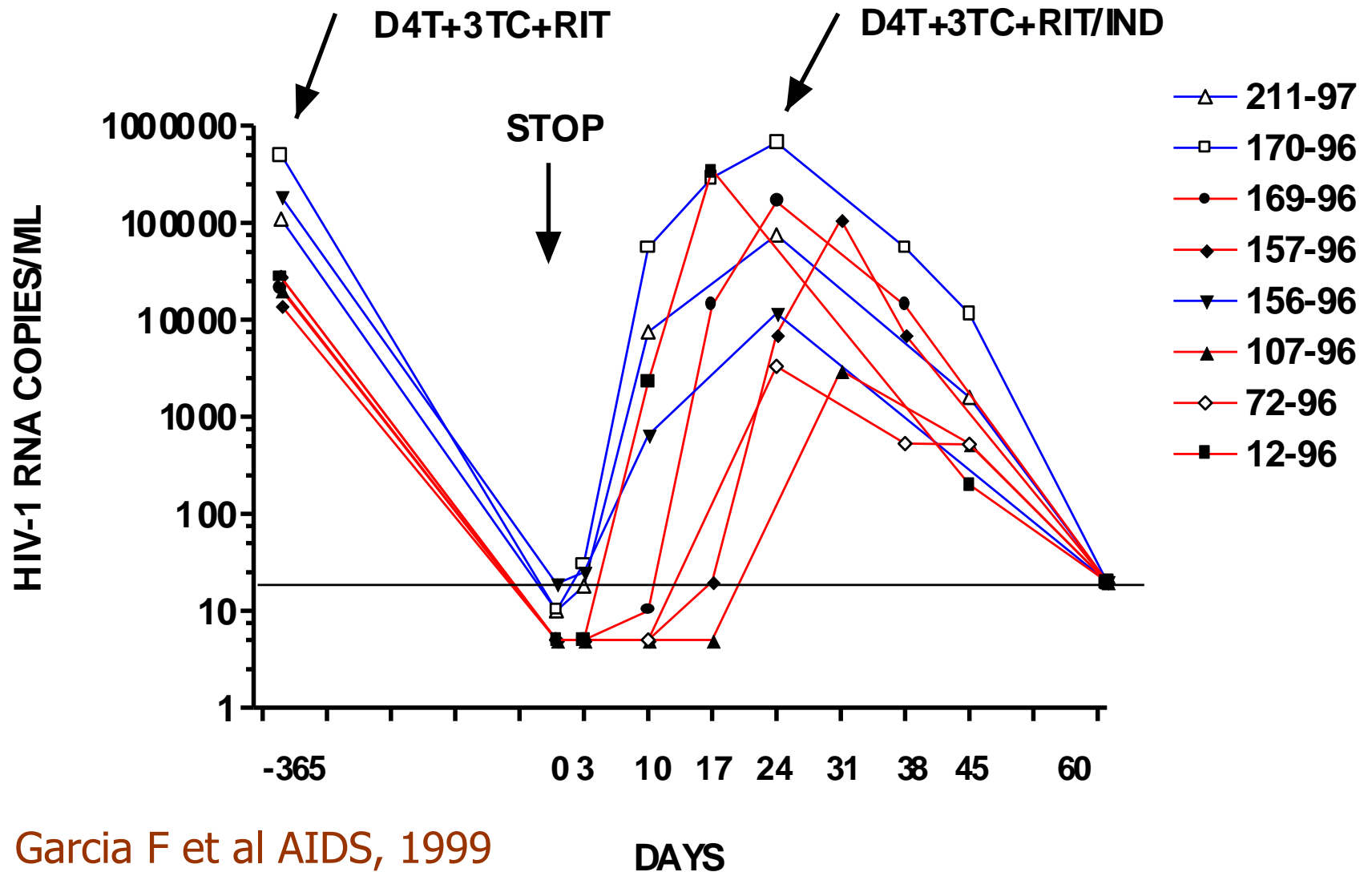
Exitus por año sobre pacientes activos





* Often a convenient, single pill & well tolerated regimen

**SPANISH EARTH-1 STUDY (CD4>500 AND VL >10000).
STOP THERPAY AFTER 1 YEAR OF D4T+3TC+RIT/IND AND VL<20**



Garcia F et al AIDS, 1999

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THERAPEUTIC VACCINES (TV) & OTHER IMMUNE INTERVENTIONS (IBT) IN HIV INFECTION: 2013

2. Untreated patients. TV/IBT to control productive HIV replication or restore CD4's

Biological model:

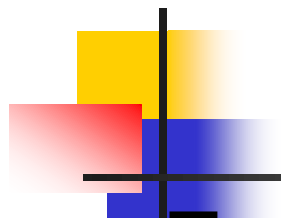
Capacity of the immune system (HIV-specific CTL's and T-helper cells) to partially control viral replication in HIV natural infection and establishing a viral set point lower than peak viremia

Potential objectives:

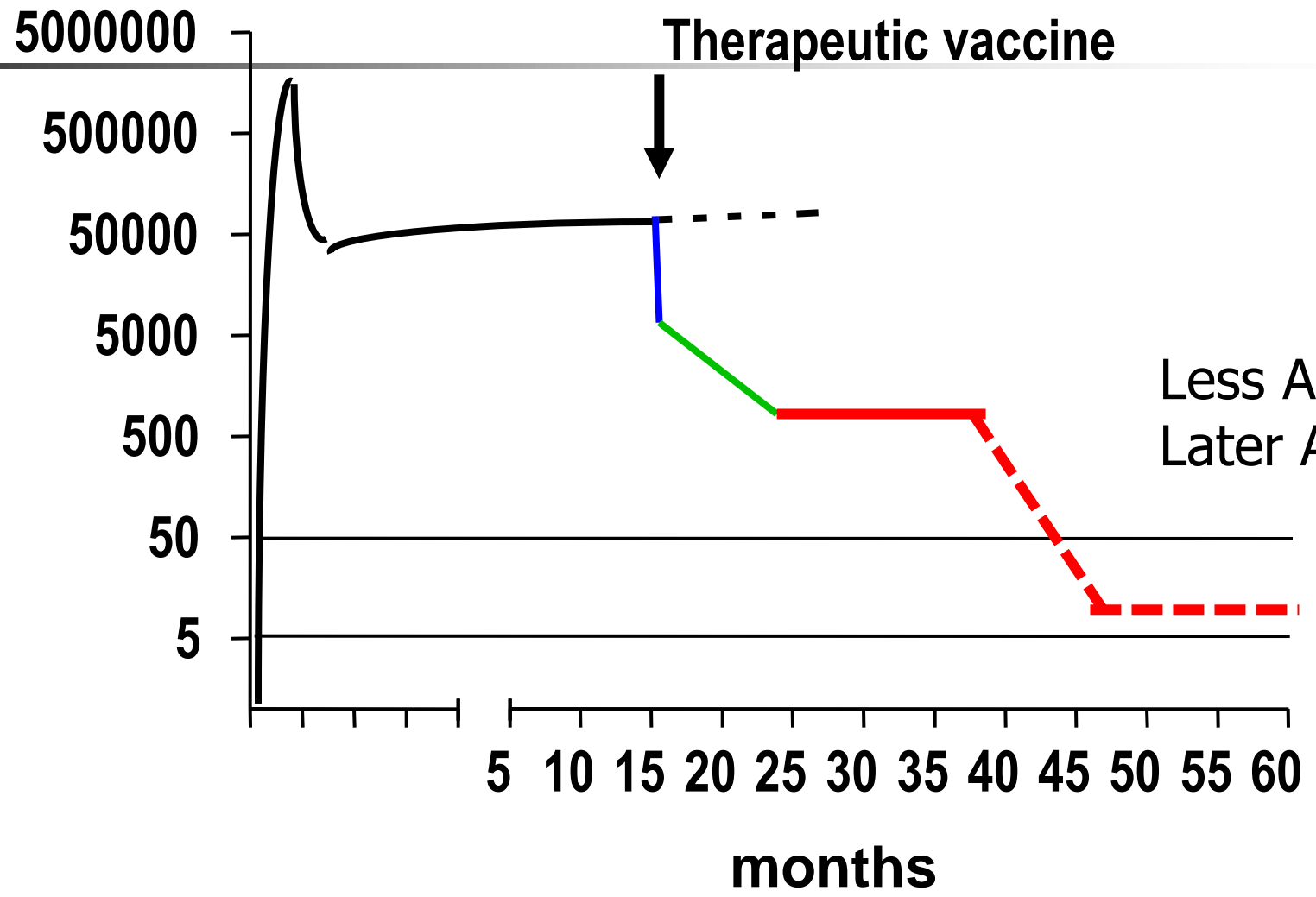
Replace ART

Partially replace ART (less drugs)

Delay ART



plasma viral load





IL-2

GSK-biologicals 732426

Passive transfer of Abs

Autologous dendritic cells based vaccines pulsed with inactivated (AT2, heat) autologous virus

ARTICLES

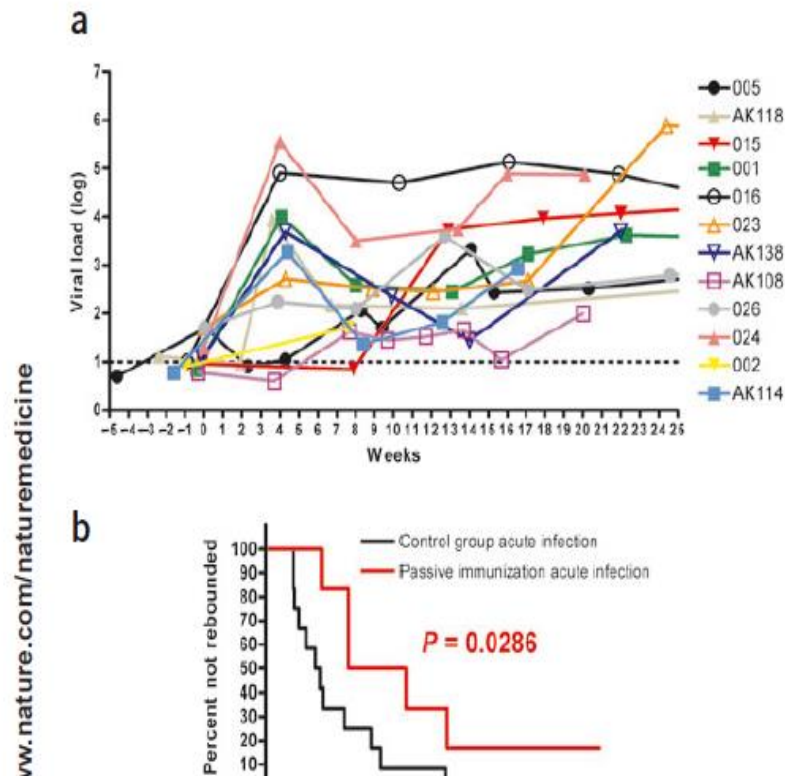
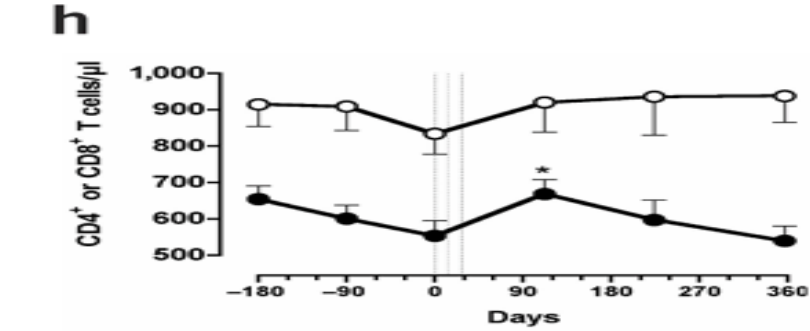
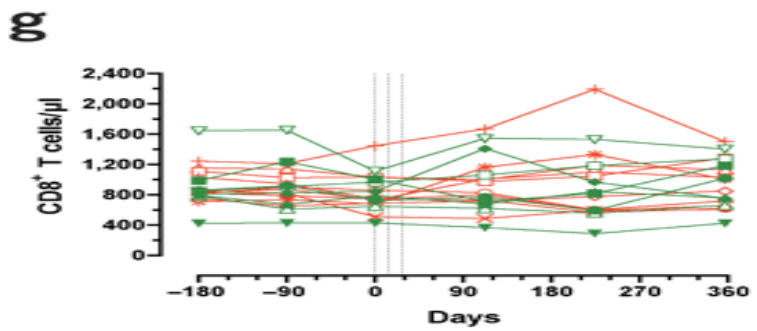
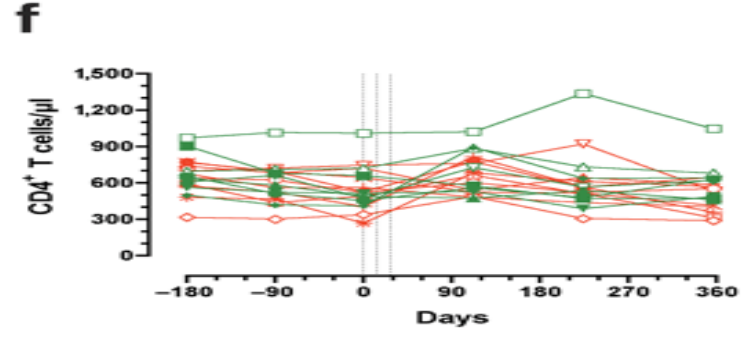
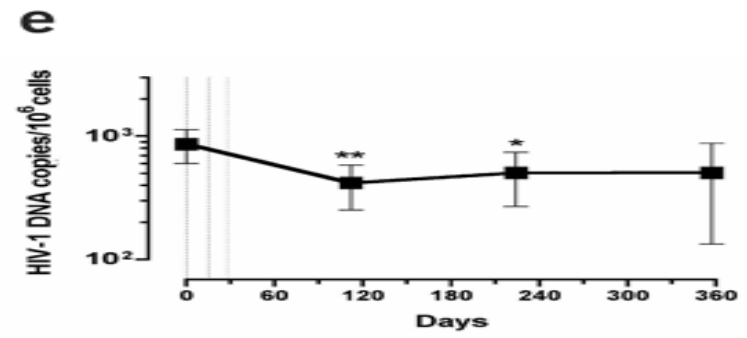
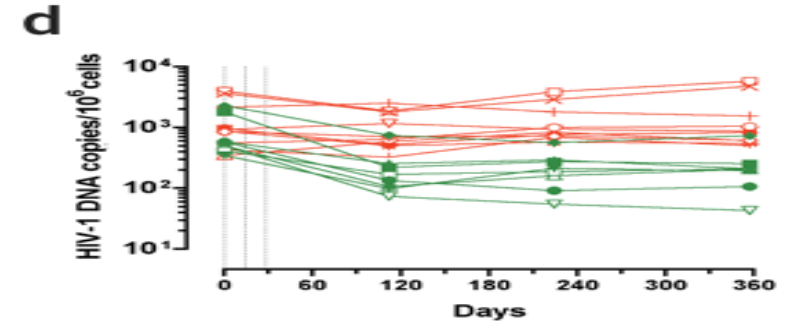
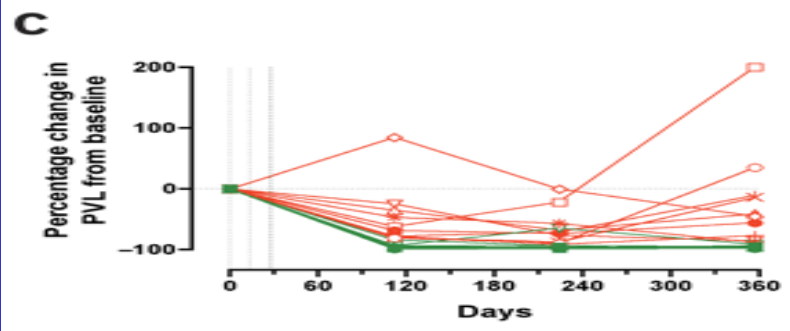
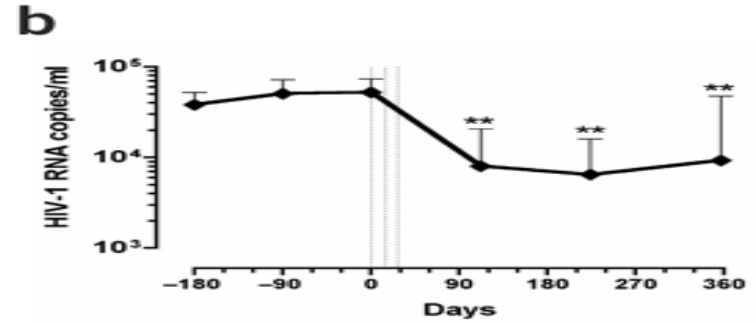
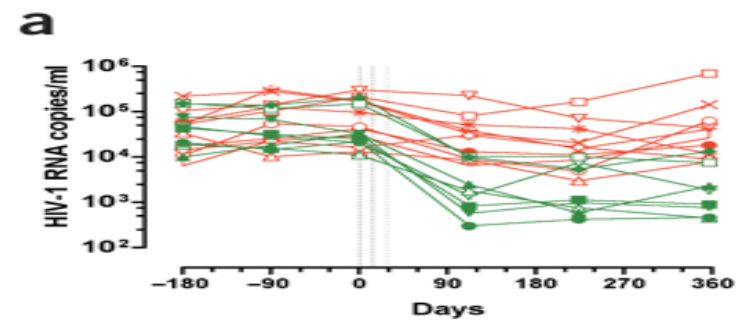


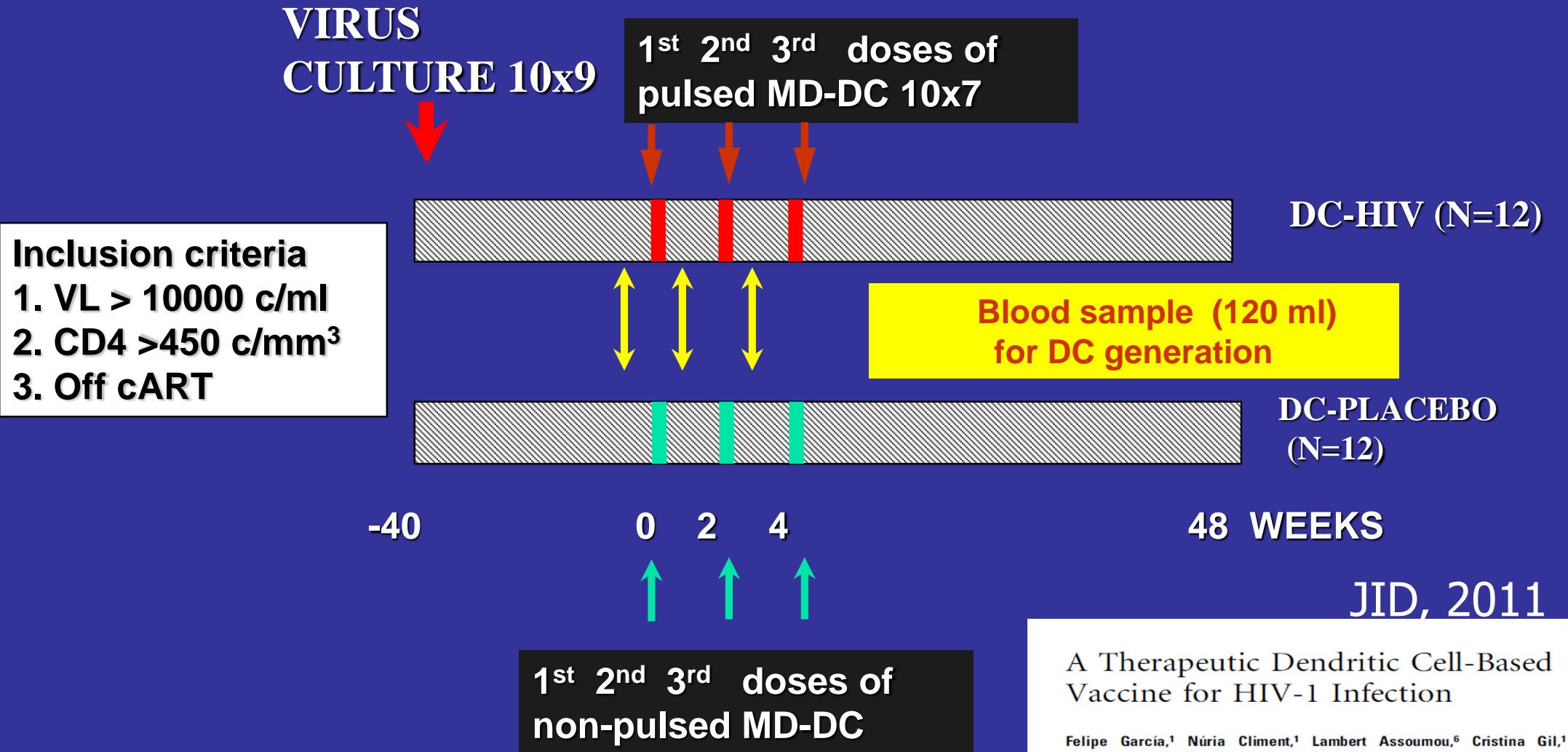
Figure 2 Comparison of virus rebound in acutely infected subjects with and without passive immunization. (a) Control group of subjects with acute HIV infection undergoing treatment interruption: viral load profiles of 12 subjects who initiated ART during acute infection and subsequently underwent treatment interruption without receiving antibody treatment are shown. Viral load is the log HIV RNA copies/ml in plasma. The dotted line indicates the detection limit. (b) Time until rebound of viremia (first time viral load detectable at >10 RNA copies/ml, increase over day 0 value) was determined in the control group and in acutely infected subjects who received passive immunization. The fraction of subjects without rebound at a given time point was compared using Kaplan-Meier curves and log rank test. One data point (subject NAB14, week 24) was censored because rebound had not occurred in this patient.

(data not shown). Overall, plasma levels of 2G12 were significantly higher than those of 2F5 or 4E10 (Dunn multiple comparison test, $P < 0.001$ and $P < 0.01$, respectively). Of note, plasma concentrations of 2G12 and the sensitivity of the subjects' pretrial isolates to inhibition by 2G12 were higher amongst responders, whereas no significant difference in these parameters was found for 2F5 and 4E10 (Fig. 4c,d). To estimate what range of antibody concentrations are required to

**Therapeutic
 dendritic-cell
 vaccine for chronic
 HIV-1 infection**
 Wei Lu, Luiz Claudio
 Arraes, Wylla Tatiana
 Ferreira & Jean-Marie
 Andrieu
Nature Medicine **10**,
 1359 - 1365 (2004)



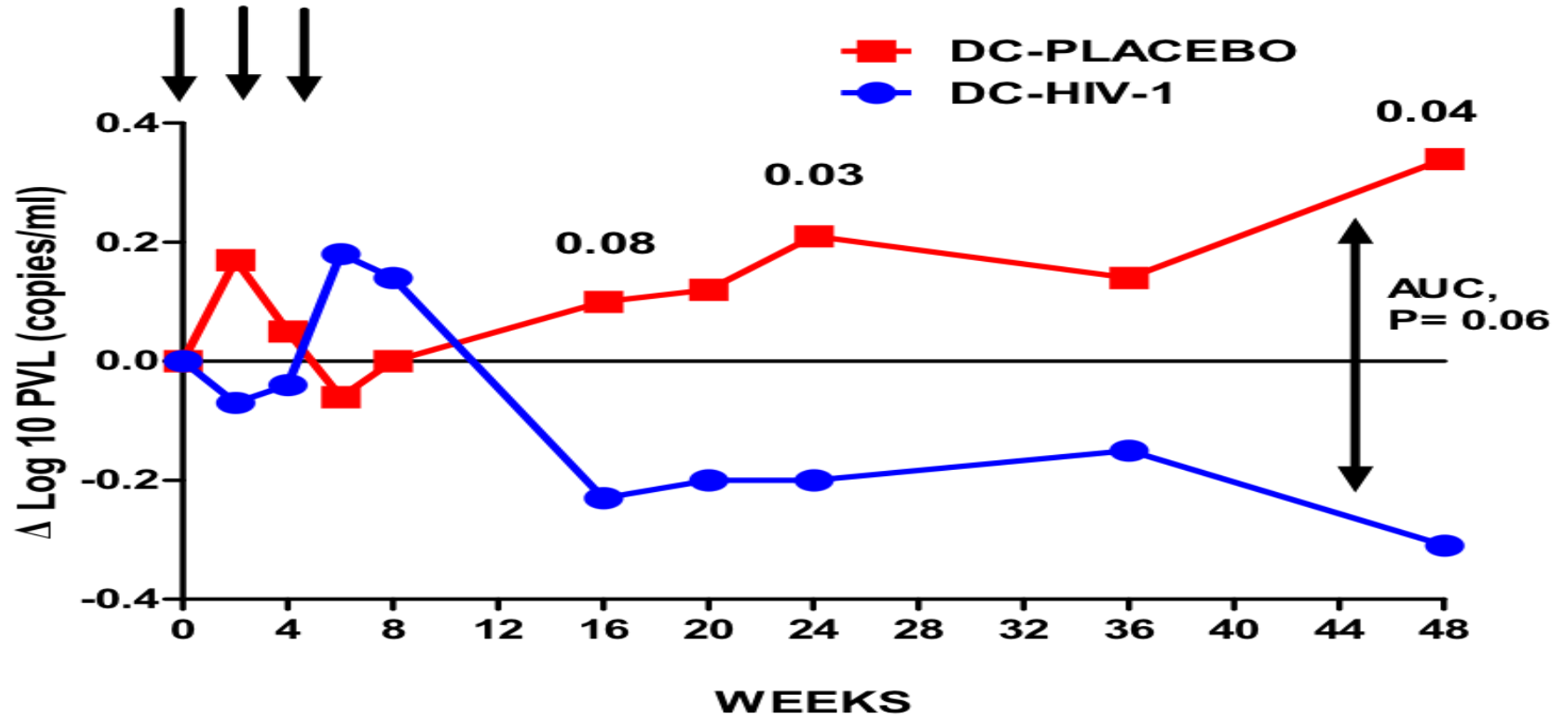
A therapeutic dendritic cell-based vaccine for HIV-1 infection.
García F et al J Infect Dis 2011;203:473-8



A Therapeutic Dendritic Cell-Based Vaccine for HIV-1 Infection

Felipe García,¹ Núria Climent,¹ Lambert Assoumou,⁶ Cristina Gil,¹ Nuria González,³ José Alcamí,³ Agathe León,¹ Joan Romeu,⁴ Judith Dalmau,⁵ Javier Martínez-Picado,^{2,5} Jeff Lifson,⁸ Brigitte Autran,⁷ Dominique Costagliola,⁶ Bonaventura Clotet,^{4,5} Josep M Gatell,¹ Montserrat Plana, and Teresa Gallart,¹ for the DCV2/MANON07- AIDS Vaccine Research Objective Study Group^a

VIRAL LOAD RESPONSES



DC-PLACEBO	12	12	12	12	11	11	11	9
DC-HIV-1	10	10	10	10	8	8	8	7

IT WAS OBSERVED A MODEST DECREASE OF VL IN VACCINATED PATIENTS

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2. TV/IBT in virologically suppressed patients with chronic HIV infection

Biological model:

Many infectious diseases (TB, Toxo, H Zoster ...)
HIV elite controllers

Potential objective:

Plasma VL BLQ without life long ART (functional cure)

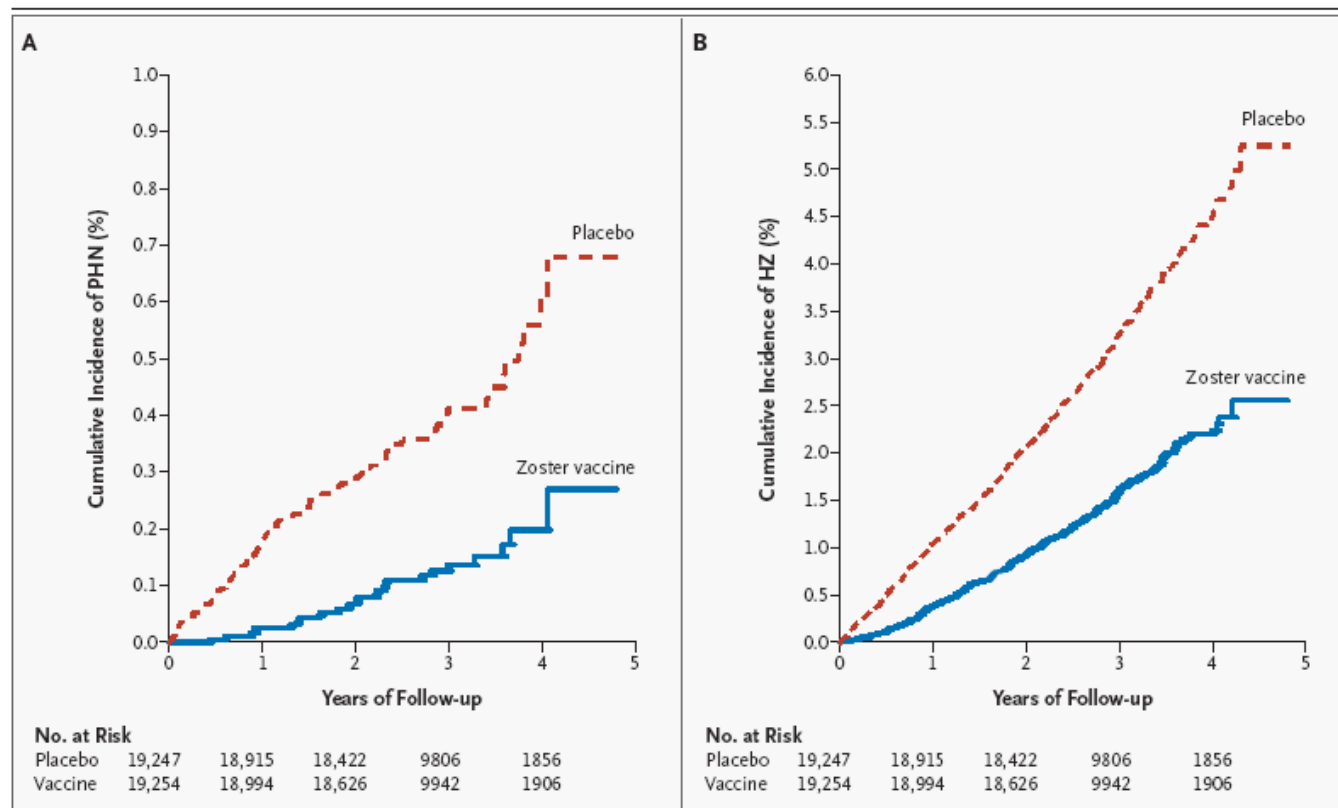
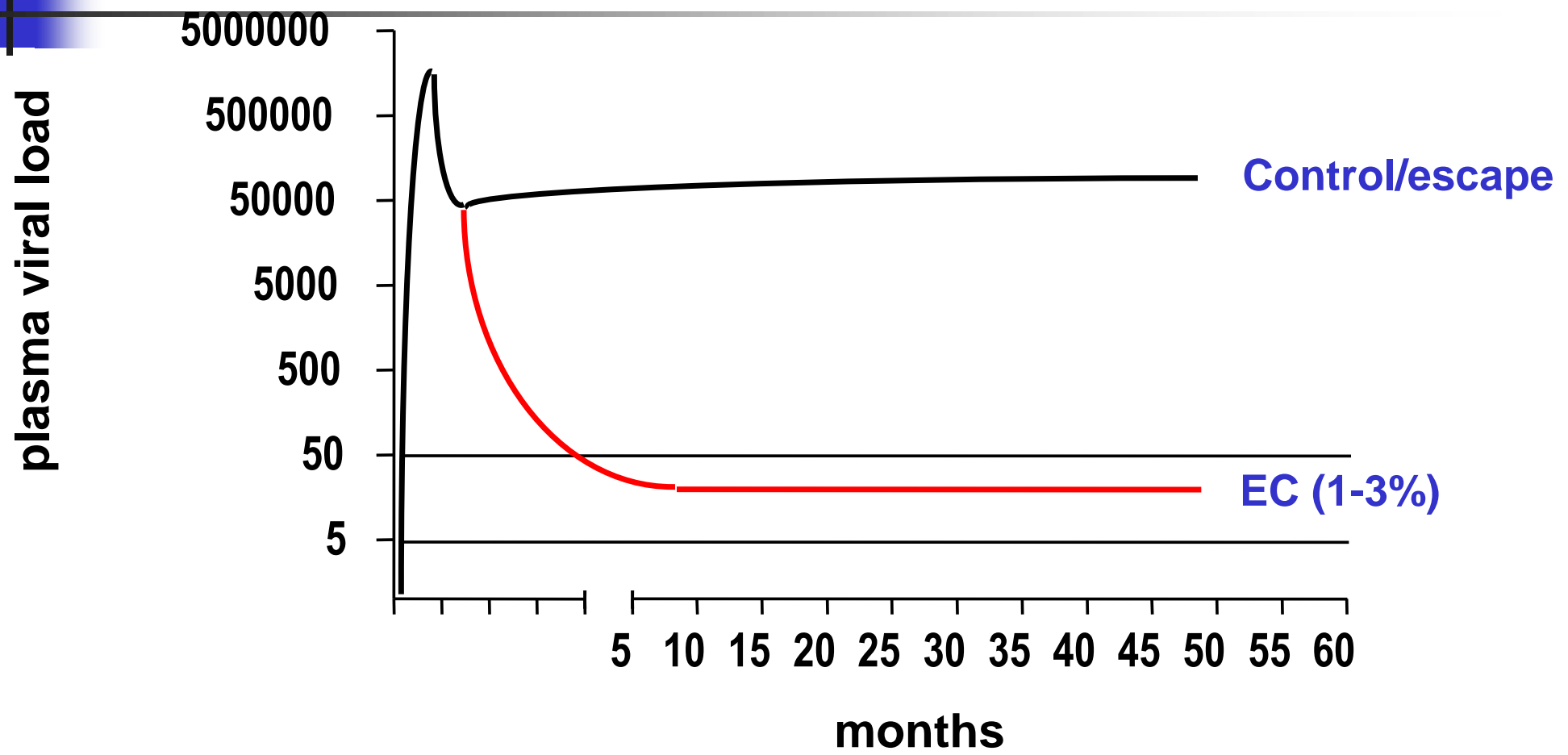
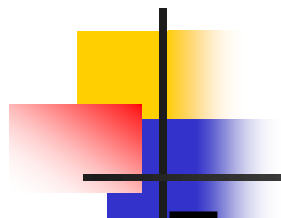


Figure 2. Kaplan–Meier Estimates of the Effect of Zoster Vaccine on the Cumulative Incidence of Postherpetic Neuralgia (Panel A) and Herpes Zoster (Panel B) in the Modified Intention-to-Treat Population.

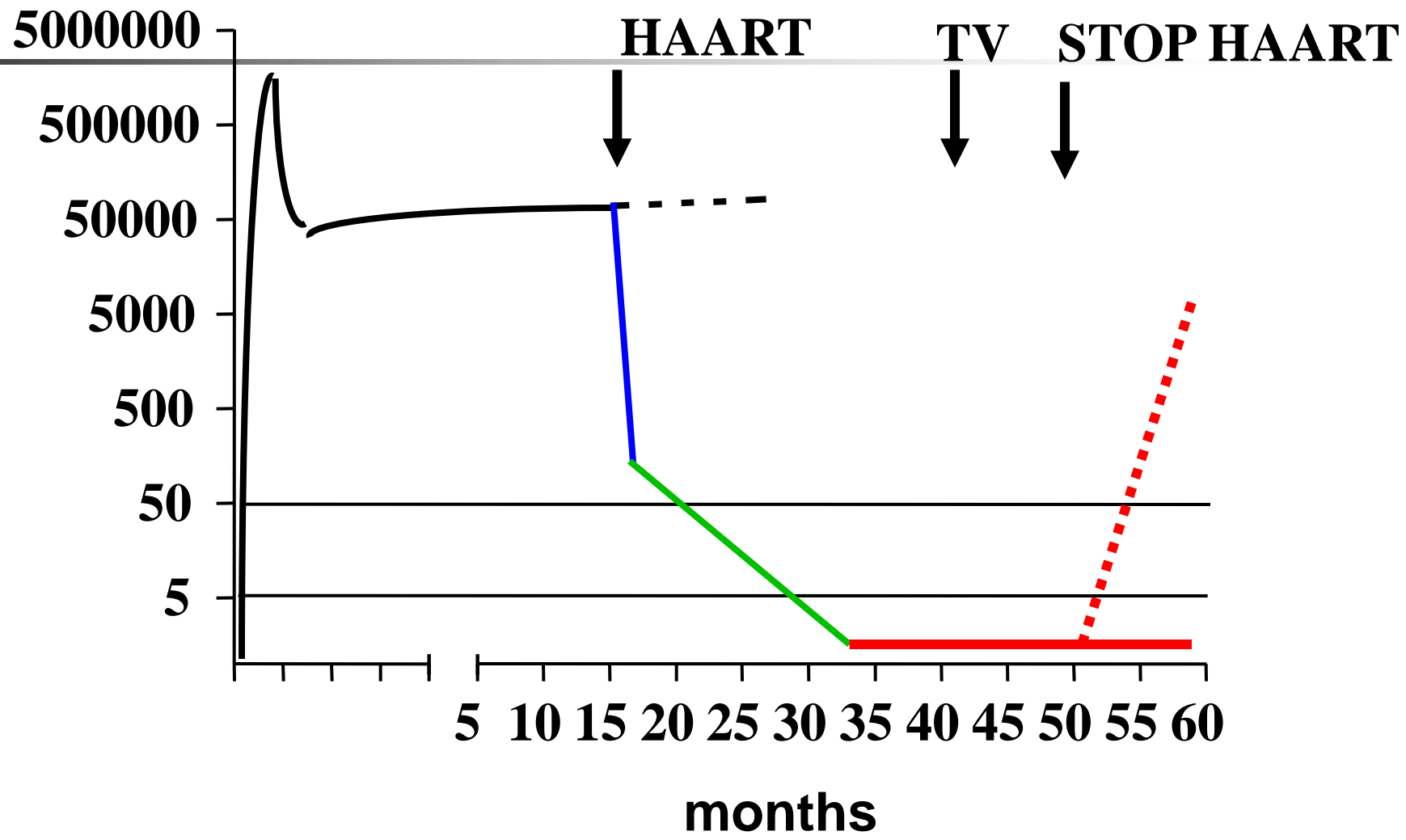
Incidence rates of postherpetic neuralgia (PHN) and herpes zoster (HZ) were significantly lower in the vaccine group than in the placebo group ($P < 0.001$, by a stratified log-rank test that pooled the results of the log-rank test from the two age groups). Cumulative incidence, expressed as a percentage of the subjects at risk, is the probability of the development of the disease during the period from 30 days after vaccination to the follow-up time.

CTL's





plasma viral load





Viral vectors based vaccines (poxviruses, adenoviruses,)

Replicative viral vectors based vaccines (herpesviruses)

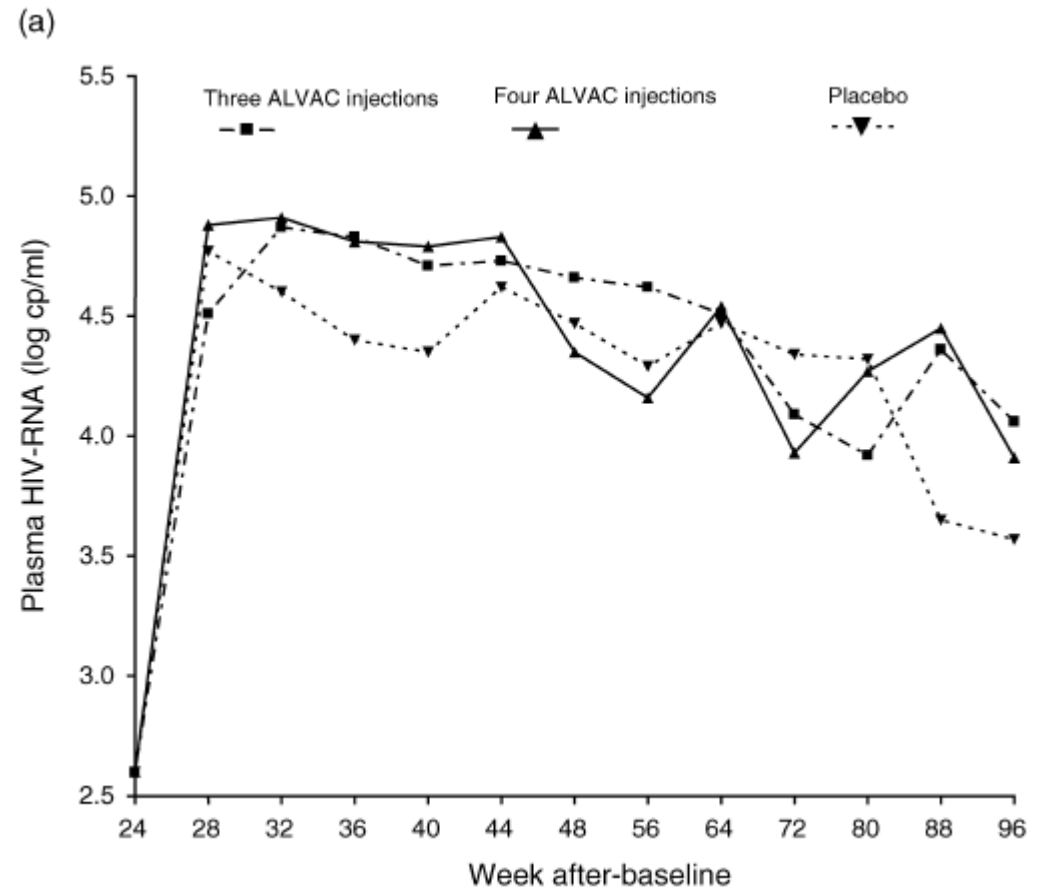
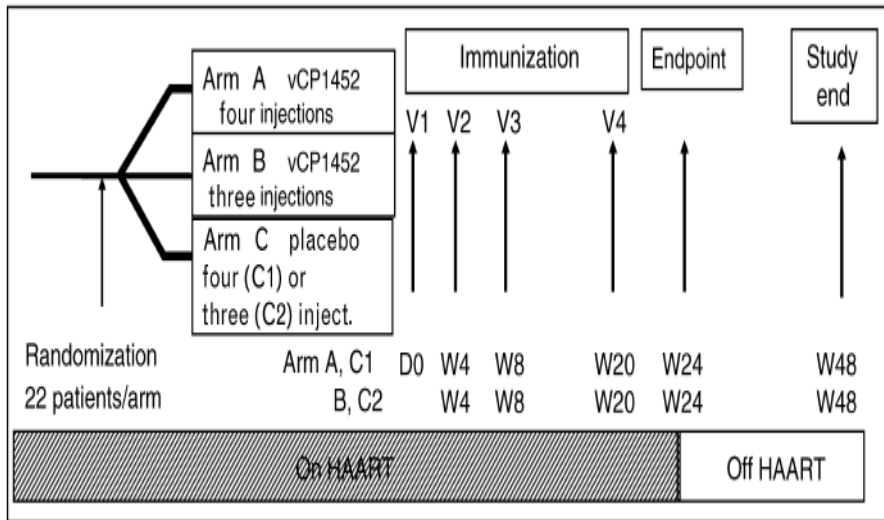
Autologous dendritic cells based vaccines pulsed with

Other modalities (proteins, peptides) / combinations

Passive transfer of nAbs

Greater viral rebound and reduced time to resume antiretroviral therapy after therapeutic immunization with the ALVAC-HIV vaccine (vCP1452)

Brigitte Autran^{a,b,c}, Robert L. Murphy^{d,e,f}, Dominique Costagliola^{d,e,g}, Roland Tubiana^{d,e,g}, Bonaventura Clotet^h, Jose Gatellⁱ, Schlomo Staszewski^j, Norma Wincker^k, Lambert Assoumou^{e,g}, Raphaelle El-Habib^l, Vincent Calvez^{m,n}, Bruce Walker^o, Christine Katlama^{d,e,g} and the ORVACS Study Group



Safety, Immunogenicity and Dynamics of Viral Load Rebound After cART Interruption in Chronic HIV Infected Patients Receiving MVA-B Vaccination

Beatriz Mothe¹, Nuria Climent², Montserrat Plana², Miriam Rosas¹, José Luis Jiménez³, María Angeles Muñoz-Fernández³, Judit Pich², Joan Albert Arnaiz², Jose M Gatell², Bonaventura Clotet¹, Mariano Esteban⁴, Juan Carlos López Bernaldo de Quirós³, Felipe García² and Christian Brander¹ for the RISVAC-03 Study.

1. Irsicaixa-HIVACAT, Hospital Germans Trias i Pujol, Badalona, Spain

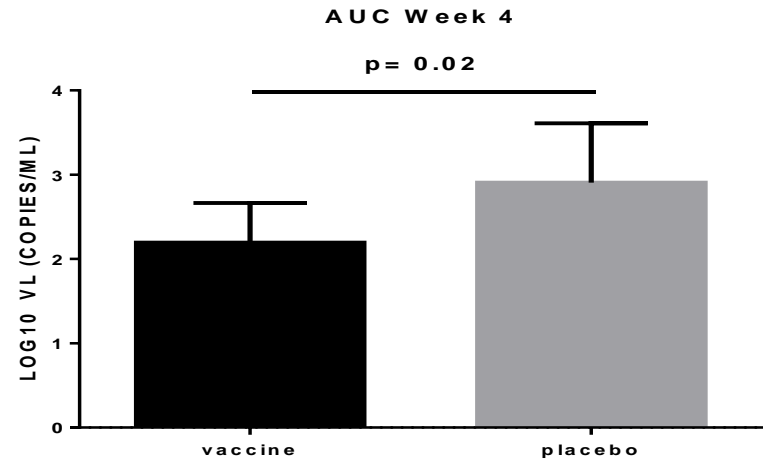
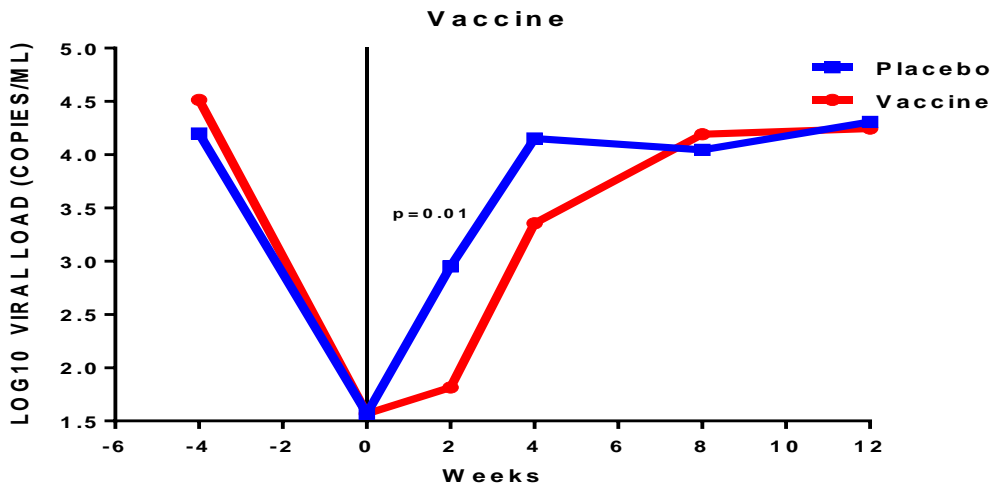
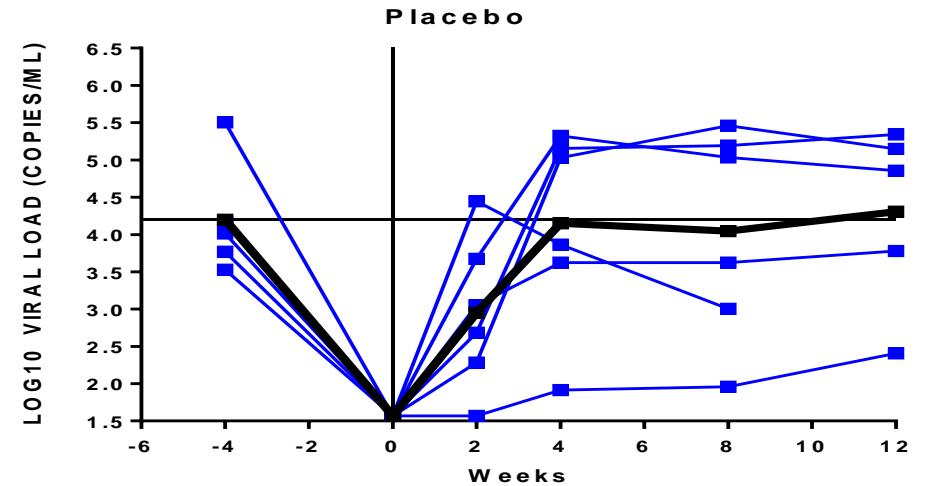
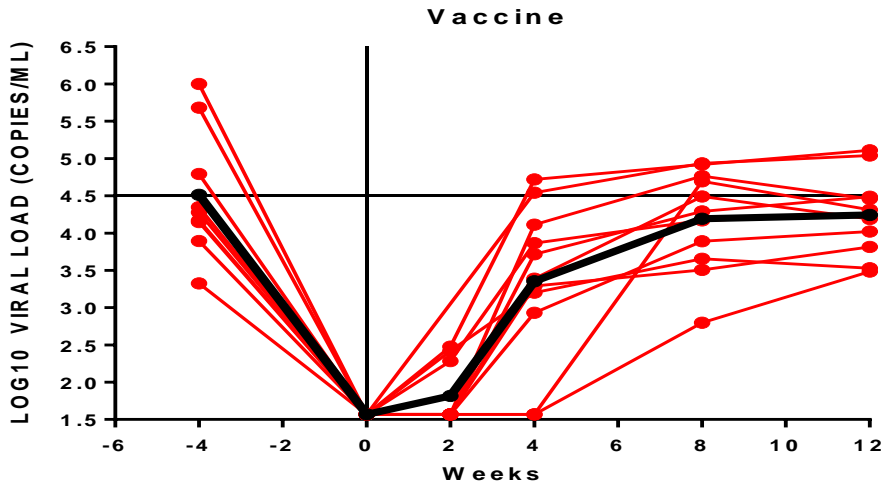
2. Hospital Clínic-HIVACAT, IDIBAPS, University of Barcelona, Spain

3. Hospital Gregorio Marañón, Madrid. Spain

4. Centro Nacional de Biotecnología, Madrid. Spain



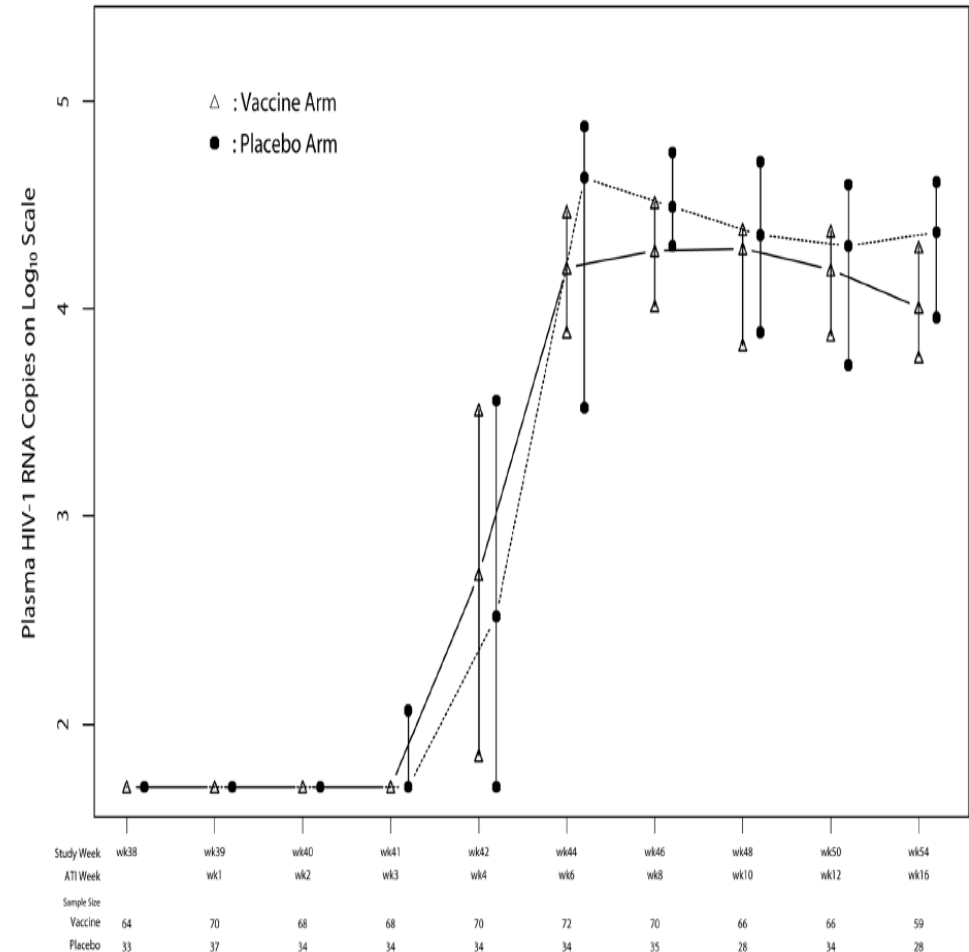
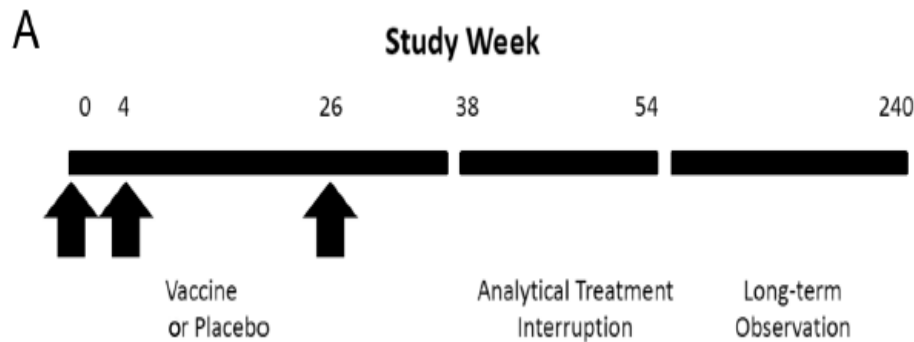
VL rebound after analytical treatment interruption in MVA-B (n=11) vs placebo (6) recipients



JID, 2010

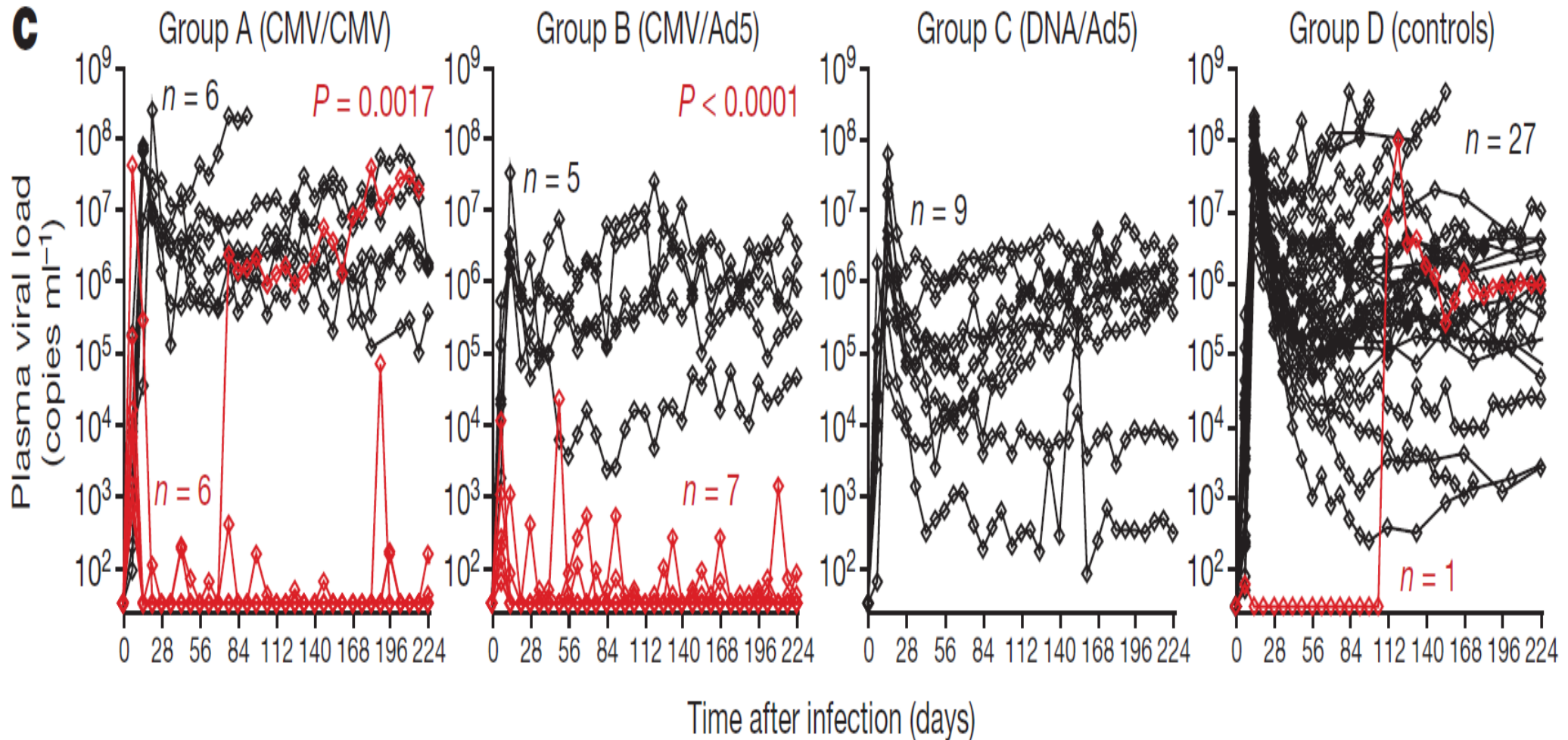
AIDS Clinical Trials Group 5197: A Placebo-Controlled Trial of Immunization of HIV-1–Infected Persons with a Replication-Deficient Adenovirus Type 5 Vaccine Expressing the HIV-1 Core Protein

Robert T. Schooley,¹ John Spritzler,⁴ Hongying Wang,⁴ Michael M. Lederman,⁵ Diane Havlir,² Daniel R. Kuritzkes,⁵ Richard Pollard,³ Cathy Battaglia,⁷ Michael Robertson,⁸ Devan Mehrotra,⁸ Danilo Casimiro,⁸ Kara Cox,⁸ Barbara Schock,⁹ and the AIDS Clinical Trials Group 5197 Study Team



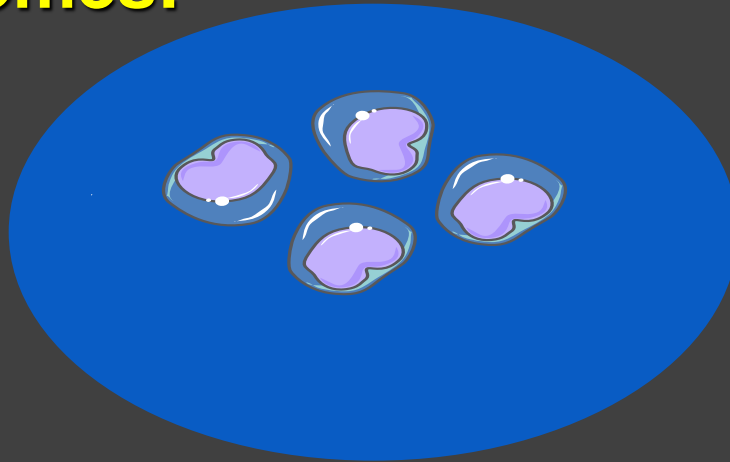
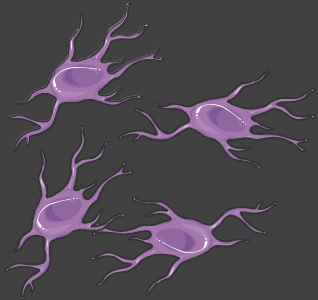
Profound early control of highly pathogenic SIV by an effector memory T-cell vaccine

Scott G. Hansen¹, Julia C. Ford¹, Matthew S. Lewis¹, Abigail B. Ventura¹, Colette M. Hughes¹, Lia Coyne-Johnson¹, Nathan Whizin¹, Kelli Oswald², Rebecca Shoemaker², Tonya Swanson¹, Alfred W. Legasse¹, Maria J. Chiuchiolo³, Christopher L. Parks³, Michael K. Axthelm¹, Jay A. Nelson¹, Michael A. Jarvis¹, Michael Piatak Jr², Jeffrey D. Lifson² & Louis J. Picker¹



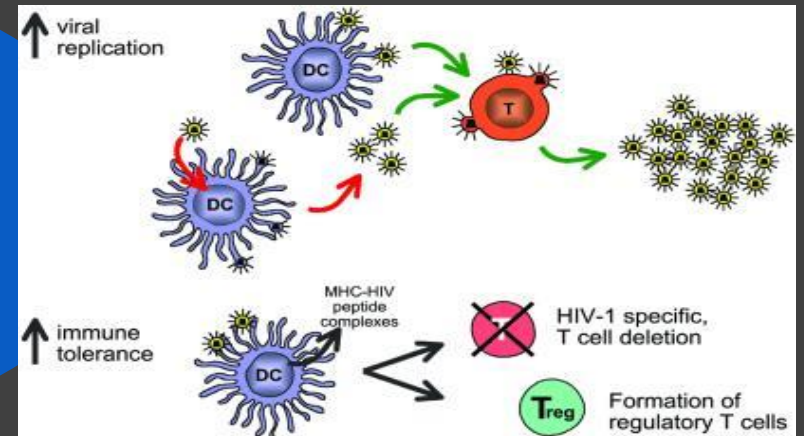
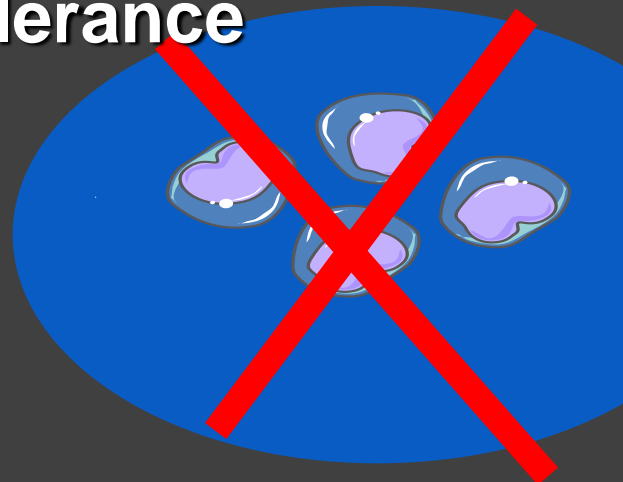
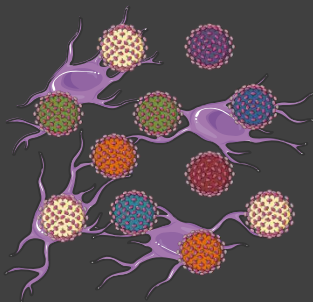
DCs have a central role in HIV infection.

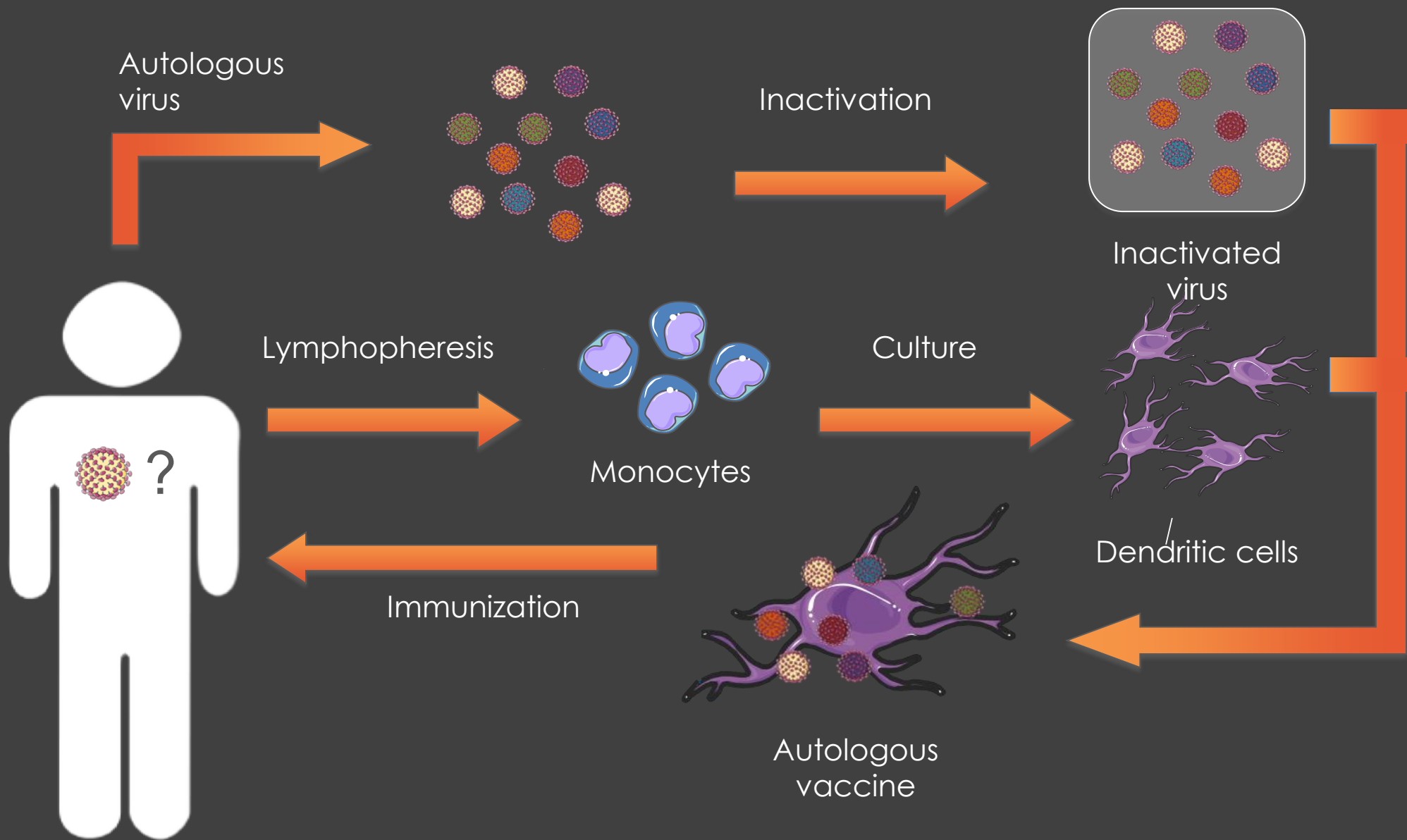
the initial contact of HIV-1 with DCs can result in opposite outcomes:



beneficial in inducing strong HIV-specific T-cell responses

deleterious in promoting the dissemination of HIV-1 and/or immunotolerance





- **Different immunogens (load or pulse):**
 - autologous inactivated virus (heat, AT-2)
 - HIV-1 proteins
 - Peptides
 - mRNA
 - recombinant virus vectors nanoparticles

Therapeutic Immunization with Dendritic Cells Loaded with Heat-Inactivated Autologous HIV-1 in Patients with Chronic HIV-1 Infection

**Felipe García,¹ Merylene Lejeune,² Nuria Climent,² Cristina Gil,³
José Alcamí,⁸ Vanessa Morente,⁴ Lluçia Alós,⁴ Alba Ruiz,⁵
Javier Setoain,⁵ Emilio Fumero,¹ Pedro Castro,¹ Anna López,²
Anna Cruceta,¹ Carlos Piera,⁵ Eric Florence,¹ Arturo Pereira,⁶
Agnes Libois,¹ Nuria González,⁸ Meritxell Guilá,³ Miguel Caballero,⁷
Francisco Lomeña,⁵ Joan Joseph,¹ José M Miró,¹ Tomás Pumarola,³
Montserrat Plana,² José M Gatell,¹ and Teresa Gallart²**

Received 29 September 2004; accepted 3 December 2004; electronically published 11 April 2005.

Reprints or correspondence: Dr. Felipe García, Infectious Diseases Unit, Hospital Clínic, Villarroel, 170, 08036 Barcelona, Spain (fgarcia@clinic.ub.es).

The Journal of Infectious Diseases 2005;191:1680–5

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0022-1899/2005/19110-0014\$15.00

**ORVACS
MANON 03 STUDY**

DCV-1 study

Figure 3A

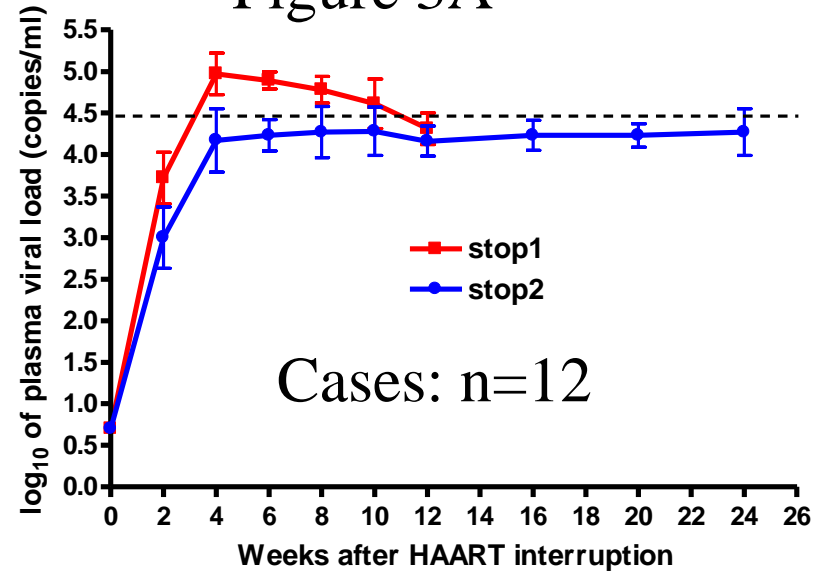


Figure 3B

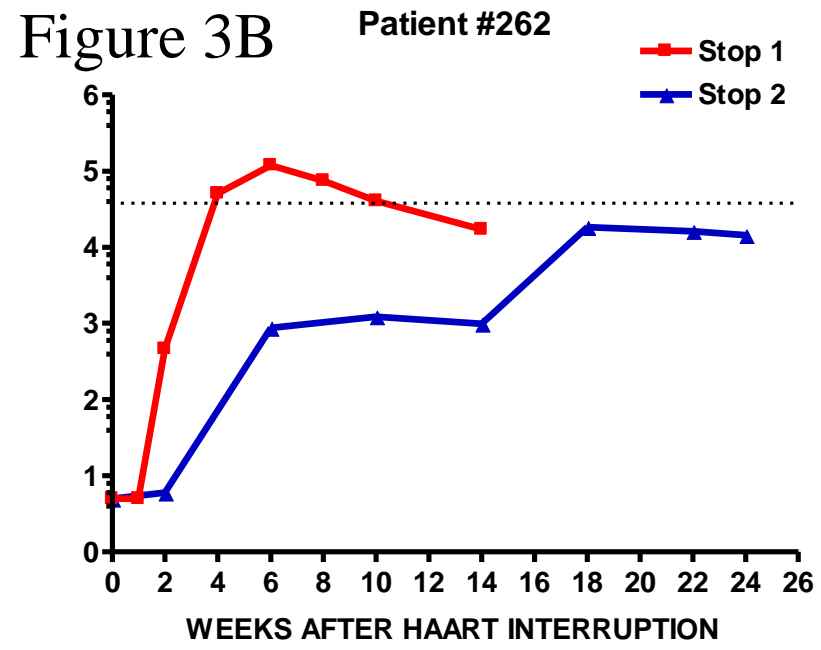


Figure 3C

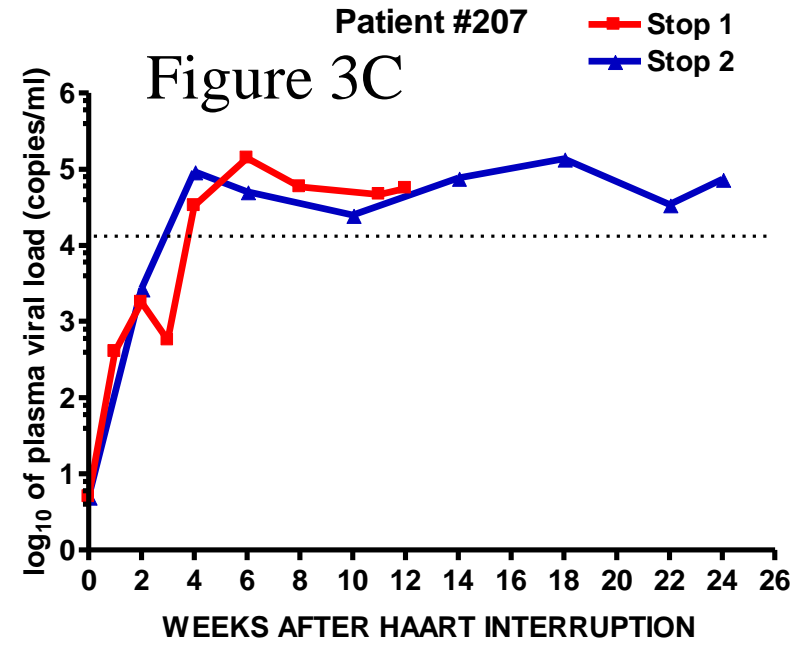
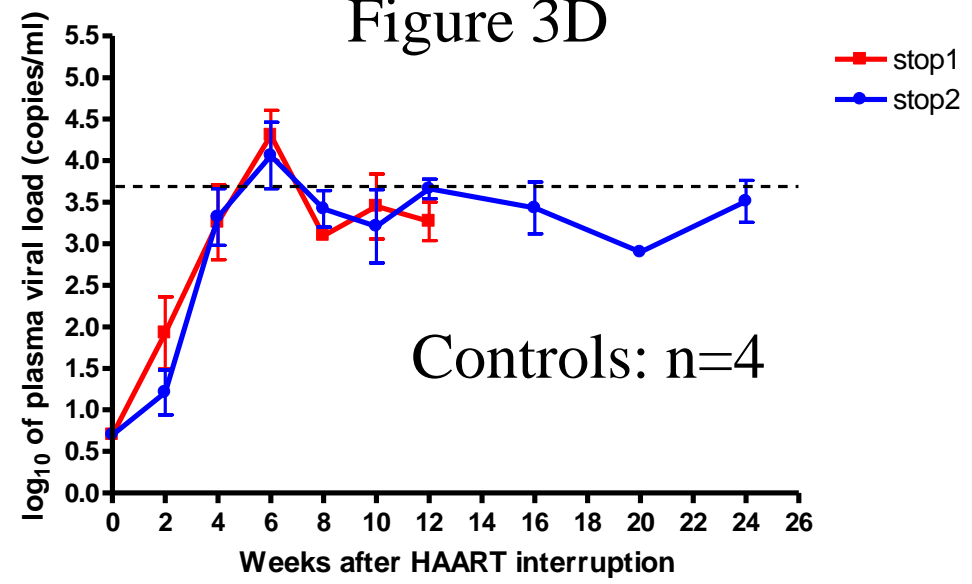


Figure 3D



• **Main differences:**

**Manon 03
(JID 2005)**

**Manon07 part II
(STM 2013)**

• **IMMUNOGEN**

- Pulsing dose 10⁶ virions/ml
- Source of HIV plasmapheresis
- Inactivation Heat
- No. of DCs per dose 10⁶
- No. Doses 4

- 10⁹⁻¹⁰ virions/ml
- culture
- Heat
- 10⁷
- 3

• **CLINICAL TRIAL**

- Schedule every 6 weeks
- cART Yes
- Design Open randomized
- Number 18 (12:6)

- every 2 weeks
- yes
- Blinded, placebo
- 36 (24-12)

• **OUTCOME**

- - 4/12 (>0.5 log; 6mo.)
- 0/4 controls
- - No differences between arms
- - No sig.change in VL

- -12/22 (>1 log; 3mo.)
- 1/11 controls
- - Sig diff. bet arms
- - Drop VL 1.2log

High dose virus and MD-DCs in patients on cART

RESEARCH ARTICLE

HIV

A Dendritic Cell–Based Vaccine Elicits T Cell Responses Associated with Control of HIV-1 Replication

Felipe García,^{1*†} Nuria Climent,^{1*} Alberto C. Guardo,¹ Cristina Gil,¹ Agathe León,¹ Brigitte Autran,² Jeffrey D. Lifson,³ Javier Martínez-Picado,^{4,5} Judit Dalmau,⁴ Bonaventura Clotet,⁴ Josep M. Gatell,¹ Montserrat Plana,^{1*} Teresa Gallart,^{1*} For the DCV2/MANON07-ORVACS Study Group

Combination antiretroviral therapy (cART) greatly improves survival and quality of life of HIV-1–infected patients; however, cART must be continued indefinitely to prevent viral rebound and associated disease progression. Inducing HIV-1–specific immune responses with a therapeutic immunization has been proposed to control viral replication after discontinuation of cART as an alternative to “cART for life.” We report safety, tolerability, and immunogenicity results associated with a control of viral replication for a therapeutic vaccine using autologous monocyte-derived dendritic cells (MD-DCs) pulsed with autologous heat-inactivated whole HIV. Patients on cART with CD4⁺ >450 cells/mm³ were randomized to receive three immunizations with MD-DCs or with nonpulsed MD-DCs. Vaccination was feasible, safe, and well tolerated and shifted the virus/host balance. At weeks 12 and 24 after cART interruption, a decrease of plasma viral load setpoint ≥ 1 log was observed in 12 of 22 (55%) versus 1 of 11 (9%) and in 7 of 20 (35%) versus 0 of 10 (0%) patients in the DC–HIV-1 and DC-control groups, respectively. This significant decrease in plasma viral load observed in immunized recipients was associated with a consistent increase in HIV-1–specific T cell responses. These data suggest that HIV-1–specific immune responses elicited by therapeutic DC vaccines could significantly change plasma viral load setpoint after cART interruption in chronic HIV-1–infected patients treated in early stages. This proof of concept supports further investigation of new candidates and/or new optimized strategies of vaccination with the final objective of obtaining a functional cure as an alternative to cART for life.

DCV2-b study

HAART

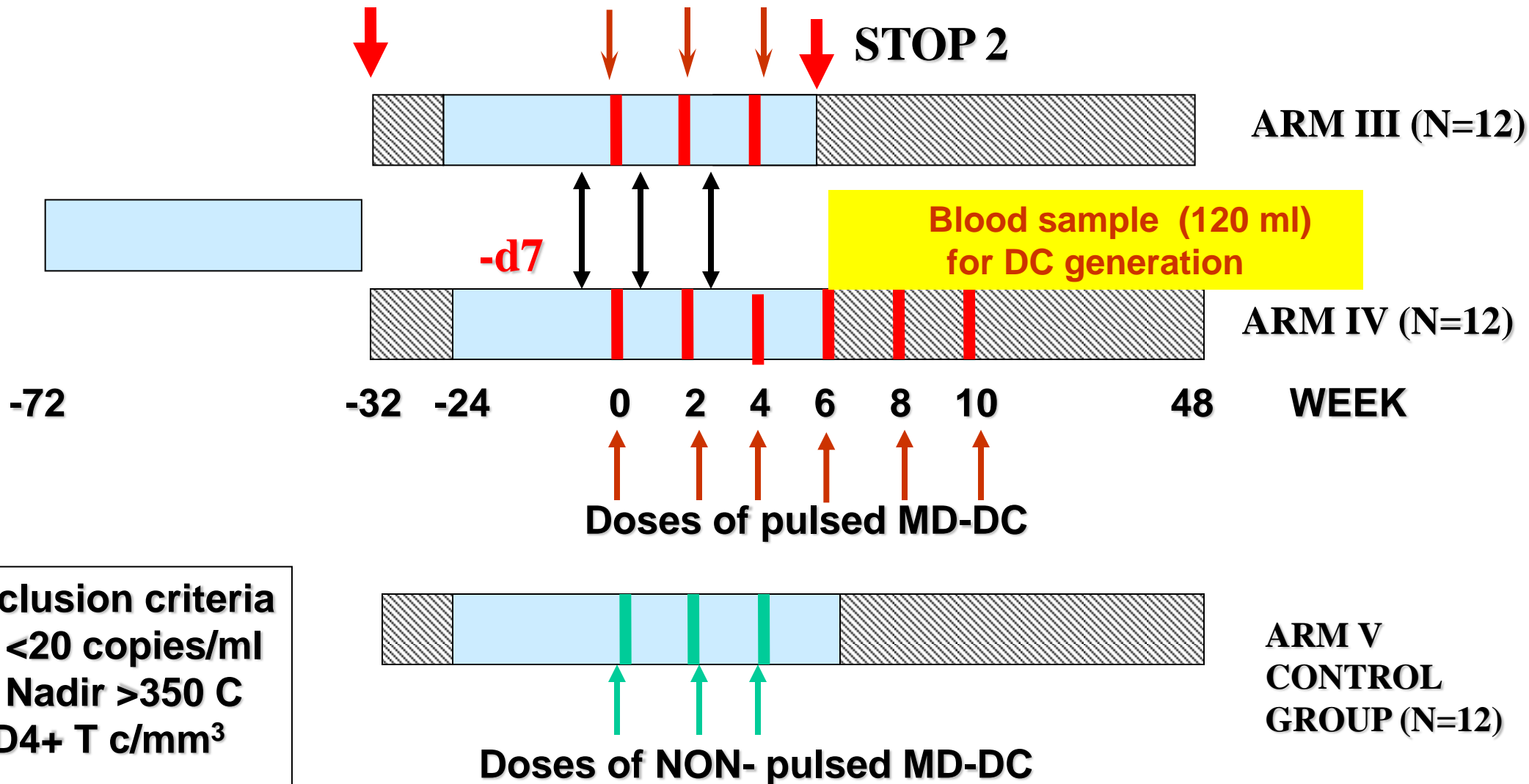
Stop HAART

STOP 1

Virus culture

Doses of pulsed MD-DC

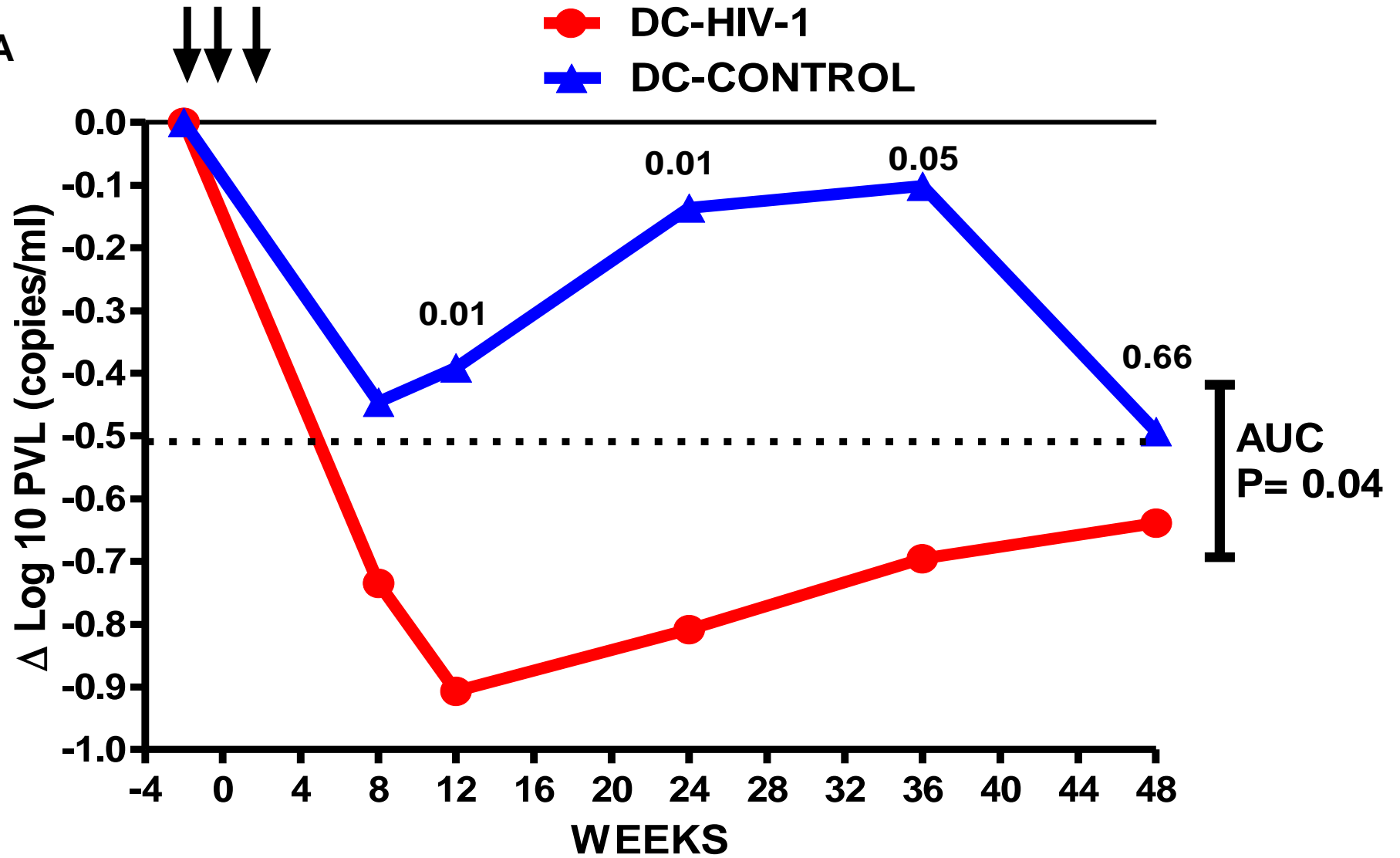
STOP 2



Inclusion criteria

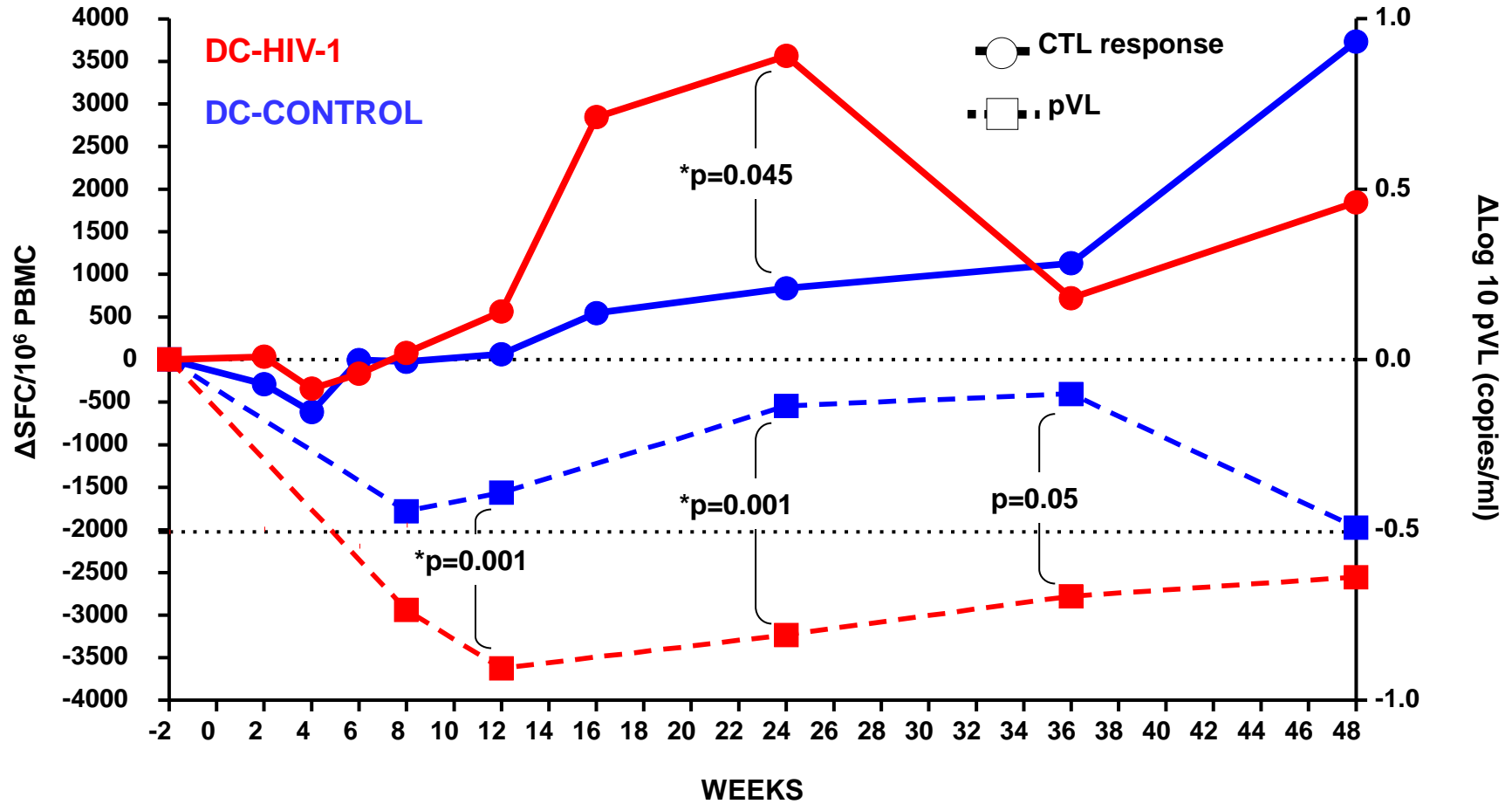
1. <20 copies/ml
2. Nadir >350 C
CD4+ T c/mm³

Figure 2A



DC-HIV-1	24	23	22	21	20	17
DC-CONTROL	11	11	11	10	9	6

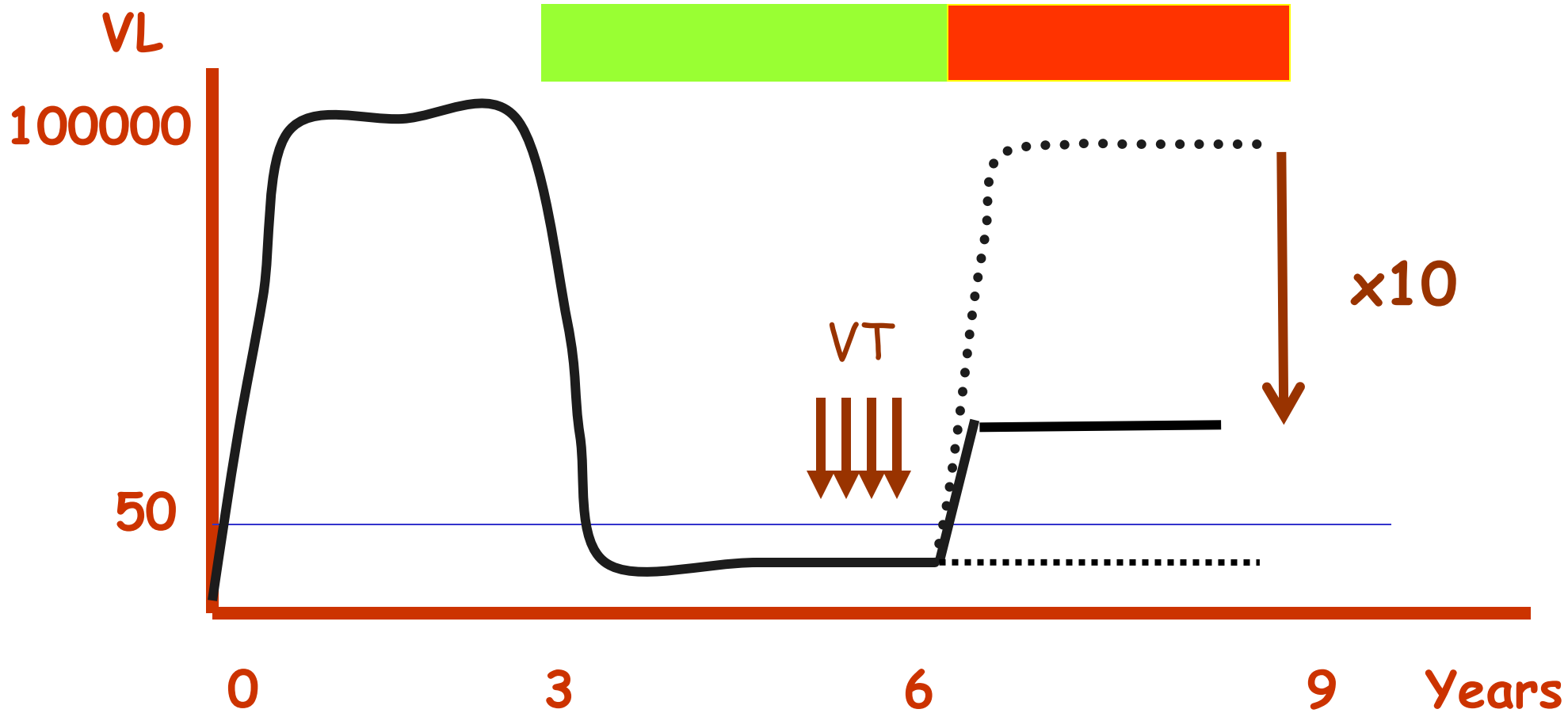
CHANGES IN IFN- γ PRODUCING HIV SPECIFIC T CELLS




CONCLUSIONS

- Therapeutic vaccination was **feasible, safe and well tolerated**.
- A consistent and significant **decrease in VL (1 log)** was observed in vaccine recipients and was correlated with an increase in **CD4 T cell count**.
- **86%** of vaccinated patients had a significant **lower set point VL** when compared to baseline and this was maintained in **52%** of patients at week 48

ART
No ART



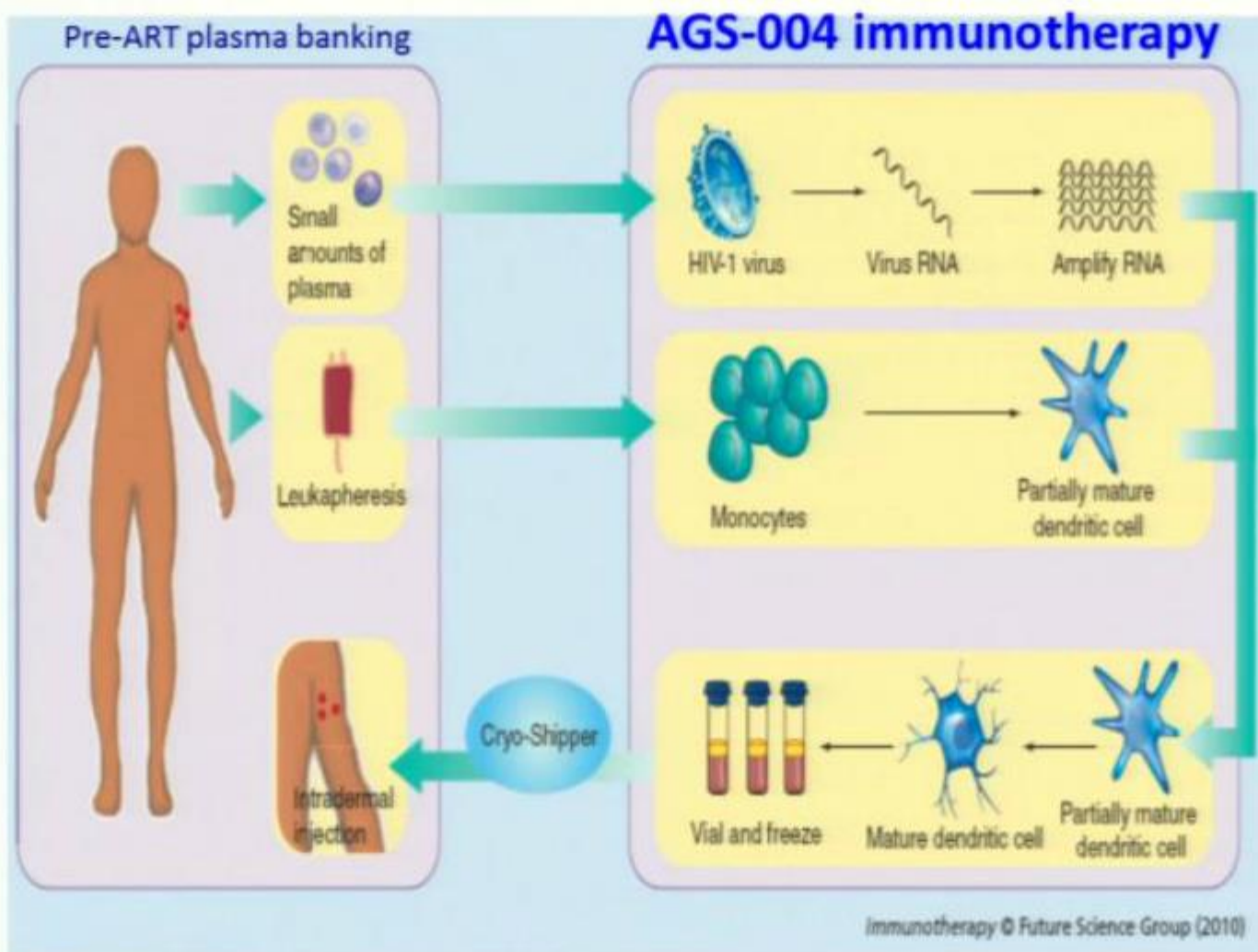


Editor's Summary: Putting the Vaccine Before the cART

Combination antiretroviral therapy has turned HIV infection from a death sentence to a manageable disease. However, current treatment requires “cART for life,” a less than ideal situation for HIV-infected individuals because of drug cost and worries about resistance. New vaccine strategies are attempting to control viral replication after infection, thus allowing discontinuation of cART and a “functional cure.” Garcia *et al.* report a dendritic cell (DC)-based vaccine that elicits an HIV-1-specific immune response and may change the setpoint of viral load.

The authors pulsed the patient's own DCs with heat-inactivated whole HIV and then used these DCs as a therapeutic vaccine. The vaccine was safe and well tolerated. They observed a decrease in viral setpoint after cART interruption in vaccinated patients with a concomitant increase in HIV-1-specific T cell responses. Although not yet a functional cure, these results support future studies optimizing a therapeutic vaccine to maintain HIV-1-infected patients.

Presentation: Image



Immunotherapy © Future Science Group (2010)

Routy, Nicolette Immunotherapy. 2010

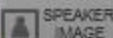
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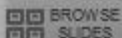
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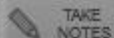
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SPEAKER
IMAGE



BROWSE
SLIDES



TAKE
NOTES

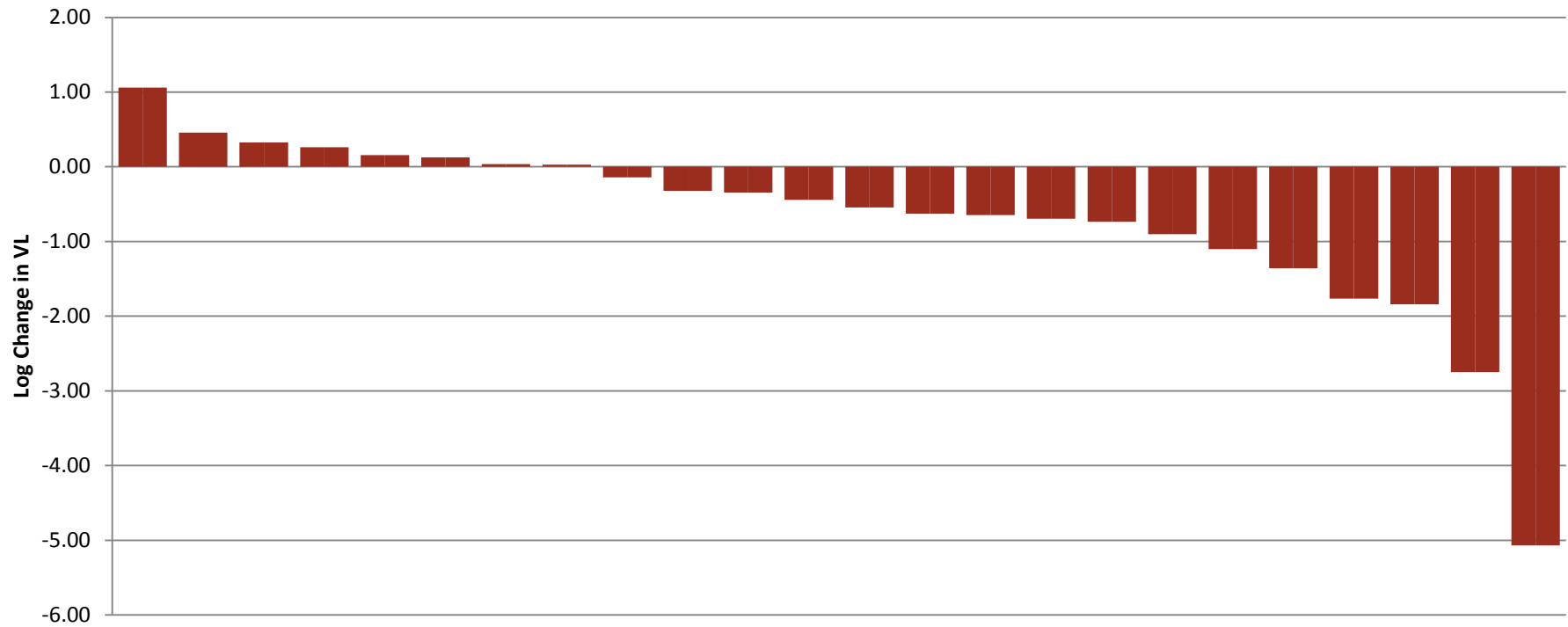


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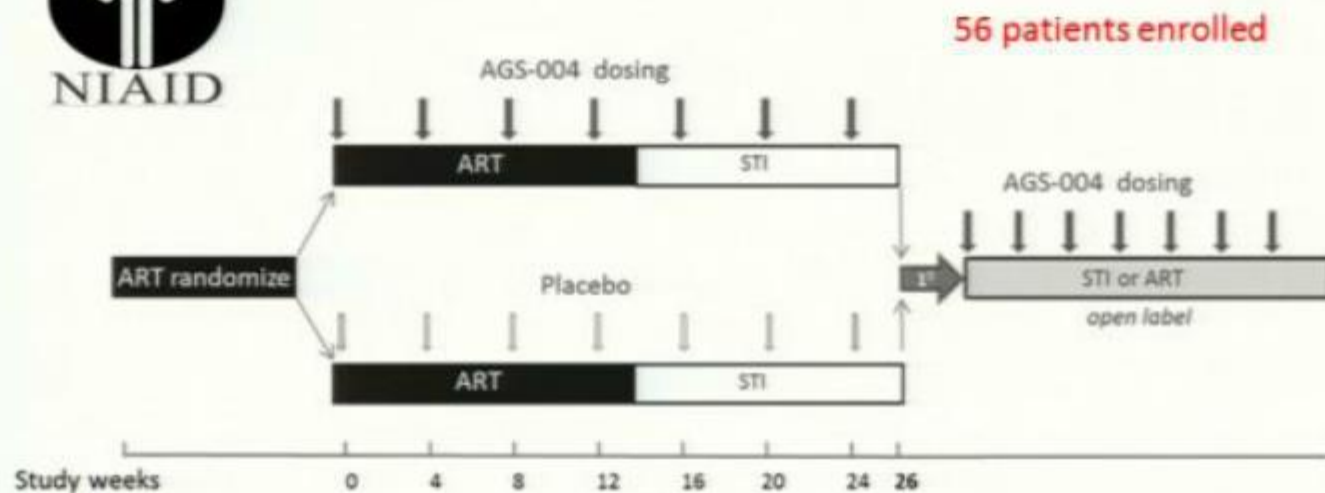
SLIDE IMAGE

Pre-ART vs. Week 12 of STI Log Change in Viral Load



Presentation: Image

Phase 2b Study Schematic: Chronic Cohort*: USA and Canada



Involving participants from private
community medical clinics

Global PI: J M. Jacobson

Phase 2b data expected mid 2014

*All patients were chronically infected for more than 6 months prior to initiating ART

iHIV^ARNA



Vrije Universiteit Brussel

The iHIV^ARNA consortium

Academic partners



Vrije Universiteit Brussel



Non-academic partners

Regulatory
affairs



Administrative
coordinator

SYNAPSE

SME (mRNA production)

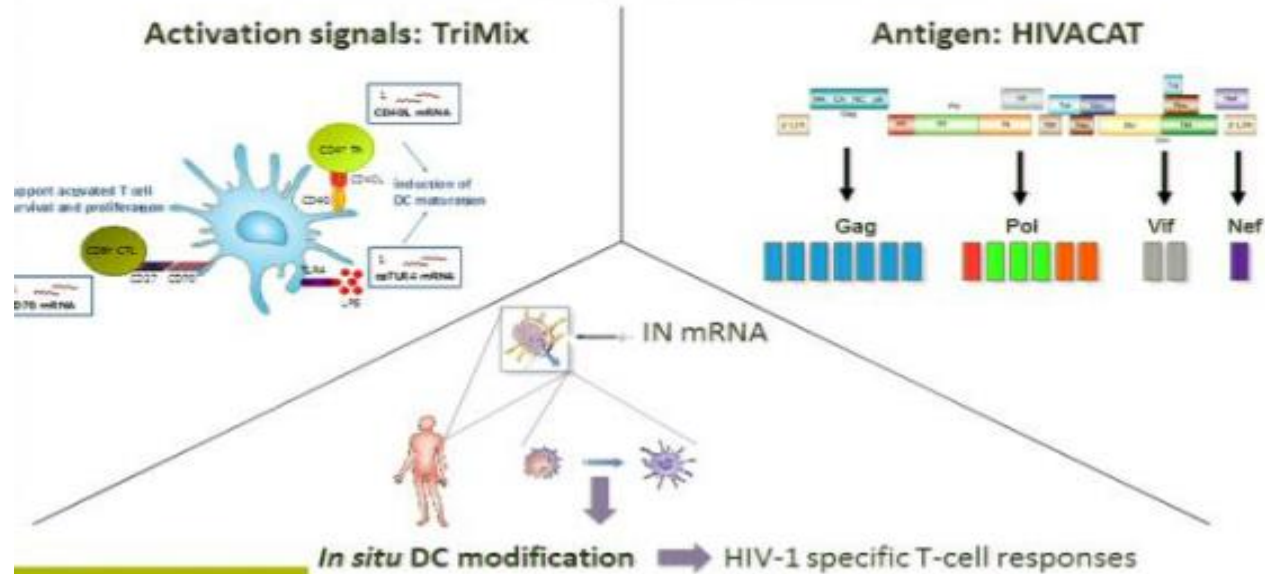




Vrije Universiteit Brussel

Concept of iHIVARNA

Intranodal vaccination of HIV-1 infected patients with mRNA encoding **TriMix** and **HIVACAT**



THERAPEUTIC VACCINES (TV) & OTHER IMMUNE INTERVENTIONS (IBT) IN HIV INFECTION: 2013

1. Where are we with ART
2. Untreated patients. TV/IBT to control productive HIV replication or restore CD4's
3. TV/IBT in virologically suppressed patients with chronic HIV infection
4. TV/IBT to reduce the size of the reservoirs and/or to control already depleted reservoirs
5. Final considerations

THERAPEUTIC VACCINES (TV) & OTHER IMMUNE INTERVENTIONS (IBT) IN HIV INFECTION: 2013

2. TV/IBT to reduce the size of the reservoirs and/or to control already depleted reservoirs

Biological model (functional cure)
Visconti patients

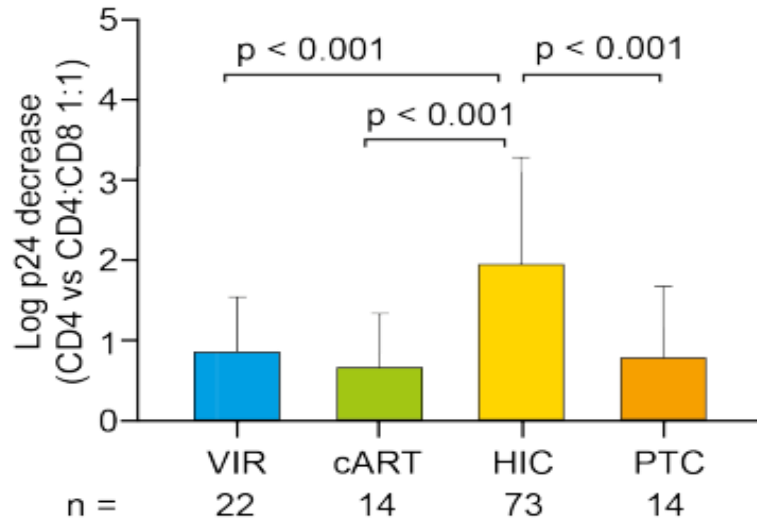
Reservoirs can be reduced (purged ?):

ART alone early after PHI

ART + TV ?

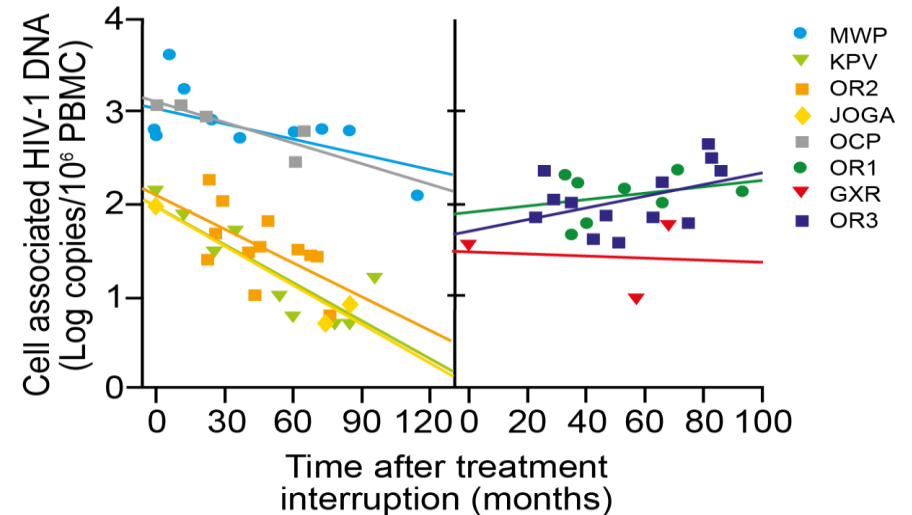
ART+ mobilizing agent + TV ?

The VISCONTI cohort: the possibility of post-treatment control



Capacity of CD8+ T cells to suppress HIV infection of CD4+ T cells

Determined by log-fold decrease in the level of secreted p24 (CD4 vs CD4:CD8 1:1 cell cultures).



Evolution of cell-associated HIV DNA after treatment interruption in PBMCs from 8 PTCs.

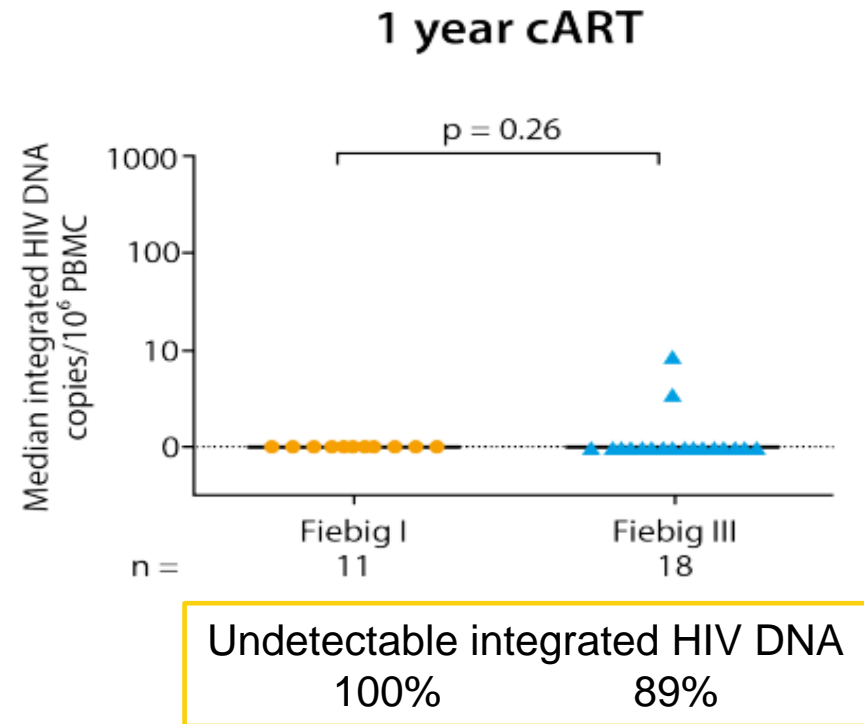
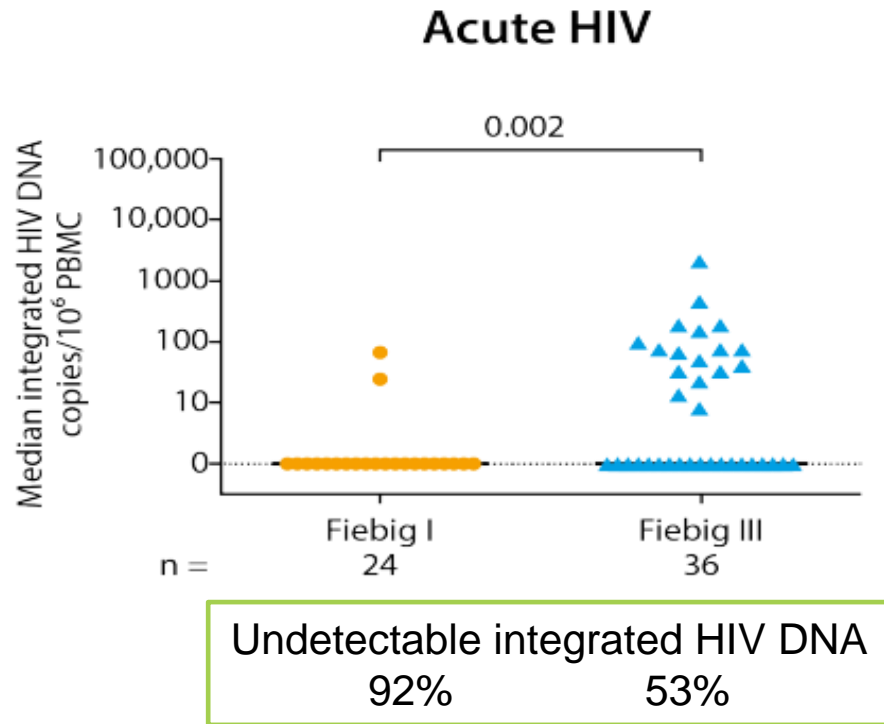
Left: five PTCs experienced a decline in their cell-associated HIV DNA levels

Right: two PTCs maintained stable levels and a positive slope was calculated for OR3

VIRs, viraemic patients; ARTs, treated patients; HICs, HIV controllers; PTCs, post-treatment controllers

Saez-Cirión A, et al. PLoS Pathog 2013;9:e1003211.

Very early treatment in adults: restricted reservoir formation?

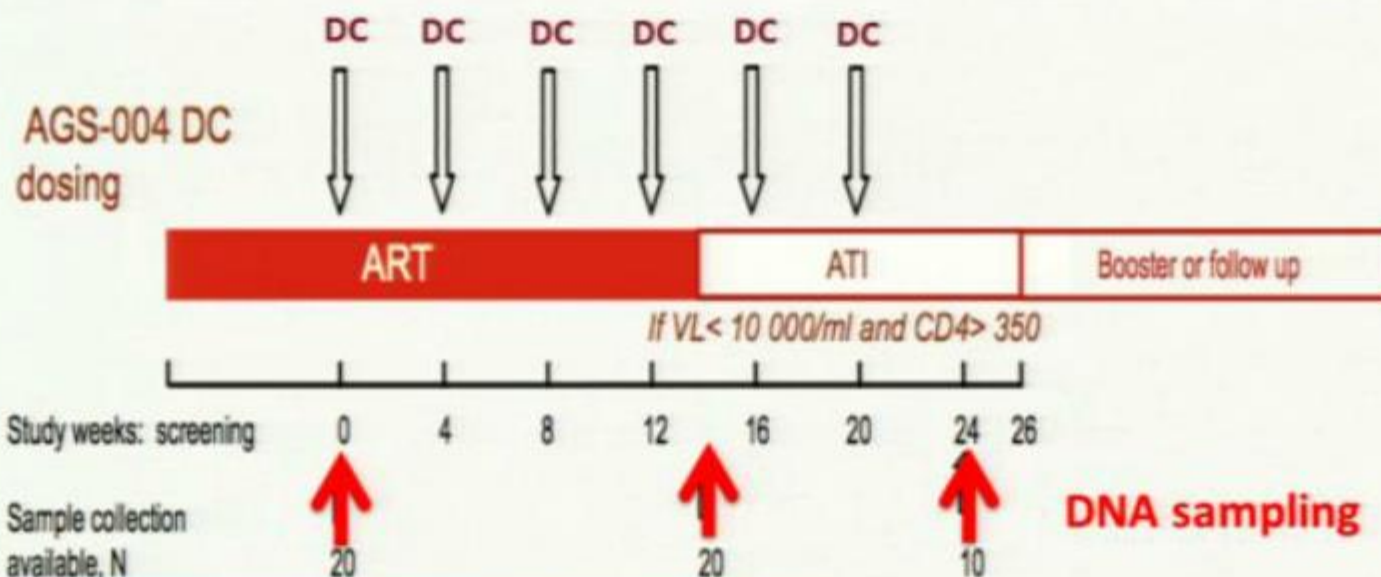


Ananworanich et al. CROI 2013. Abstract 47. Available online at : <http://en.trcarc.org/?p=1436> [Accessed August 2013]

Ananworanich, ANRS satellite symposium, IAS 2013. Available online at: <http://pag.ias2013.org/session.aspx?s=42> [Accessed August 2013]

Presentation: Image

DC vaccine and HIV reservoir



	Total Subjects (N=29) Mean (SD)
Age	39.27 (8.60)
Pre-ART CD4 ⁺ T cell nadir (cells/mm ³)	306.5 (137.1)
Log Pre-ART HIV-1 RNA (copies/mL)	4.91 (0.59)
Baseline CD4 ⁺ T cell (cells/mm ³)	637.3 (203.9)
Duration of ART (years)	3.14 (2.11)

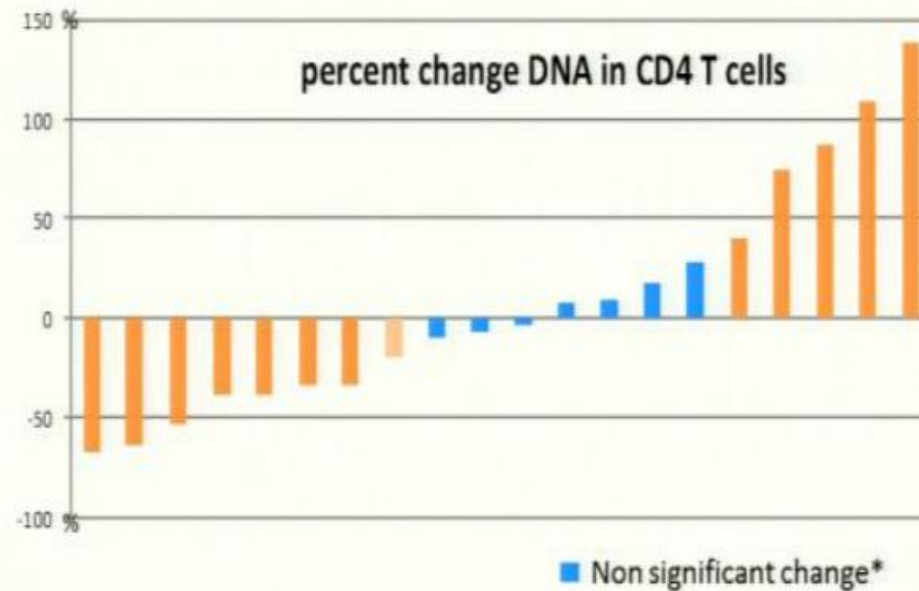
8 clinical sites in Canada:
Including 3 private community
medical centres

Tcherepanova et al. PO4.35 LB
AIDS vaccine 2013

Presentation: Image

shrink →

Pro viral DNA change (%) at week 14 vs. week 0 after 4 doses of AGS-004 on ART



*Significant change when > 1.3 fold change (28%) based on inter assay variability

Tcherepanova et al. PO4.35 LB AIDS vaccine 2013

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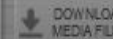
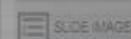
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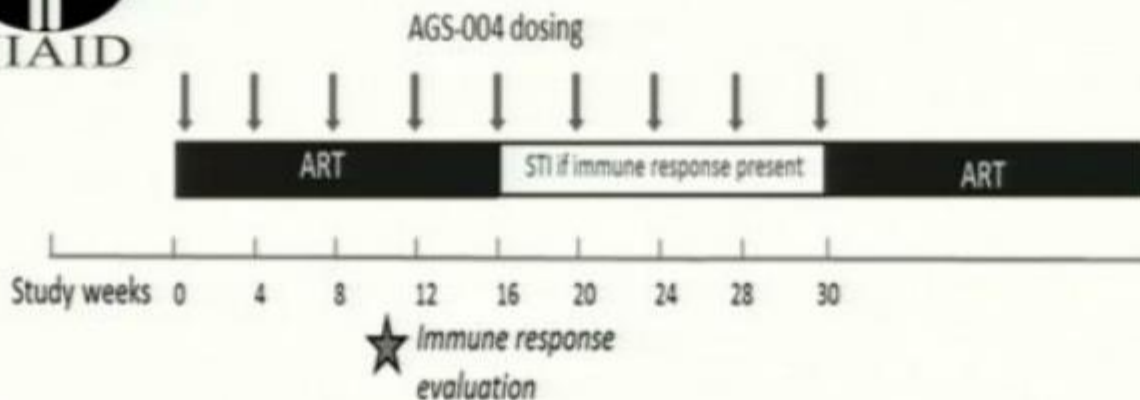


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AGS-004-003 Acute infection study Uncontrolled, Open Label



*AHI=acute HIV infection
initiated ART within 45 days of primary infection)

PI: DM Margolis
6 patients recruited

3
0

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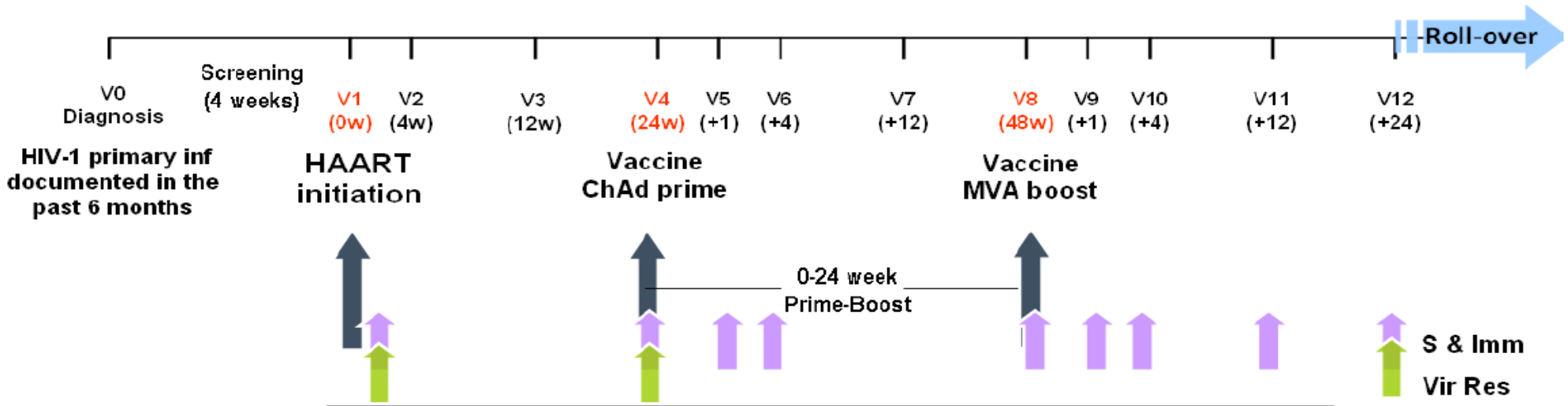
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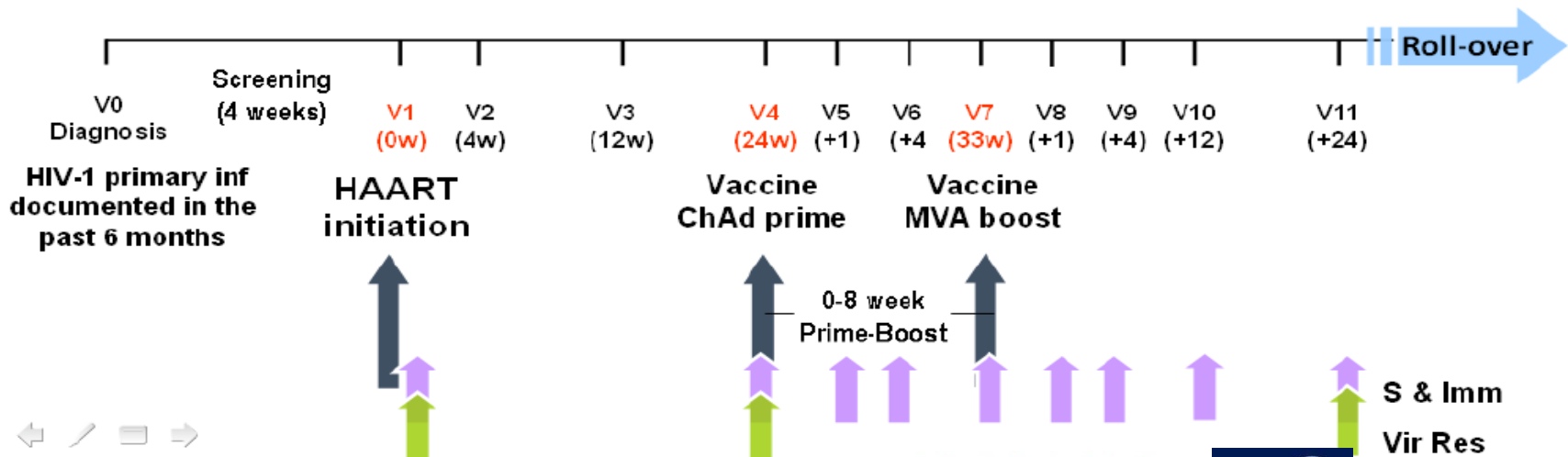
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SLIDE IMAGE

ARM A: TDF/FTC + RAL 0-24 week vaccination (individuals 0 to 12)

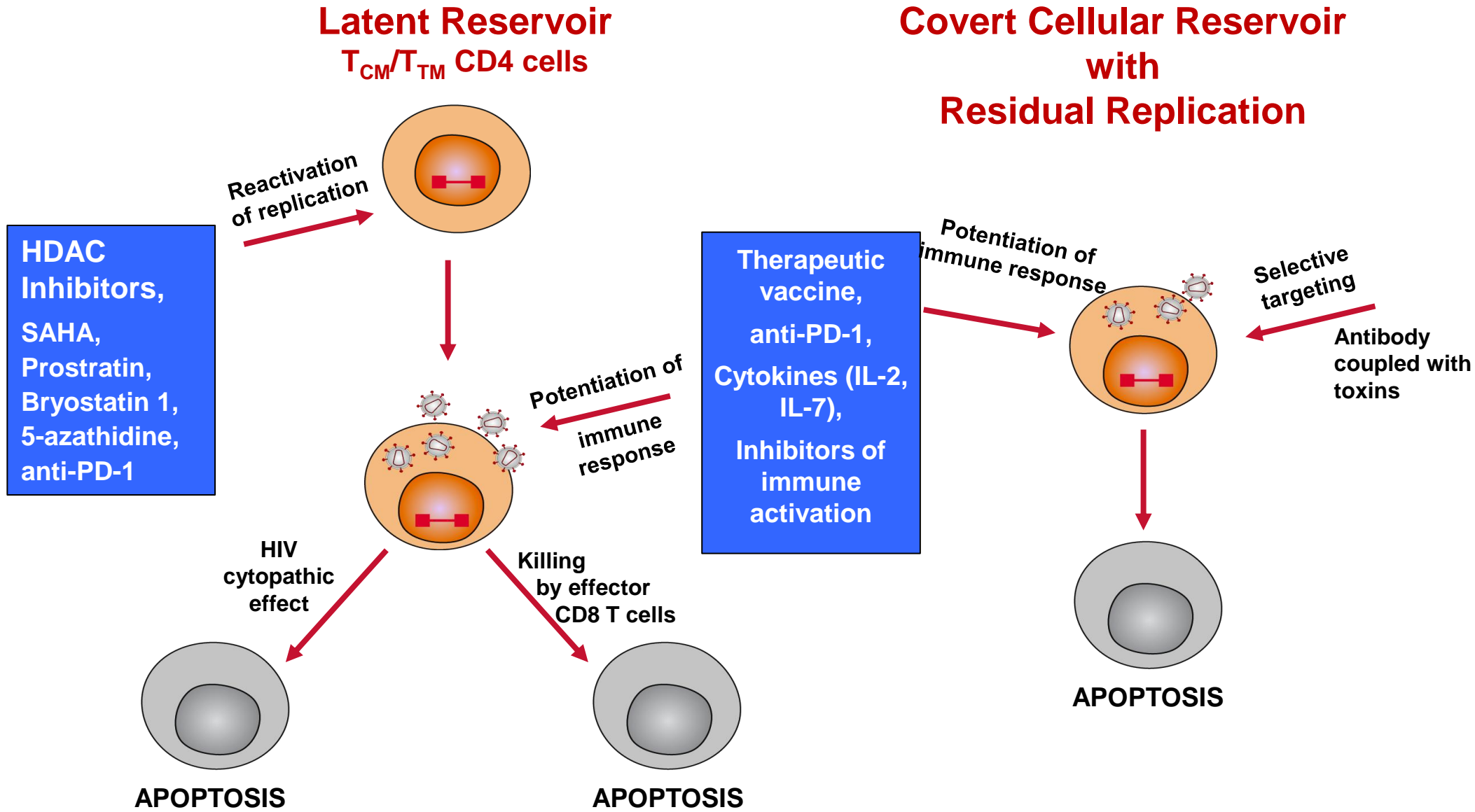


ARM B: TDF/FTC + RAL 0-8 week vaccination (individuals 13 to 24)



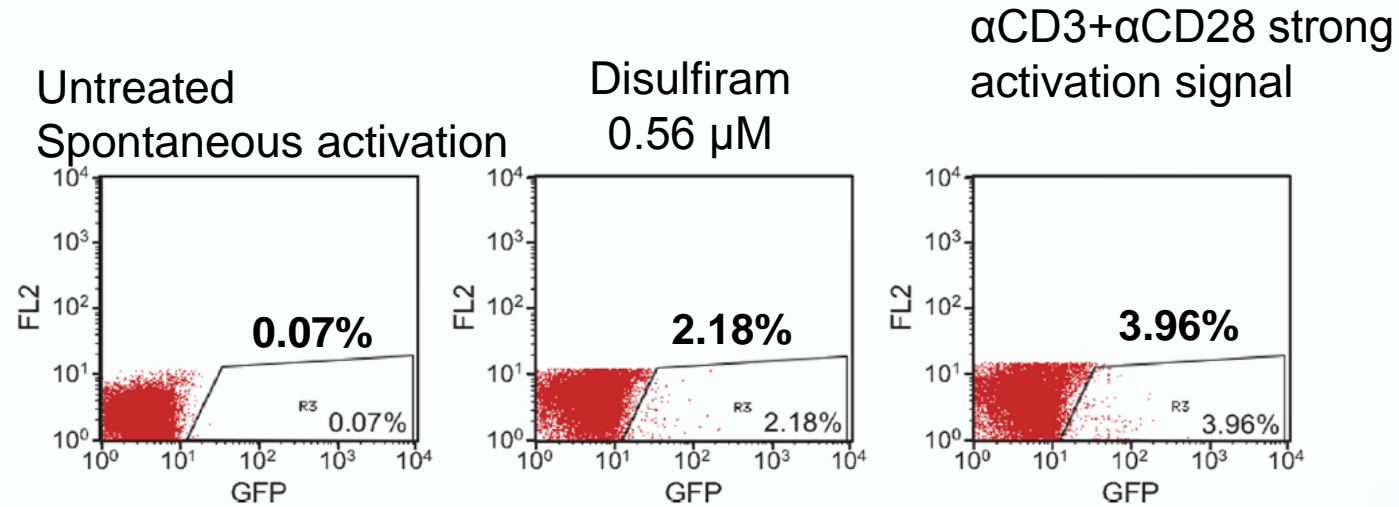
Combination Strategies To Purge The HIV Reservoir

Yves Levy



G. Pantaleo, IAS HIV cure, 2012

Disulfiram Reactivates Latent HIV-1 without Inducing T Cell Activation



❖ But it is not yet clear that disulfiram can reactivate latent HIV-1 in vivo

Stimulation ^a	Treatment Time Course (days)						
	0	2	3	4	5	6	7
Media Alone	67	UD	UD	UD	41	77	134
Disulfiram 0.4 μM	UD ^c	366	76	88	UD	263	204
anti-CD3 + anti-CD28 ^b	49	22,169	65,697	40,489	12,969	7,510	3,383

Dynamics of Viral Load (VL) Rebound After cART Interruption in Chronic HIV Infected Patients Receiving MVA-B plus Disulfiram.

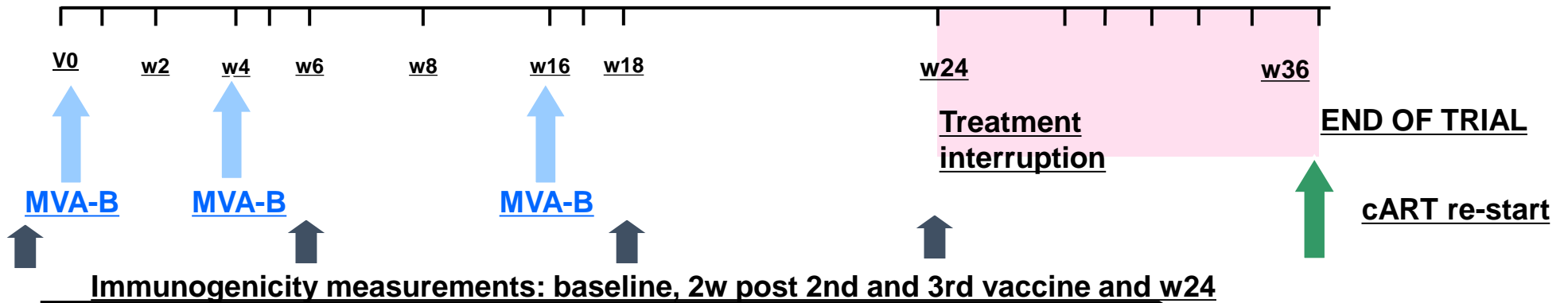
Beatriz Mothe¹, Sonsoles Sánchez², Saray Corral³, Nuria Climent², Alberto C. Guardo², Lorna Leal², Berta Torres², José Luis Jiménez³, Judit Pich², Joan Albert Arnaiz², Agathe León², María Angeles Muñoz-Fernández³, Jose M Gatell², Bonaventura Clotet¹, Mariano Esteban⁴, Montserrat Plana², Juan Carlos López Bernaldo de Quirós³, Christian Brander¹, Felipe García² for the RISVAC-03 Study.

1. Irsicaixa-HIVACAT, Hospital Germans Trias i Pujol, Badalona 2. Hospital Clinic-HIVACAT, IDIBAPS, University of Barcelona 3. Hospital Gregorio Marañón, Madrid 4.- Centro Nacional de Biotecnología, Madrid. Spain

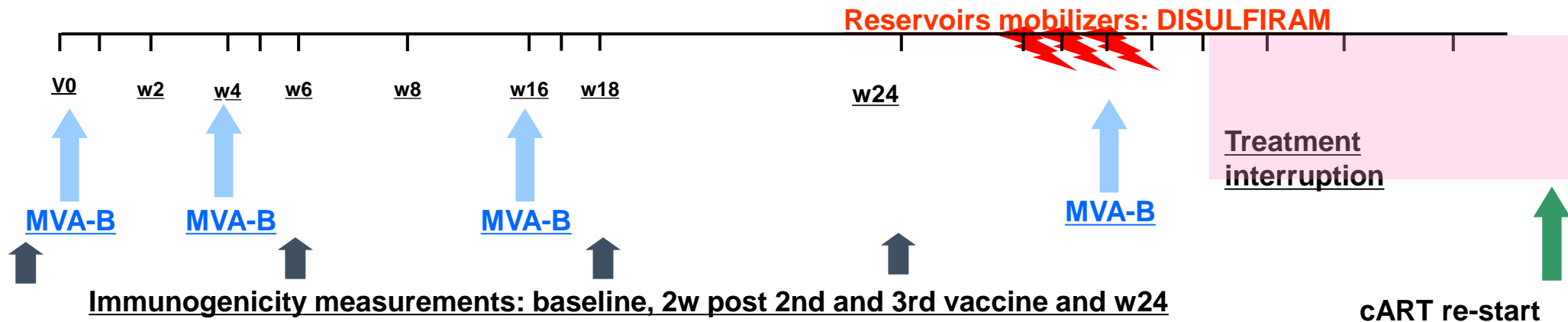


Clinical Trial Design

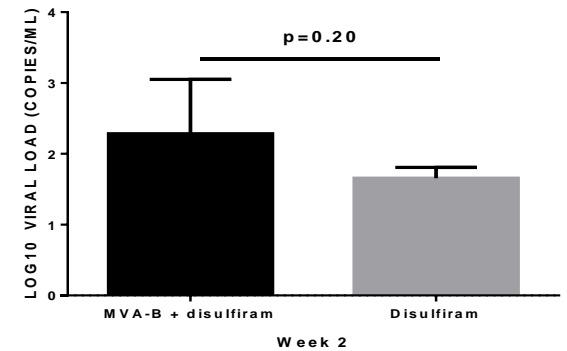
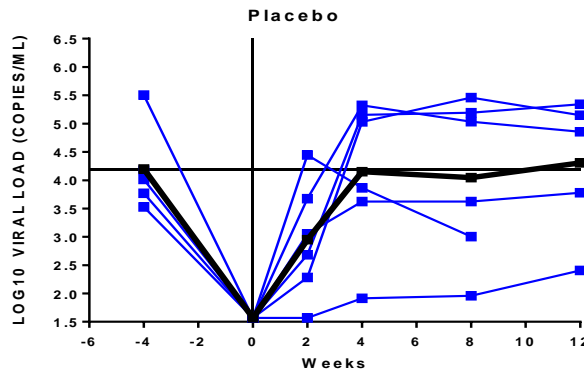
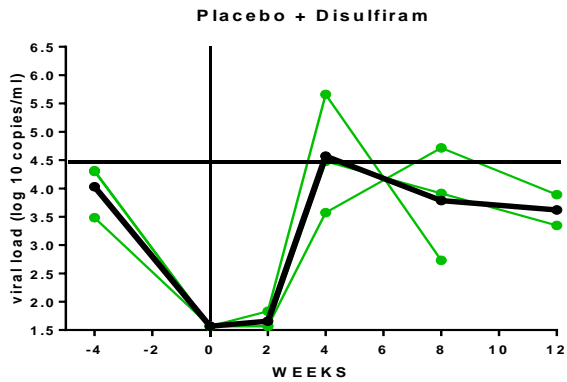
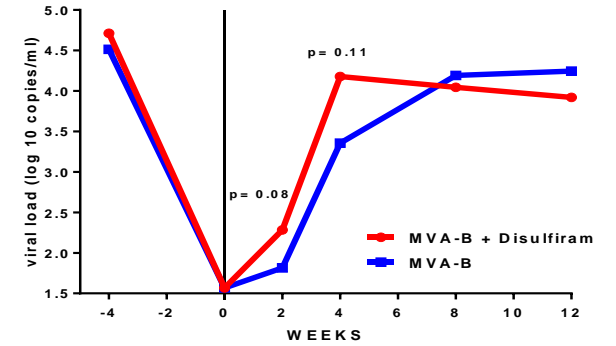
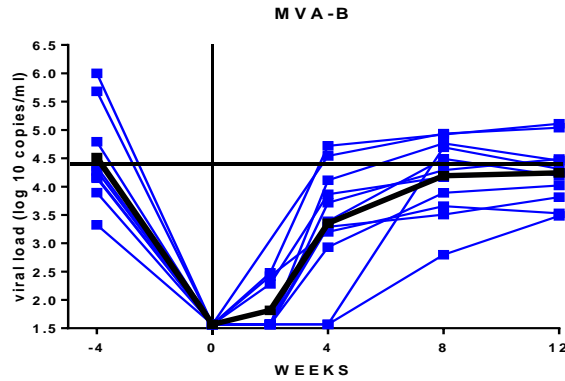
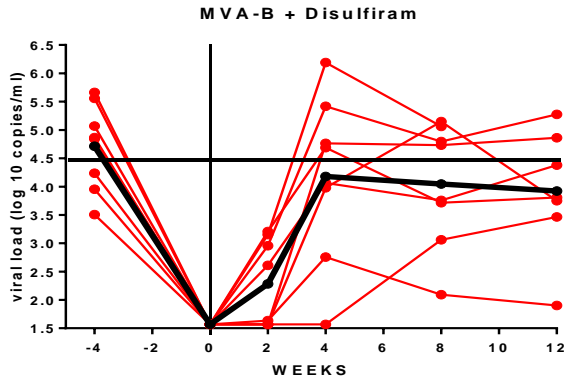
ARM A: VACCINE/PLACEBO ARM (n=18, randomized 2:1)



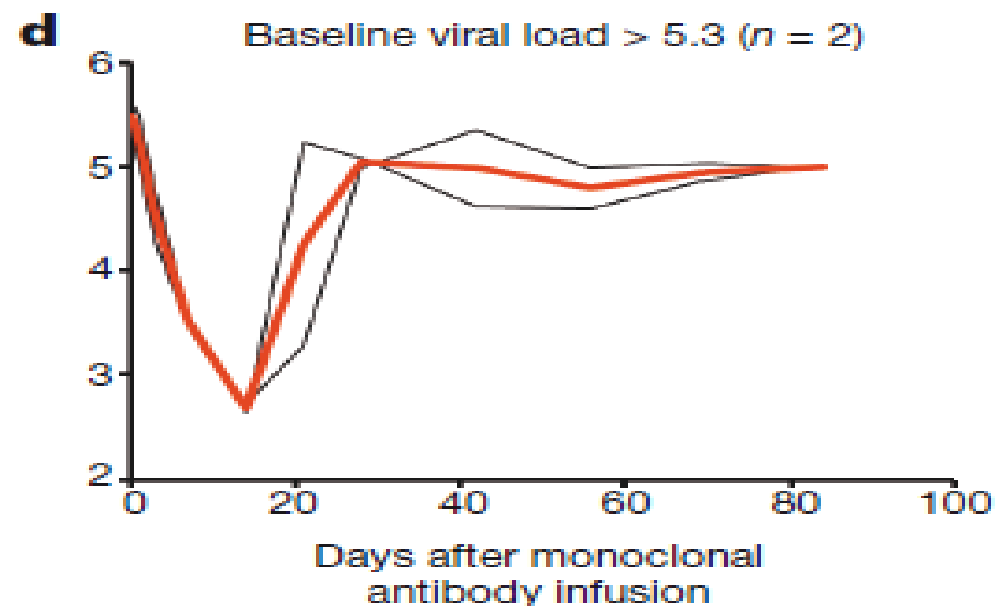
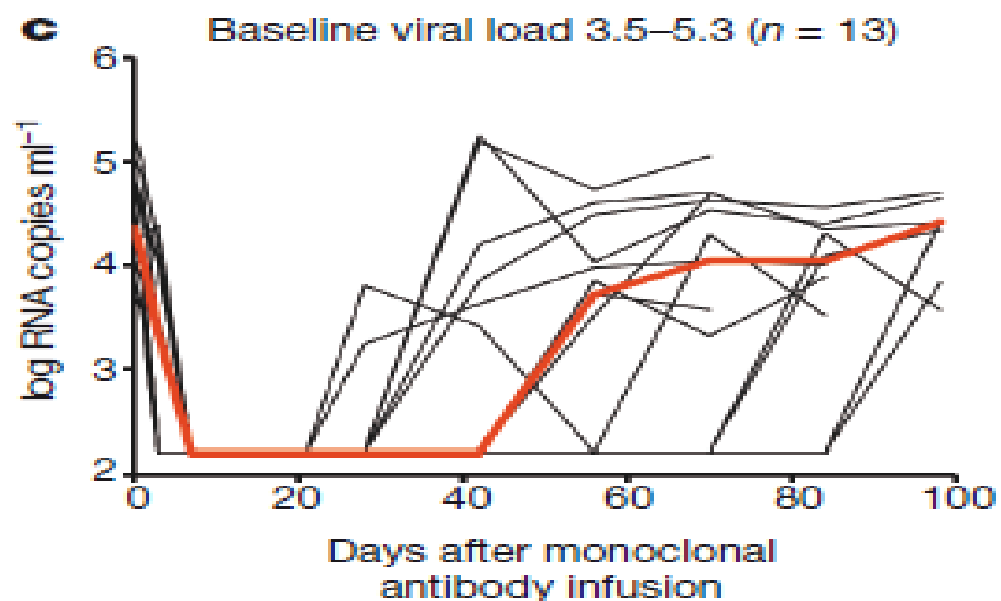
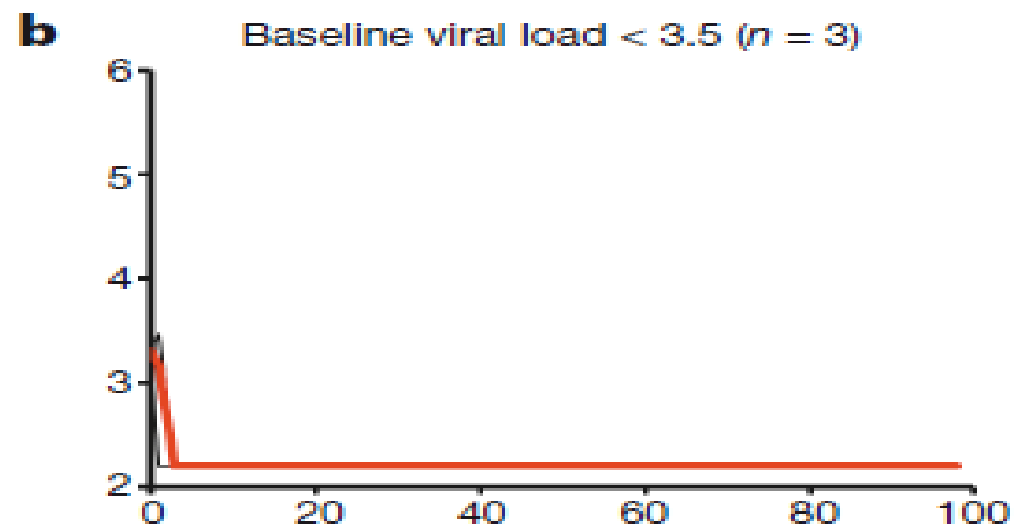
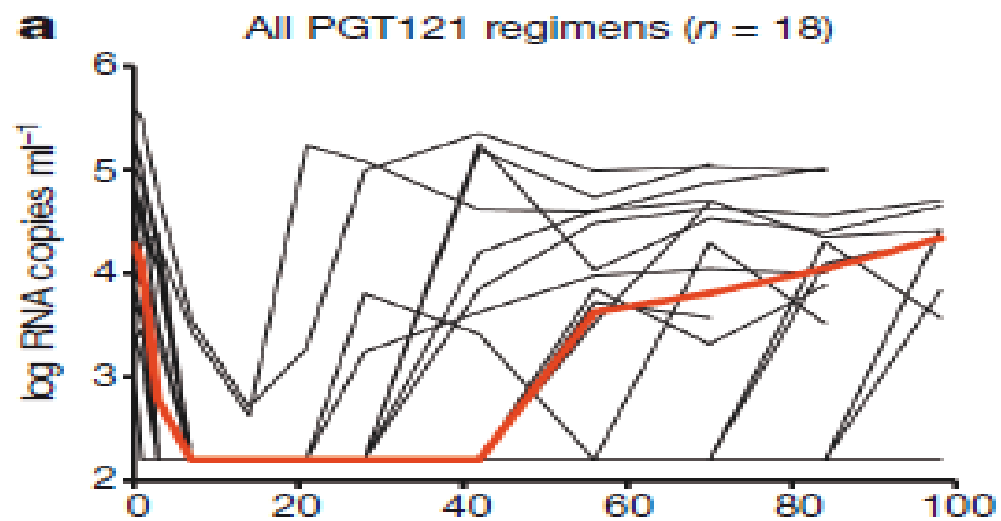
ARM B: VACCINE/PLACEBO + MOBILIZERS (n=12)



Viral load rebound after vaccination vs vaccination plus disulfiram. Absolute numbers and changes as compared with baseline viral load before any cART



Barouch et al. Nature 2013



THERAPEUTIC VACCINES (TV) & OTHER IMMUNE INTERVENTIONS (IBT) IN HIV INFECTION: 2013

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5. Final considerations

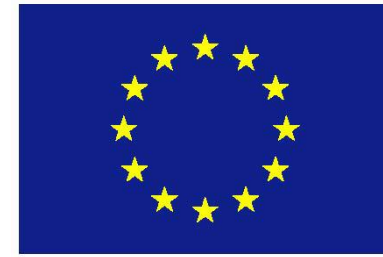
- HIV therapeutic vaccines may play a role to overcome some of the limitations of ART
 - Delay or avoid VL rebound after ART interruption
 - Deplete the reservoirs
 - Purge the reservoirs shock & kill strategies
- Most promising results so far, in humans, have been obtained with dendritic cells based therapeutic vaccines



 <p>Program Directors</p>	 <p>Scientific Dr</p>	 <p>INSTITUT PASTEUR</p>		 <p>HARVARD UNIVERSITY</p>	
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RETIC-RIS | Red Española de
Investigación en SIDA (RIS)



HIVACAT

Projecte de Recerca de la Vacuna de la Sida

 Generalitat de Catalunya
Departament de Salut

 Generalitat de Catalunya
Departament d'Innovació,
Universitats i Empresa

ESTEVE

 **Obra Social**
Fundació "la Caixa"

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August Pi i Sunyer