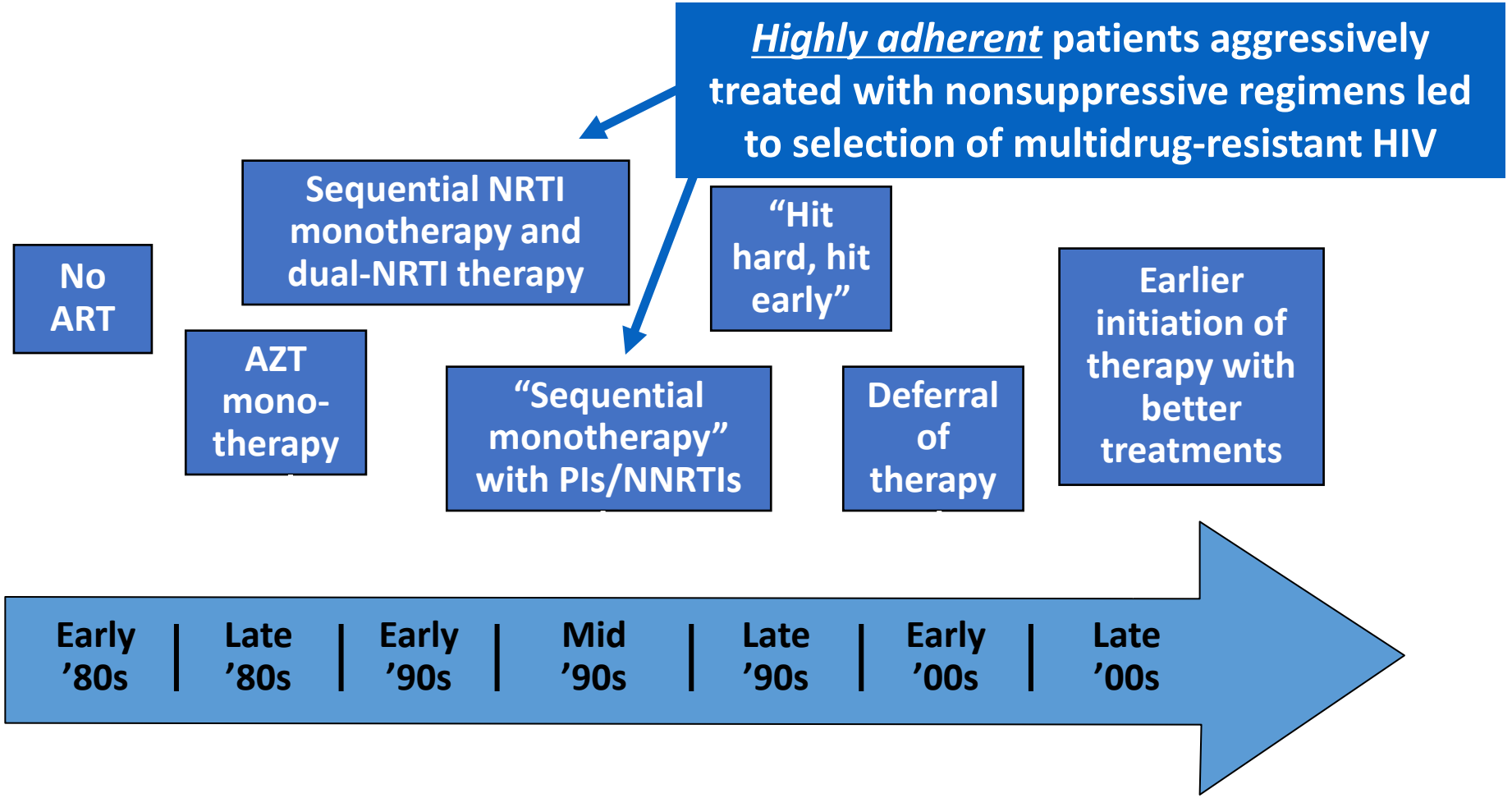
Current and Emerging Treatment Options for People with HIV Multi-Drug Resistance (MDR) & Immunologic Non-Response (INR)

A Brief Activist & Patient Perspective

Nelson Vergel
50+ Strong & Healthy Webinar
May 26, 2023

Who Are the People With Multidrug Resistant HIV (MDR)?

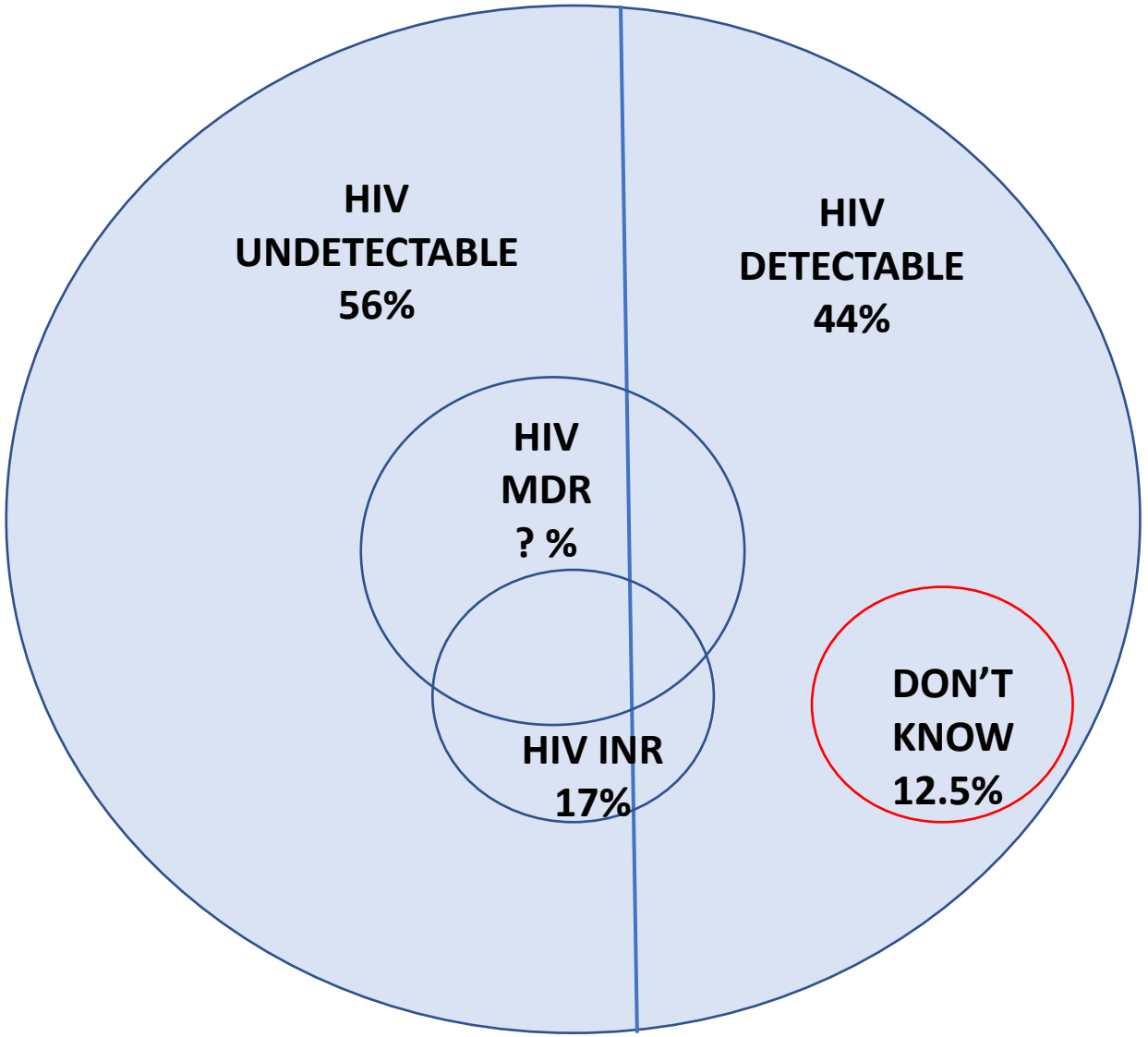


Slide credit: clinicaloptions.com

People Living with HIV in the U.S. in 2019

HIV MDR: People with HIV Multi-Drug Resistance- 15-20+%? 2-4 HV ARV class resistance

HIV INR: People with Immunological Non-Response. CD4< 300 cells/mL. 17%?



- There were approximately **1.2 million** people living with HIV in the US[9]
- There were **34,800 new infections** in the US, which represented an **8% decrease** since 2015[9]
- An estimated **1 in 8** people living with HIV in the US did not know they had it[7]
- About **66%** of people living with HIV received some HIV care, **50%** were retained in care, and **56%** were virally suppressed.

Source: CDC. Diagnoses of HIV infection, by race/ethnicity and selected characteristics, 2019. HIV Surveillance Supplemental Report. 2019;32.

A Clinical Challenge: Heavily Treatment–Experienced People With HIV

- ART with novel mechanisms of action plays a critical role for a small proportion of people with HIV: those with **resistance to multiple drug classes and no/limited treatment options**[1,2]
- 2 primary target populations[3-5]
  1) Older people with HIV treated in early days of ART with less potent regimens that had low resistance barriers
  2) Younger people with congenital HIV infection, now adults

1. Struble. AIDS Lond Engl. 2005;19:747. 2. Richman. AIDS Lond Engl. 2004;18:1393. 3. Weinstock. J Infect Dis. 2004;189:2174. 4. Yazdanpanah. Clin Infect Dis. 2009;49:1441. 5. Tassiopoulos. Clin Infect Dis. 2020;71:133. 6. Emu. NEJM. 2018;379:645. 7. Reeves. J Virol. 2005;79:4991. 8. Kozal. NEJM. 2020;382:1232.

Slide credit: clinicaloptions.com

HIV Medications Currently Used for Multi-Drug Resistance

Entry Inhibitors



RUKOBIA
fostemsavir
One 600 mg tablet twice a day for people with HIV treatment experience. Take with or without food.



SELZENTRY
maraviroc
One 150 mg, 300 mg (shown) or 600 mg tablet twice a day, depending on other meds used, for people with HIV treatment experience. Take with or without food.



TROGARZO
ibalizumab
A long-acting injectable administered intravenously as a single loading dose of 2,000 mg followed by a maintenance dose of 800 mg every two weeks for people with HIV treatment experience.



PIFELTRO
doravirine
One 100 mg tablet once a day. Take with or without food.

Non-Nucleoside Reverse Transcriptase Inhibitor

Sunlenca (lenacapavir) | N/A | Sunlenca is a long-acting injectable HIV medication taken every six months. People who wish to use Sunlenca have two initiation options:
Option 1:
Two Sunlenca tablets on Day 1 and Day 2 plus two subcutaneous injections on Day 1.
Option 2:
Two Sunlenca tablets on Day 1 and Day 2, one tablet on Day 8 and two subcutaneous injections on Day 15.
After initiation, Sunlenca is given by injection every six months.

HIV Capsid Inhibitor

SUNLENCA Is a Long-acting SC Injectable Administered Only Twice a Year



Treatments for HIV+ People with Immunological Non-Response (INR)

Nelson Vergel- Program for Wellness Restoration

Poor CD4+ Cell Recovery

Most people on ART will have a CD4+ cell count increase for at least a decade[1]

- Most rapid increase seen in first 3 months of suppressive ART, followed by steady increases over time

Maintenance of ART-mediated viral suppression results in most individuals eventually recovering to normal range CD4+ cell counts (>500 cells/mm^3)

- **15%-20% of people who start ART at low CD4+ cell counts may plateau at low counts and have poor CD4+ cell recovery** (eg, CD4+ count remains <300 cells/mm^3 despite having a suppressed HIV-1 RNA for 3 yr)[2-4]

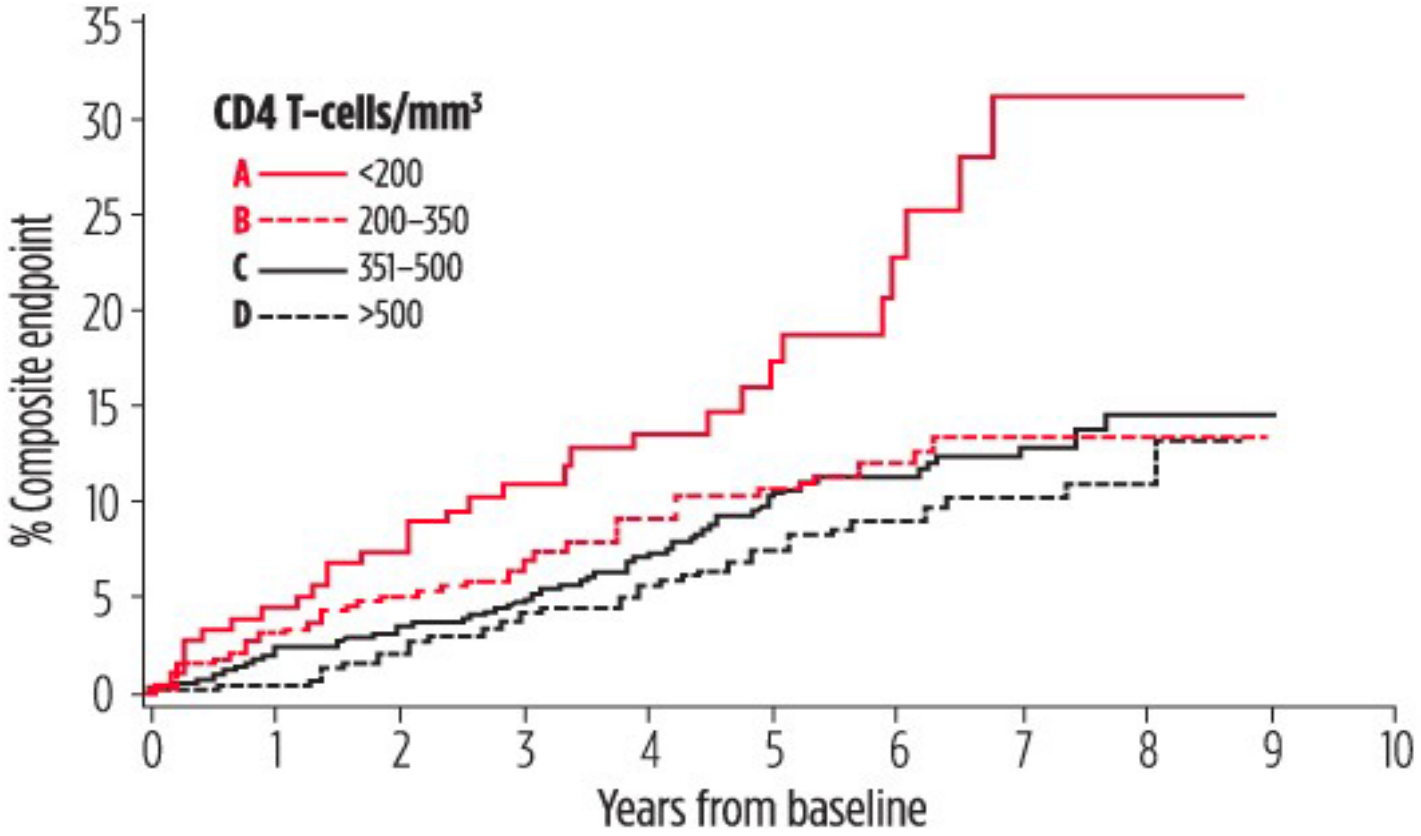
Earliest initiation of ART provides the best opportunity for maximal CD4+ cell recovery

1. linicalinfo.hiv.gov/en/guidelines/adult-and-adolescent-arv/whats-new-guidelines.
2. Kelley. Clin Infect Dis. 2009;48:787. 3. Lok. AIDS. 2010;24:1867. 4. Moore. Clin Infect Dis. 2007;44:441.

Slide credit: clinicaloptions.com

INR: Increased Risk of Illness and Death

- Most studies that have assessed risk of AIDS or non-AIDS events have also reported ~2 fold increased risk associated with suboptimal CD4 T cell recovery



Poor CD4 T-cell recovery despite suppression of viral load associated with an increased risk of death, AIDS, cancer, liver disease, and cardiovascular events (composite endpoint) in the Dutch ATHENA HIV cohort

Source: Long-term complications in patients with poor _immunological recovery despite _virological successful HAART in _Dutch ATHENA cohort

AIDS 26(4):465-474, February 20th, 2012.

HIV Activists Seek to Accelerate Development of Immune Enhancing Therapies for Immunologic Non-Responders

FOR IMMEDIATE RELEASE

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Nelson Vergel
Program for Wellness Restoration



Infusion of CCR5 Gene-Edited T Cells Allows Immune Reconstitution, HIV Reservoir Decay, and Long-Term Virological Control

Joumana Zeidan[1*ϕ], Ashish A. Sharma[1,2*], Gary Lee[3], Angie Raad[4], Remi Fromentin[5,6], Slim Fourati[1,2], Khader Ghneim[1,2], Gabriela P. Sanchez[1,2], Clarisse Benne[1], Glenda Canderan[1], Francesco A. Procopio[7], Robert Balderas[8], Georges Monette[4], Jacob P. Lalezari[9], Jane M. Heffernan[4], Laurent Sabbagh[5], Nicolas Chomont[5,6], Dale Ando[3Π], Steven G. Deeks[10], and Rafick-Pierre Sekaly[1,2ϕ]

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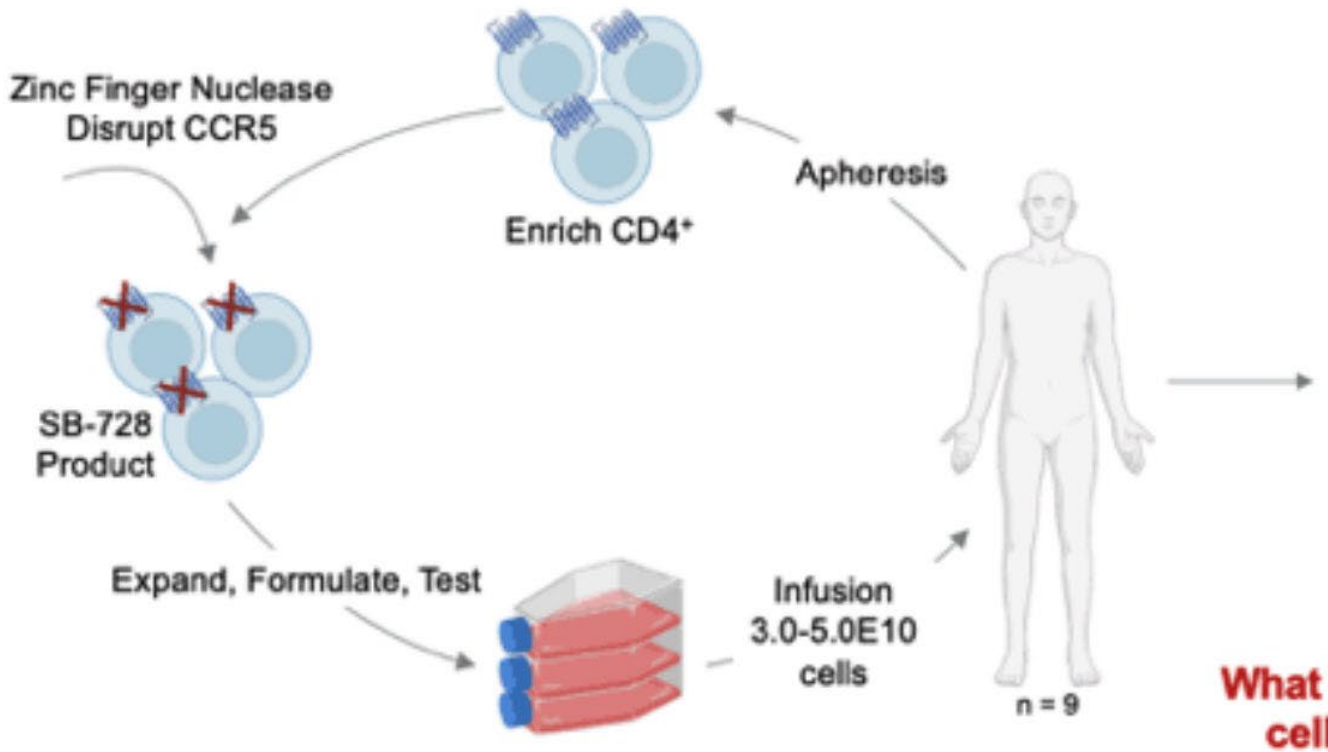
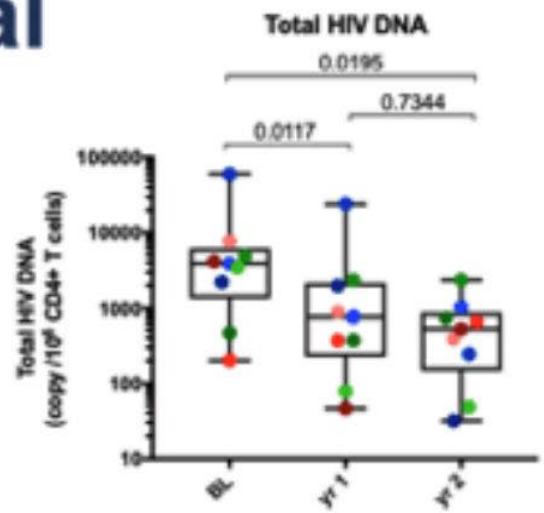
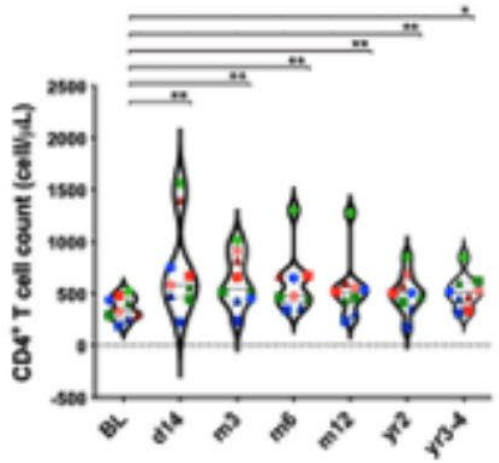
[2]Emory University, Atlanta, Georgia, USA
[3]Sangamo Therapeutics, Richmond, California, USA
[4]Centre for Disease Modelling, Mathematics & Statistics, York University, Toronto, Ontario, Canada
[5]Université de Montréal, Faculty of Medicine, Department of Microbiology, Infectiology, and Immunology, Montreal, Quebec, Canada
[6]Université de Montréal, Centre de Recherche du CHUM, Montreal, Quebec, Canada
[7]Lausanne University Hospital (CHUV), Lausanne, Switzerland
[8]BD Biosciences, San Jose, California, USA
[9]Quest Clinical Research, San Francisco, California, USA
[10]University of California, San Francisco and San Francisco General Hospital, San Francisco, California, USA

SB-728-902 Trial

- Immune non-responder PLWH on ART
  - Aviremic
  - CD4 counts: 200-500/µl
- Received **single-infusion**, remained on ART.
  - Sampled at baseline (BL) and up to 4 years post-infusion.

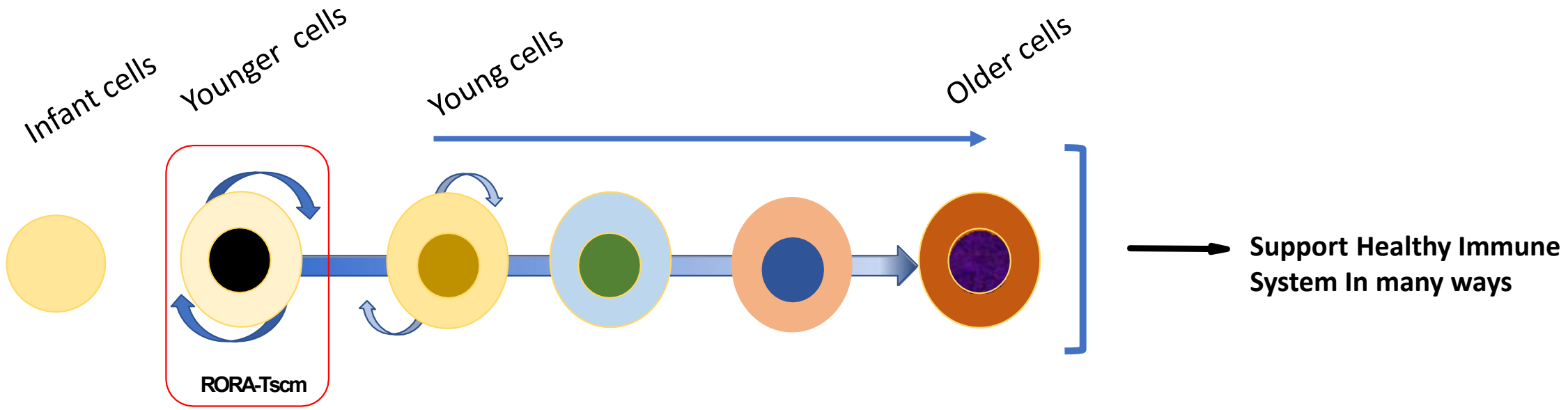






What is the phenotype of CD4 T cells in study participants?

RORA-Tscm Discovery Provides Possible Way To Make A Durable Production Line of T-cells (possibly for 6-7+ years)



Take Home:

- **RORA T-scms are at top of chain that makes new T-cells**
- **T-cells support immune system function**
- **RORA-Tscms can be found in PLWH and can be expanded in the lab to make clinical grade material**
- **RORA Tscms may Persist For 6-7 years or more**
- **RORA Tscms are basis for more durable HIV therapy**

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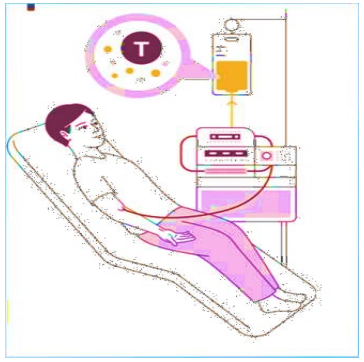
*RORA-cept™: An Experimental Cell Therapy With Potential To Restore T-cell Production Line For Years and Make It Resist HIV



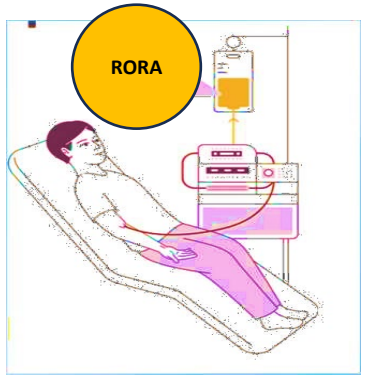
Leukapheresis (HIV-Immune Non-Responder (HIV-INR)

Expand RORA-Tscm cells at point-of-care

Clinical grade RORA-Tscm

Remove HIV Co-receptor

Clinical grade RORA-cept™



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Study Sponsor: RORA Biologics

Summary

- People living with MDR-HIV in the U.S. are now able to access some new HIV medications with different mode of action.
- Even with effective ARVs and patient assistance programs, 44% of HIV+ people have detectable viral load in the U.S.
- Some of those people (like myself) also have immunologic non-response despite having sustained undetectable HIV viral load.
- INR patients have higher risks of death and comorbidities.
- Currently, there are no FDA-approved treatment options to improve immunologic response in INRs.
- Activism is badly needed to encourage industry to develop options for INRs.
- Contact NelsonVergel@gmail.com if you want to get involved.