Immunological Non Responders: Quale Terapia?

Camilla Tincati MD, PhD

Clinica di Malattie Infettive

Dipartimento di Scienze della Salute

ASST Santi Paolo e Carlo-Presidio San Paolo

Università degli Studi di Milano

Background

- **Definition of INR**

-confine CD4+ T cell count

-increased CD4+ T- cell counts from baseline

-confine percentage of CD4+ T cell increase over baseline

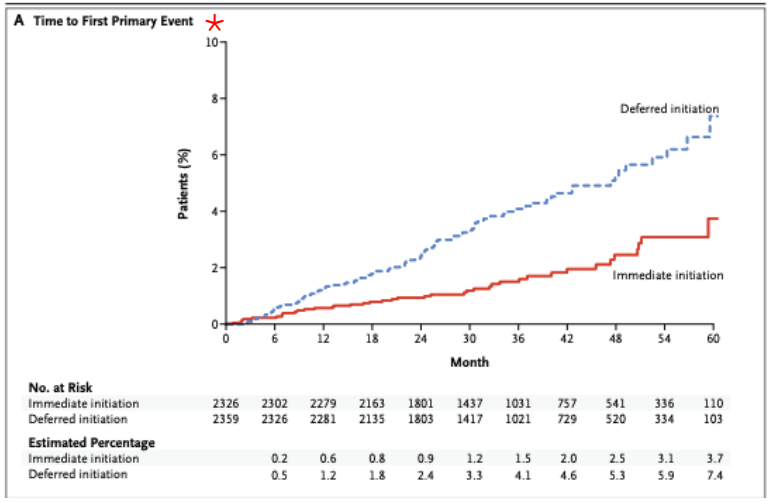
- **Clinical risk of INR**

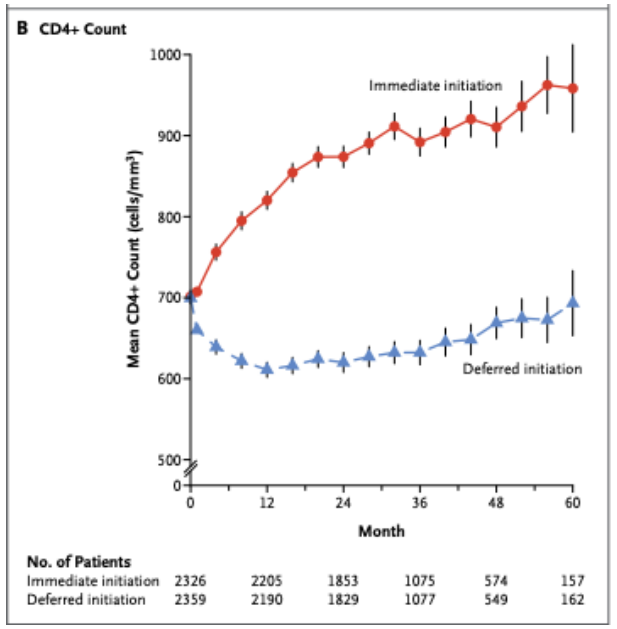
TABLE 1 Definitions of INR from the literature and guideline.

Definition of INRs	References
Increase in the CD4⁺ T cell count <200 cells/μl from baseline at 2 years after cART initiation, with an undetectable plasma VL	García et al. (2019)
Total CD4⁺ T cell counts <200 cells/μl at 2 years after cART initiation, with an undetectable plasma VL	Xie et al. (2021)
Total CD4⁺ T cell count <350 cells/μl 2 years after cART initiation, with an undetectable plasma VL	Dai et al. (2021), Rousseau et al. (2021), Shive et al. (2021)
Total CD4⁺ T cell count <350 cells/μl 2 years after cART initiation, with plasma HIV-1 RNA < 50 copies/ml	Geng et al. (2021), Malazogu et al. (2021), Vlasova et al. (2021)
Total CD4⁺ T cell count <350 cells/μl 2 years after cART initiation, with plasma HIV-1 RNA < 50 copies/ml at least 12 months	Bandera et al. (2018)
Total CD4⁺ T cell counts <350 cells/μl 8 years after cART initiation, with an undetectable plasma VL	Luo et al. (2022)
Increase in the CD4⁺ T cell count <20% from baseline at 1 year after cART initiation, with an undetectable plasma VL	Lv et al. (2021)
CD4/CD8 ratio < 1 at 24 weeks after cART initiation, with plasma HIV-1 RNA < 50 copies/ml	Russo et al. (2022)

VL, viral load.

Zhang et al. Front Microbiology 2023

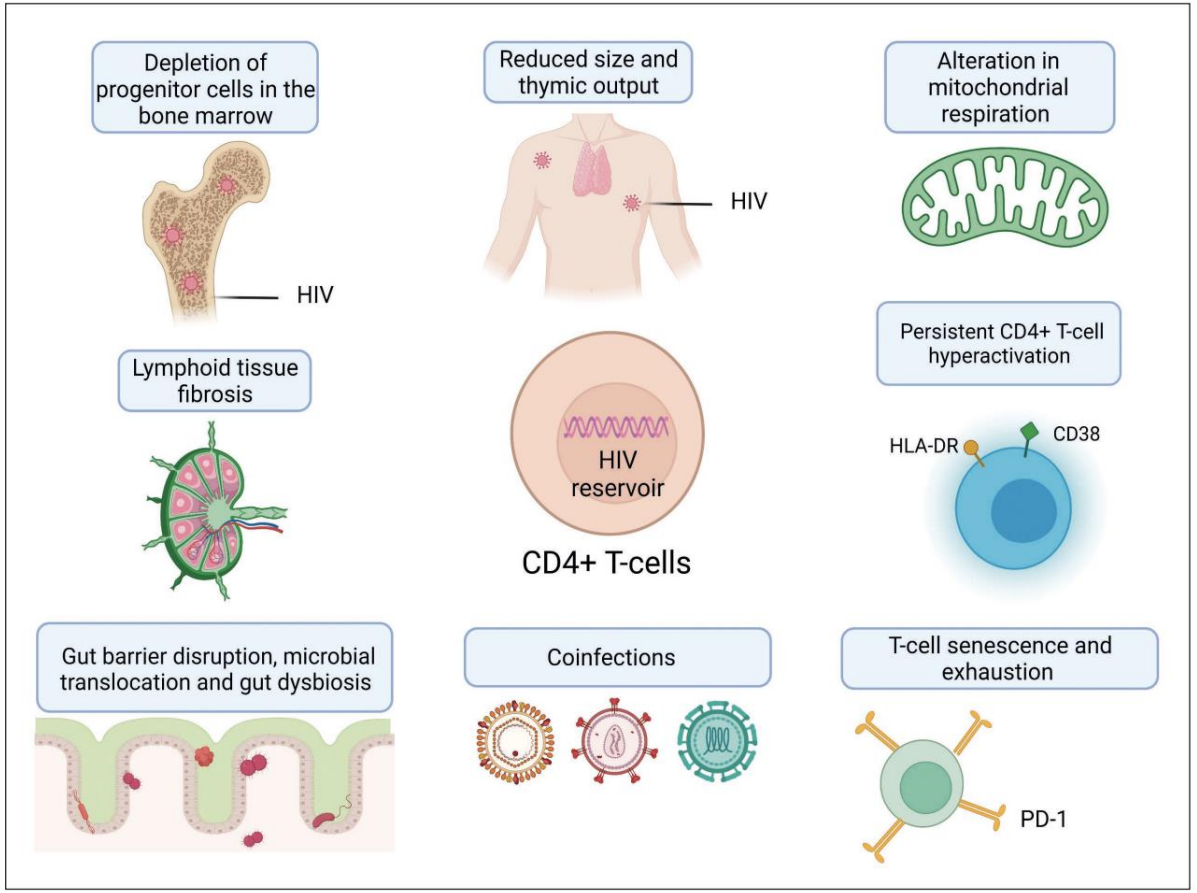




* Primary Event:
a serious AIDS-related or serious non-AIDS-related event, including death

INSIGHT START Study GroupNEJM, 2015

Pathogenesis of INR

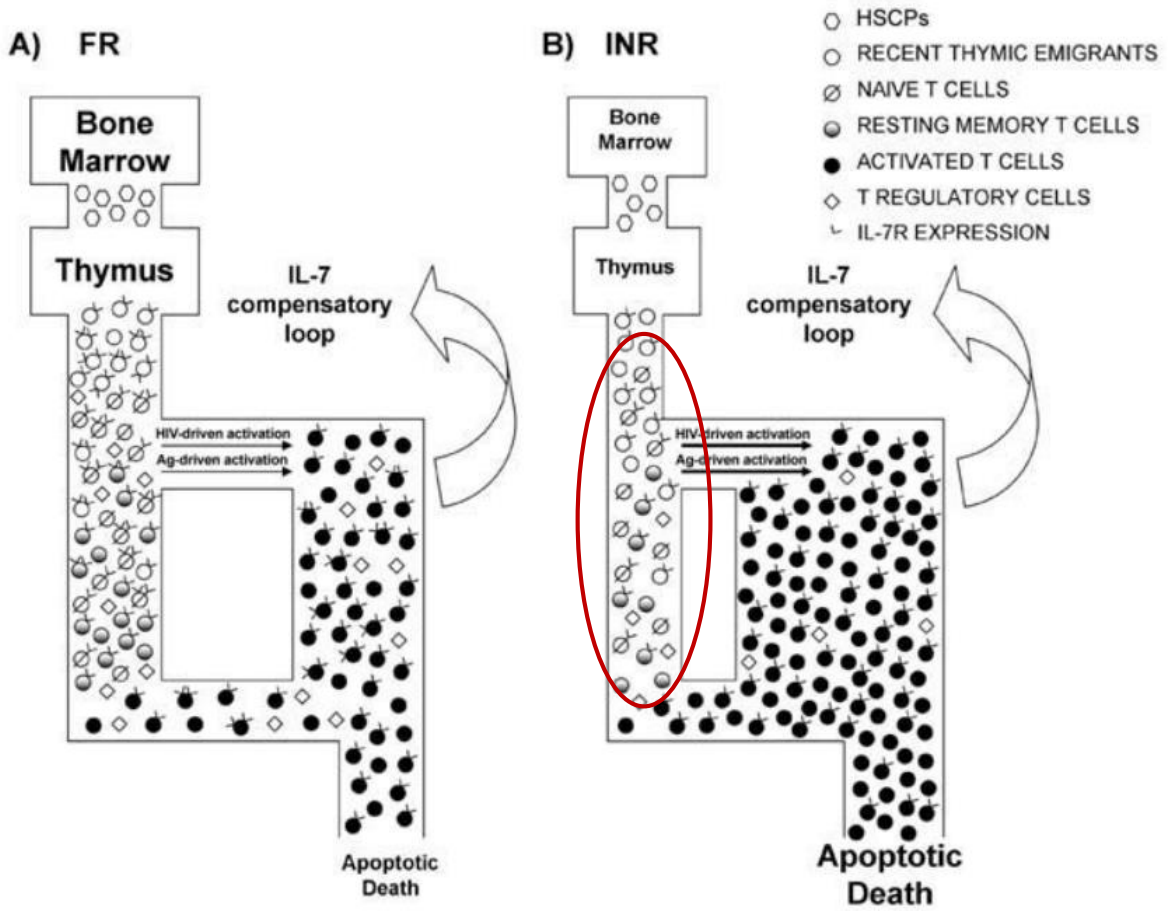


Bono, New Microbiologica, 2022

The Absence of CD4$^+$ T Cell Count Recovery Despite Receipt of Virologically Suppressive Highly Active Antiretroviral Therapy: Clinical Risk, Immunological Gaps, and Therapeutic Options

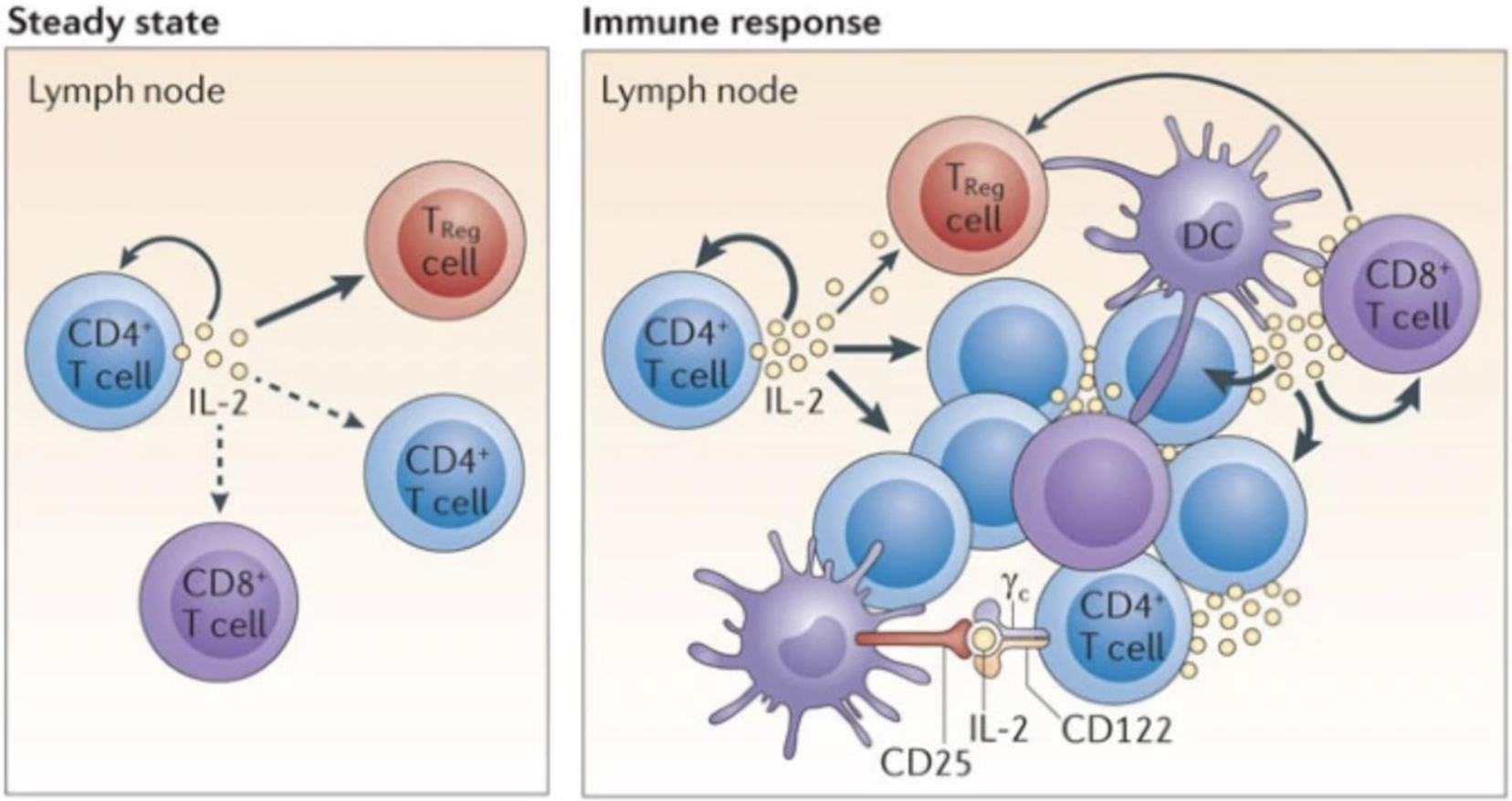
Lidia Gazzola, Camilla Tincati, Giusi Maria Bellistrì, Antonella d'Arminio Monforte, and Giulia Marchetti

Department of Medicine, Surgery, and Dentistry, Clinic of Infectious Diseases, "San Paolo" Hospital, University of Milan, Milan, Italy



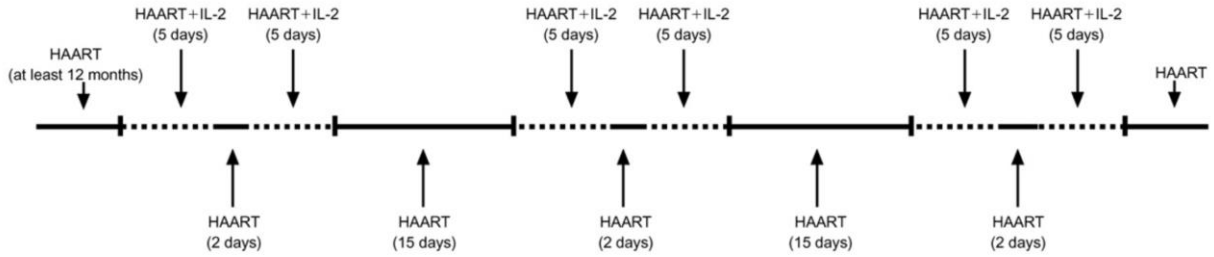
Adjuvant terapeutic strategy #1: increase peripheral CD4+ T-cell proliferation/survival

IL-2 induces T-cell proliferation

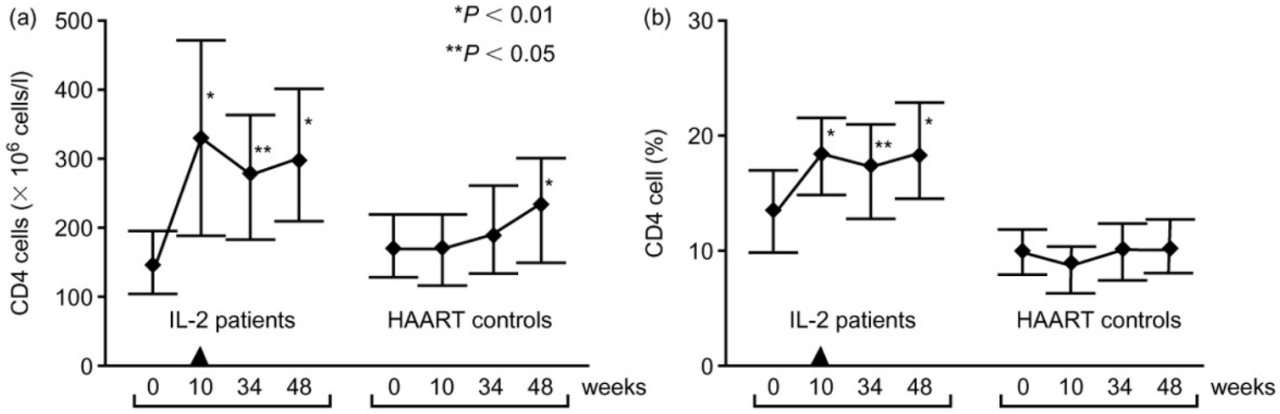


Boyman, Nat Rev Immunol, 2012

Immune benefit of IL-2 adjuvant therapy vs cART alone in HIV



Schedule of low-dose prolonged intermittent interleukin-2 (IL-2) immunotherapy in association with highly active antiretroviral therapy (HAART).



Variable	Median value (IQR) Week 0	Week 10	Week 34	Week 48
CD4/CD8 ratio				
IL-2	0.20 (0.14–0.30)	0.31 (0.29–0.41)**	0.32 (0.20–0.39)**	0.28 (0.23–0.42)**
HAART	0.14 (0.13–0.20)	0.15 (0.09–0.18)	0.14 (0.14–0.20)	0.17 (0.14–0.23)
CD8+CD38+ (%)				
IL-2	14.5 (8.3–22)	8.8 (5.9–24)	6.2 (5.5–9.2)**	11.4 (7.7–13.5)*
HAART	26 (7.5–37)	nd	nd	20 (12.3–26.5)
CD4+45RA+62L+ (per µl)				
IL-2	31 (15–37)	60 (37–93)**	65 (22–147)**	90 (26–145)**†
HAART	23 (10–77)	nd	nd	25 (9–83)
CD4+45RA− (per µl)				
IL-2	129 (68–163)	185 (152–332)**	196 (141–263)**	224 (165–319)**†
HAART	112 (105–156)	nd	nd	125 (114–215)**

Marchetti et al. AIDS 20

JAC antiviral

Journal of Antimicrobial Chemotherapy (2005) **55**, 401–409
doi:10.1093/jac/dkh557
Advance Access publication 24 February 2005

Partial immune reconstitution following highly active antiretroviral therapy: can adjuvant interleukin-2 fill the gap?

Giulia Marchetti*, Fabio Franzetti and Andrea Gori

Institute of Infectious Disease and Tropical Medicine, University of Milan, 'Luigi Sacco' Hospital, Milan, Italy

The Challenge of IL-2 Immunotherapy in HIV Disease: "No through Road" or Turning Point?

Author(s): Giulia Marchetti, Camilla Tincati, Antonella d'Arminio Monforte and Andrea Gori

Volume 6, Issue 3, 2008

Page: [189 - 199]

DOI: 10.2174/157016208784325029

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Interleukin-2 Therapy in Patients with HIV Infection

The INSIGHT–ESPRIT Study Group and SILCAAT Scientific Committee*

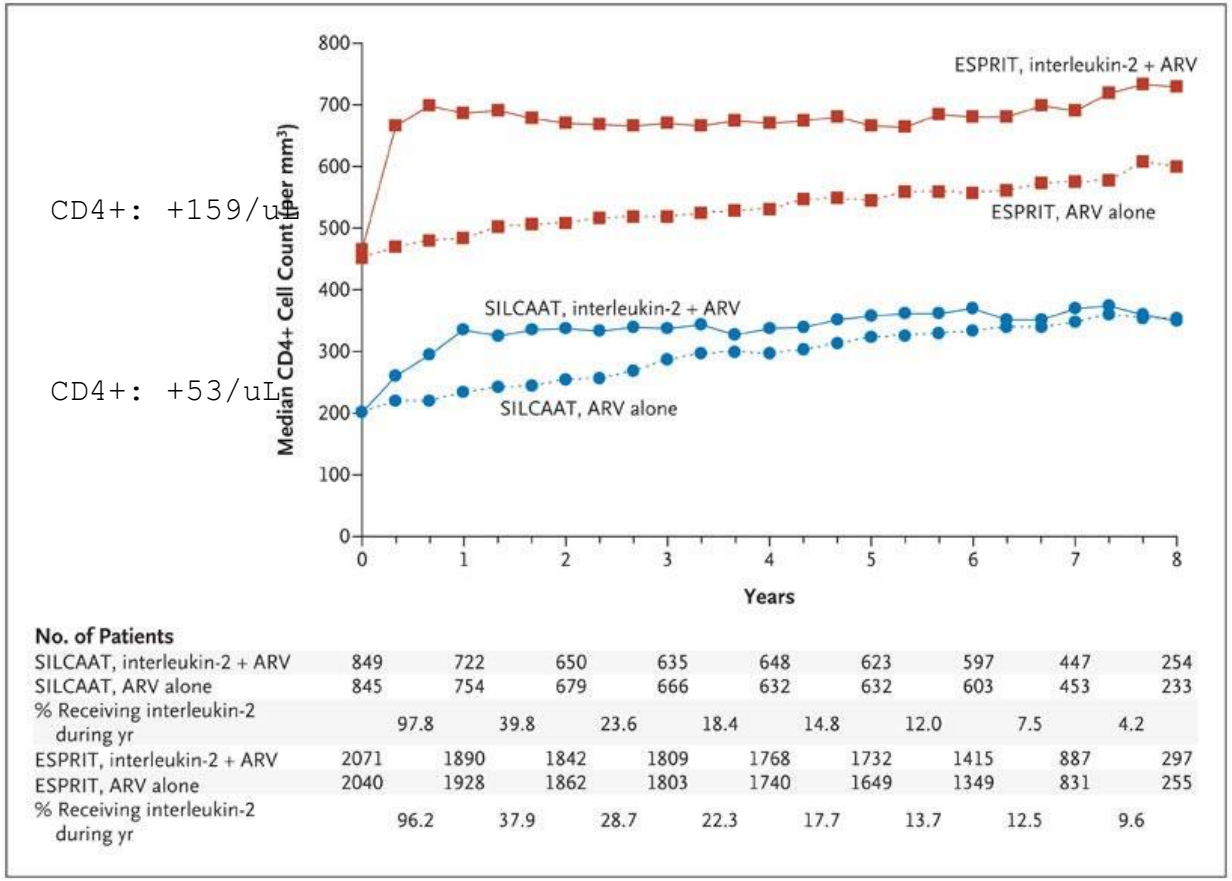
- Subcutaneous Recombinant, Human Interleukin-2 in HIV-Infected Patients with Low CD4+ Counts under Active Antiretroviral Therapy (**SILCAAT**); CD4+ cell counts of 50 to 299/uL, **n=1695**
- Evaluation of Subcutaneous Proleukin in a Randomized International Trial (**ESPRIT**); CD4+ cell counts of ≥300/uL, **n=4111**

Randomly assigned to receive interleukin-2 plus antiretroviral therapy or antiretroviral therapy alone

The primary end point of both studies was opportunistic disease or death from any cause

CD4+: +159/uL

CD4+: +53/uL

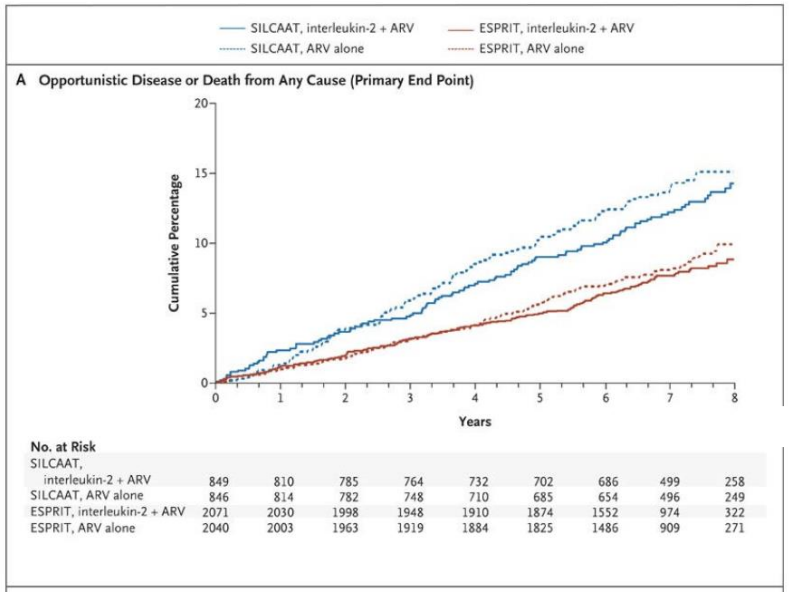


No. of Patients									
SILCAAT, interleukin-2 + ARV	849	722	650	635	648	623	597	447	254
SILCAAT, ARV alone	845	754	679	666	632	632	603	453	233
% Receiving interleukin-2 during yr	97.8	39.8	23.6	18.4	14.8	12.0	7.5	4.2	
ESPRIT, interleukin-2 + ARV	2071	1890	1842	1809	1768	1732	1415	887	297
ESPRIT, ARV alone	2040	1928	1862	1803	1740	1649	1349	831	255
% Receiving interleukin-2 during yr	96.2	37.9	28.7	22.3	17.7	13.7	12.5	9.6	

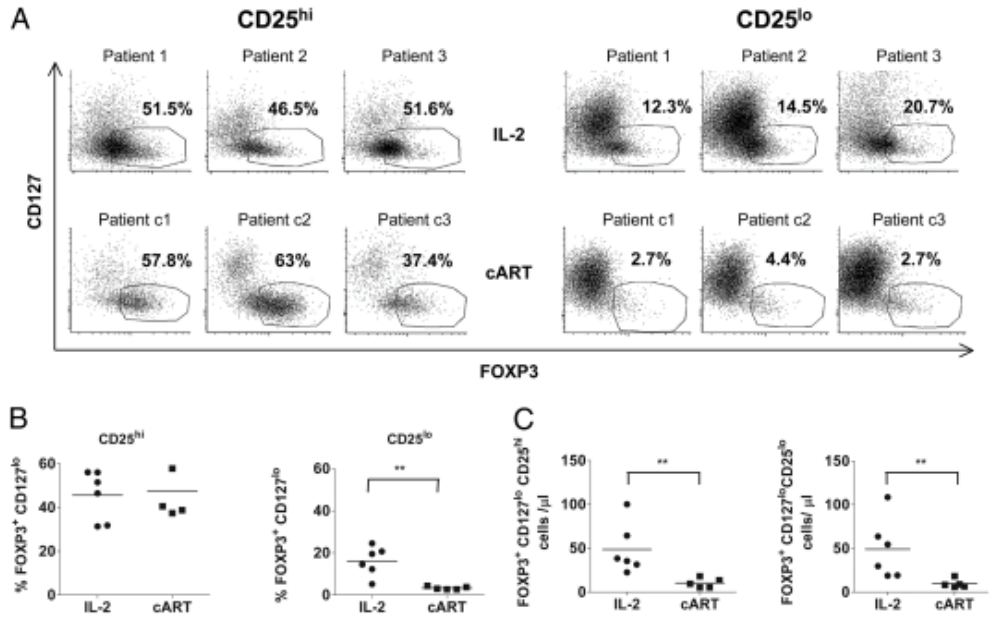
Over a median follow-up period of 7 to 8 years, the CD4+ cell count was higher in the interleukin-2 group than in the group receiving antiretroviral therapy alone

NEJM, 2009

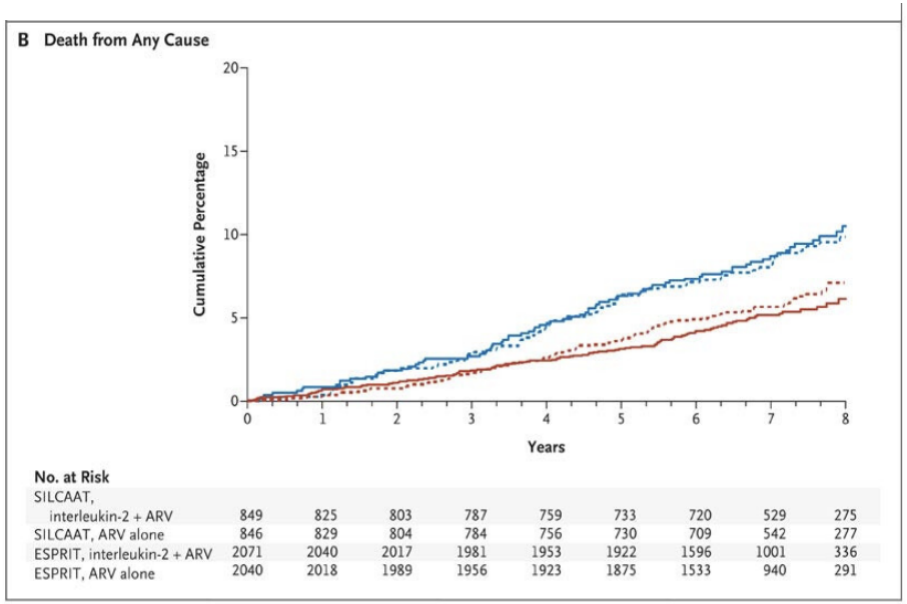
IL-2 + cART yielded no clinical benefit



Increase in Treg cells in IL-2 receipients



Weiss, PNAS, 20

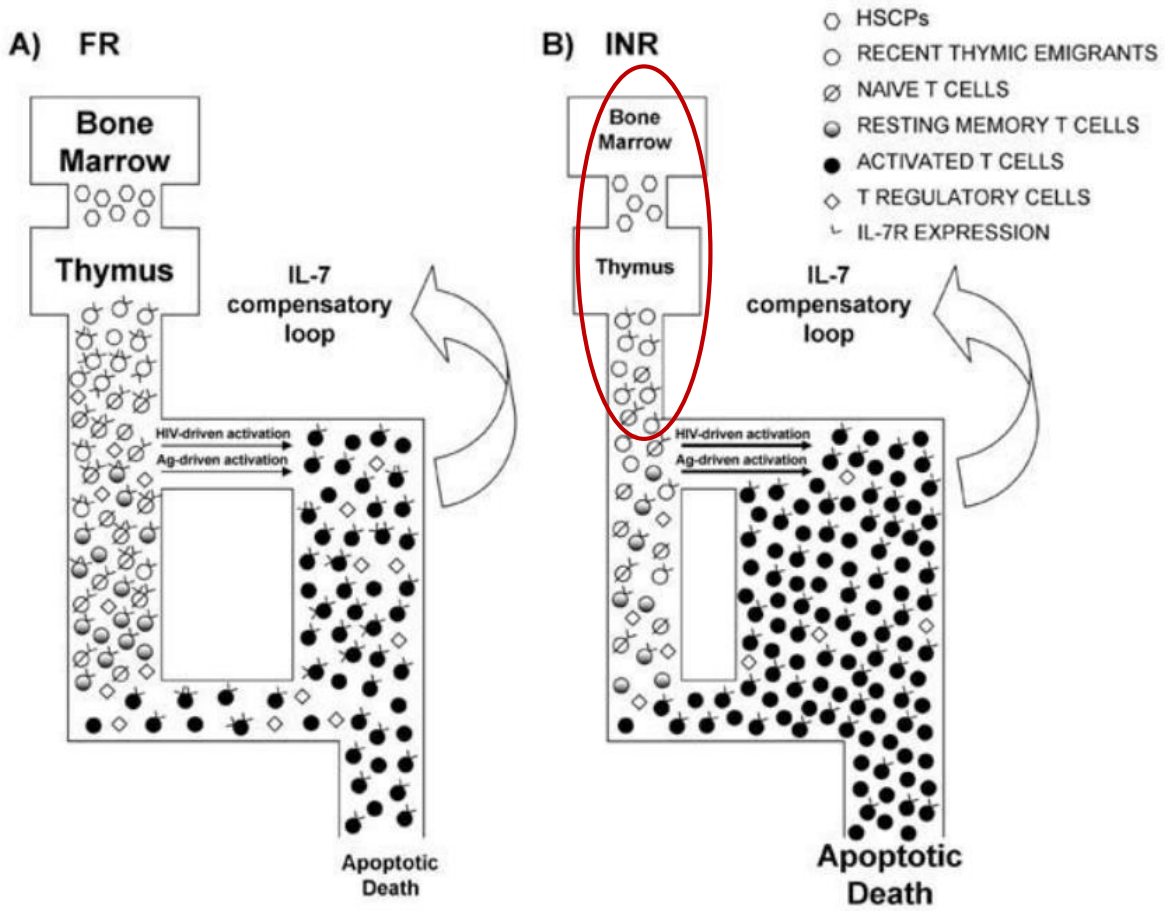


NEJM, 2009

The Absence of CD4$^+$ T Cell Count Recovery Despite Receipt of Virologically Suppressive Highly Active Antiretroviral Therapy: Clinical Risk, Immunological Gaps, and Therapeutic Options

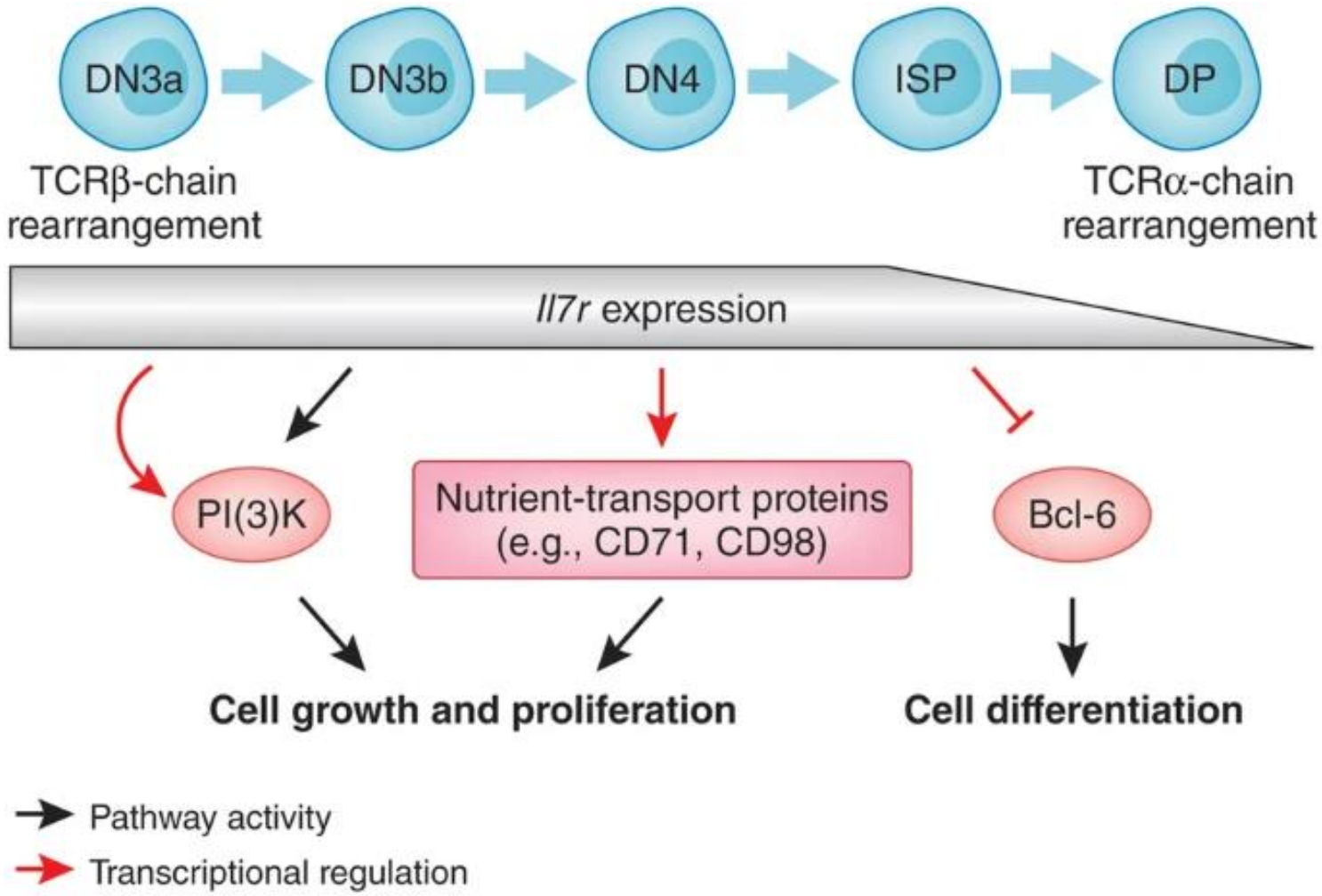
Lidia Gazzola, Camilla Tincati, Giusi Maria Bellistrì, Antonella d'Arminio Monforte, and Giulia Marchetti

Department of Medicine, Surgery, and Dentistry, Clinic of Infectious Diseases, "San Paolo" Hospital, University of Milan, Milan, Italy



Adjuvant therapeutic strategy#2: increase thymic output/*de novo* CD4+ T-cell production

IL-7 e timopoiesi



Seddon, Nat Immunol, 2015

Clinical Infectious Diseases
MAJOR ARTICLE
HIV/AIDS

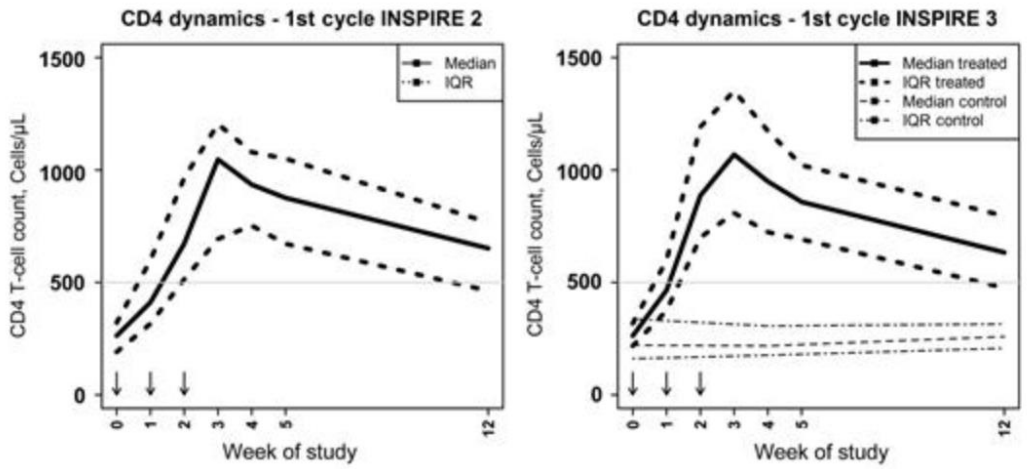
Repeated Cycles of Recombinant Human Interleukin 7 in HIV-Infected Patients With Low CD4 T-Cell Reconstitution on Antiretroviral Therapy: Results of 2 Phase II Multicenter Studies

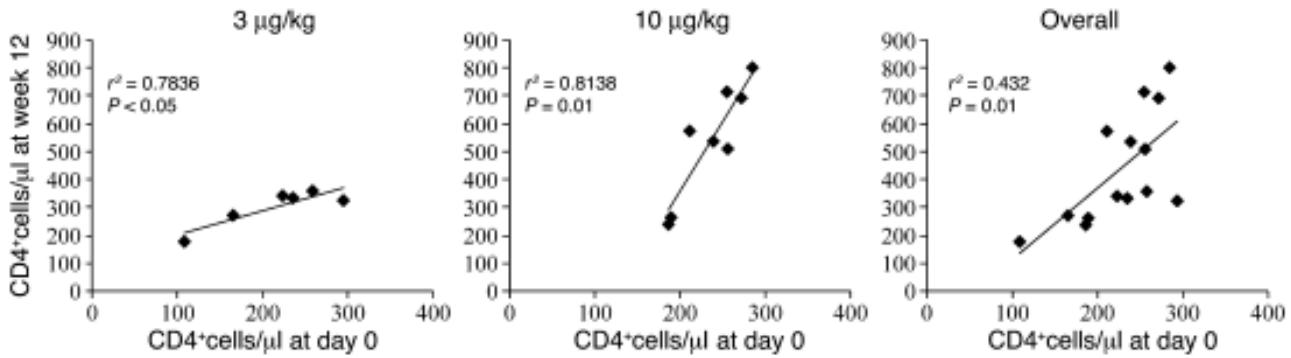
Rodolphe Thiébaut,[1] Ana Jarne,[1] Jean-Pierre Routy,[4] Irini Sereti,[5] Margaret Fischl,[7] Prudence Ive,[9] Roberto F. Speck,[11] Gianpiero D'Offizi,[12] Salvatore Casari,[13] Daniel Commenges,[1] Sharne Foulkes,[10] Ven Natarajan,[6] Thérèse Croughs,[2] Jean-François Delfraissy,[2] Guiseppe Tambussi,[14] Yves Levy,[3] and Michael M. Lederman[8]

- Eligible participants had to be receiving ART for ≥1 year with plasma HIV RNA levels <50 copies/mL and CD4 counts between 101 and 400 cells/µL
- Patients received a cycle of 3 weekly subcutaneous injections of r-hIL-7 20 µg/kg
- The study was amended 12 months after its initiation to include repeated cycles of CYT107 administration in order to maintain CD4 counts >500

Table 3. Factors Associated With CD4 T-Cell Counts Decreasing to <550 Cells/µL[a]

Factor	Hazard Ratio (95% CI)	*P* Value
Baseline CD4 T-cell count, cells/µL		
>200	1	<.001
≤200	11.10 (4.02–30.66)	
Type of IL-7 cycle		
Initial	1	.57
Maintenance	0.86 (.51–1.46)	
Injections in a given cycle		
3	1	.02
2	2.27 (.79–6.55)	
1	4.29 (1.32–13.90)	





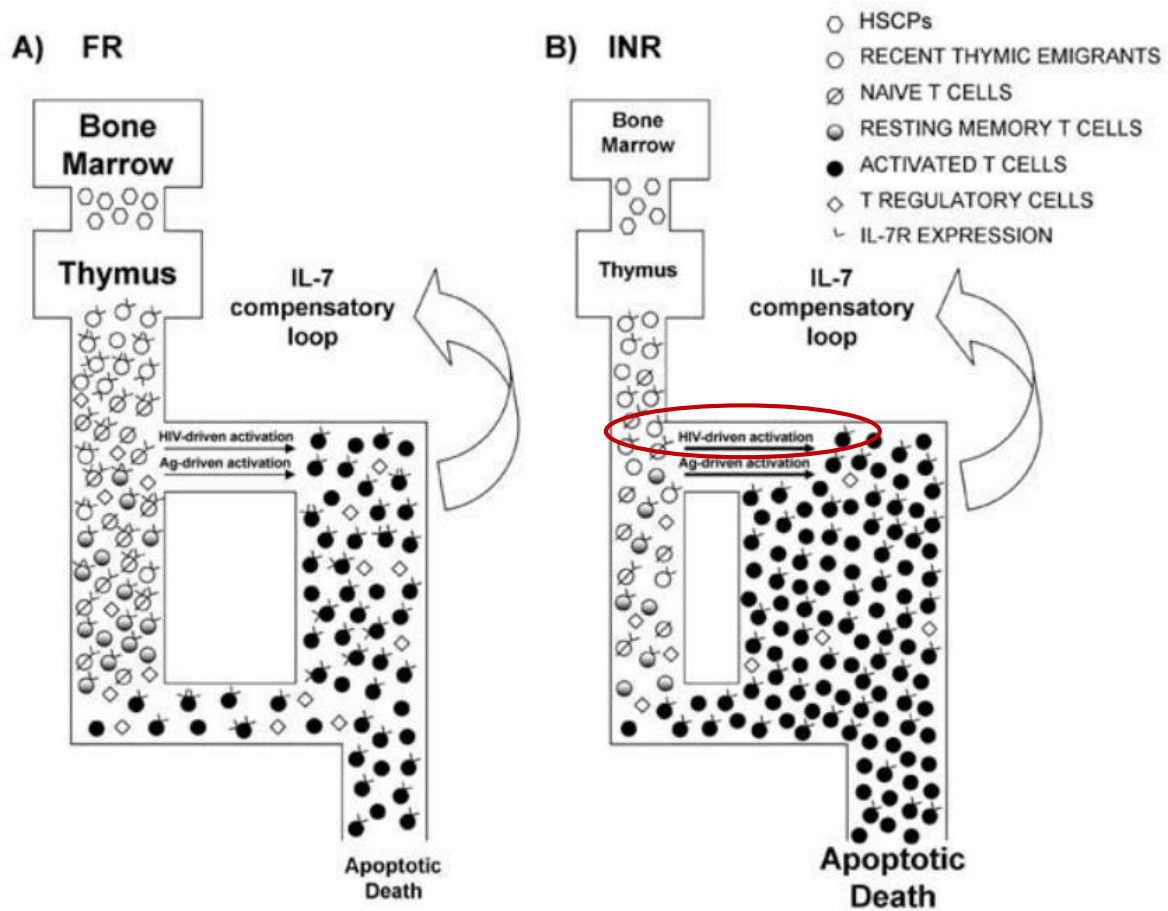
Thiebuat, CID, 2016

Levy, JCI, 200

The Absence of CD4$^+$ T Cell Count Recovery Despite Receipt of Virologically Suppressive Highly Active Antiretroviral Therapy: Clinical Risk, Immunological Gaps, and Therapeutic Options

Lidia Gazzola, Camilla Tincati, Giusi Maria Bellistrì, Antonella d'Arminio Monforte, and Giulia Marchetti

Department of Medicine, Surgery, and Dentistry, Clinic of Infectious Diseases, "San Paolo" Hospital, University of Milan, Milan, Italy

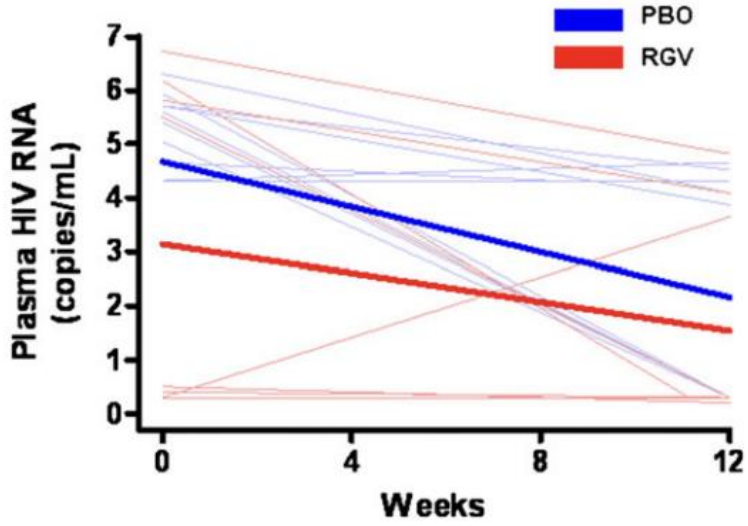


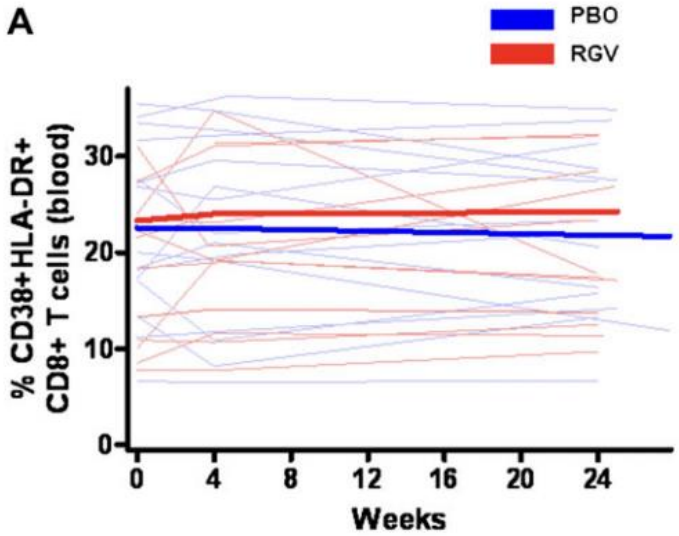
Adjuvant therapuetic strategy #3: reduce reservoirs/productive infection

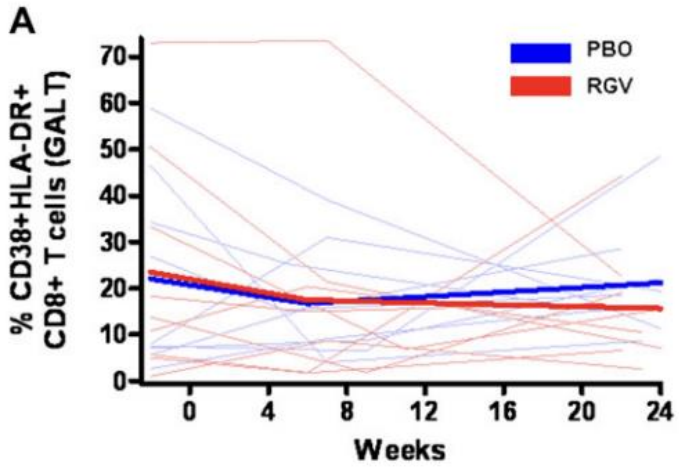
No effect on RAL intensification in INR

Table 1. Baseline Characteristics for Subjects in Raltegravir and Placebo Treatment Groups[a]

Baseline Characteristic	Raltegravir (n = 15)	Placebo (n = 15)	P
Age, median, years	48	49	.72
Sex	15 male	14 male, 1 MTF	
$CD4^+$ T cell count, median, cells/mm^3	233	231	.56
Nadir $CD4^+$ T cell count, median, cells/mm^3	17	90	.13
Plasma HIV-1 RNA, median, copies/mL[b]	2.6	5.5	.52
Time since HIV diagnosis, median, years	15	18	.23
Duration of HAART suppression, median, years	3.1	2.1	.76
Treatment with PI-containing HAART, no. of subjects	10/15	8/15	.71
HCV coinfection, no. of subjects	4/15[c]	4/15	1.00



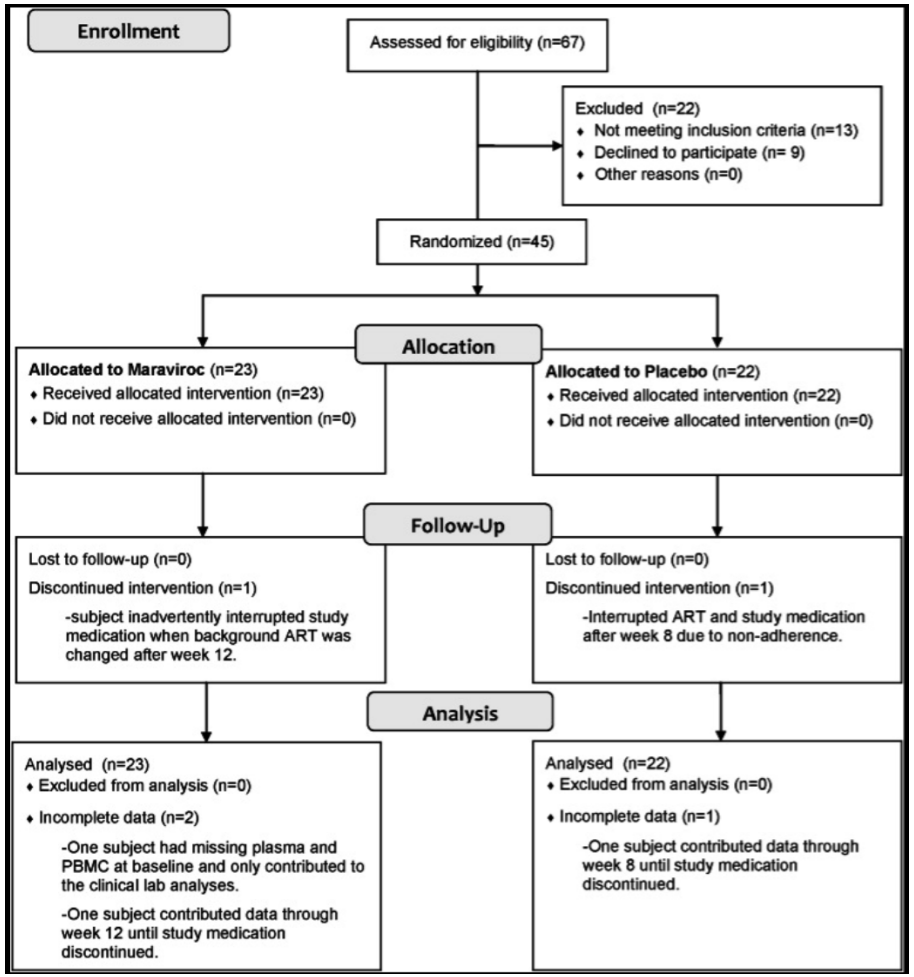


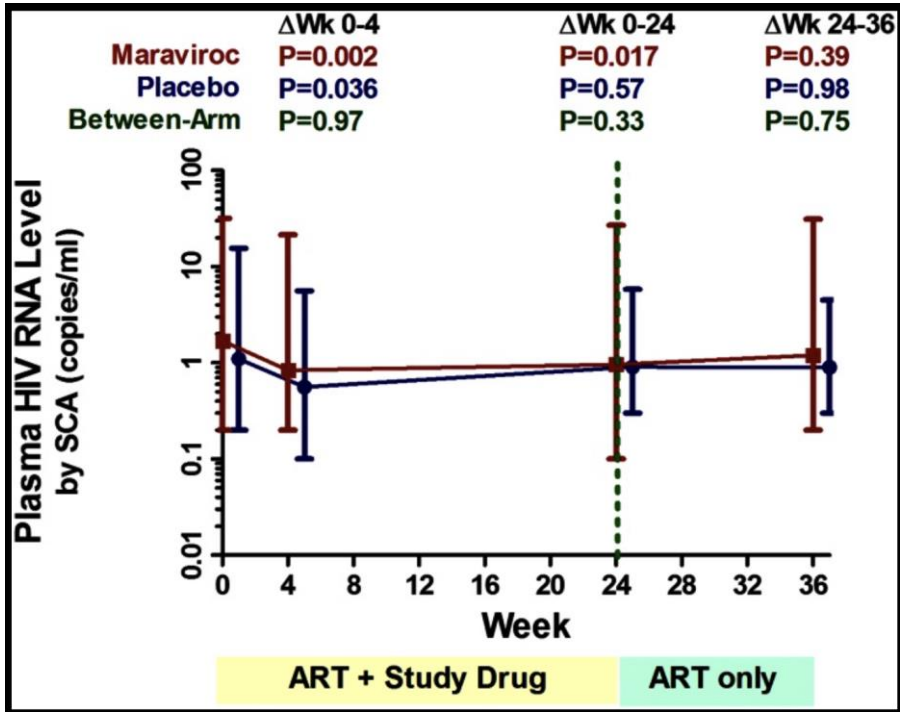


Hatano, JID, 2

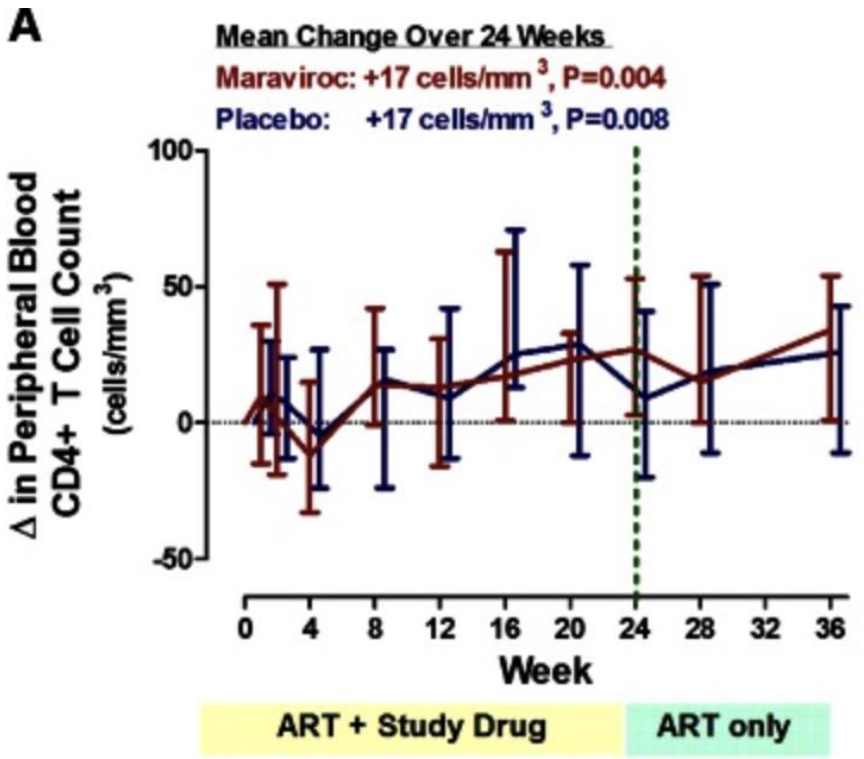
MVC intensification in INR: no effect on HIV RNA

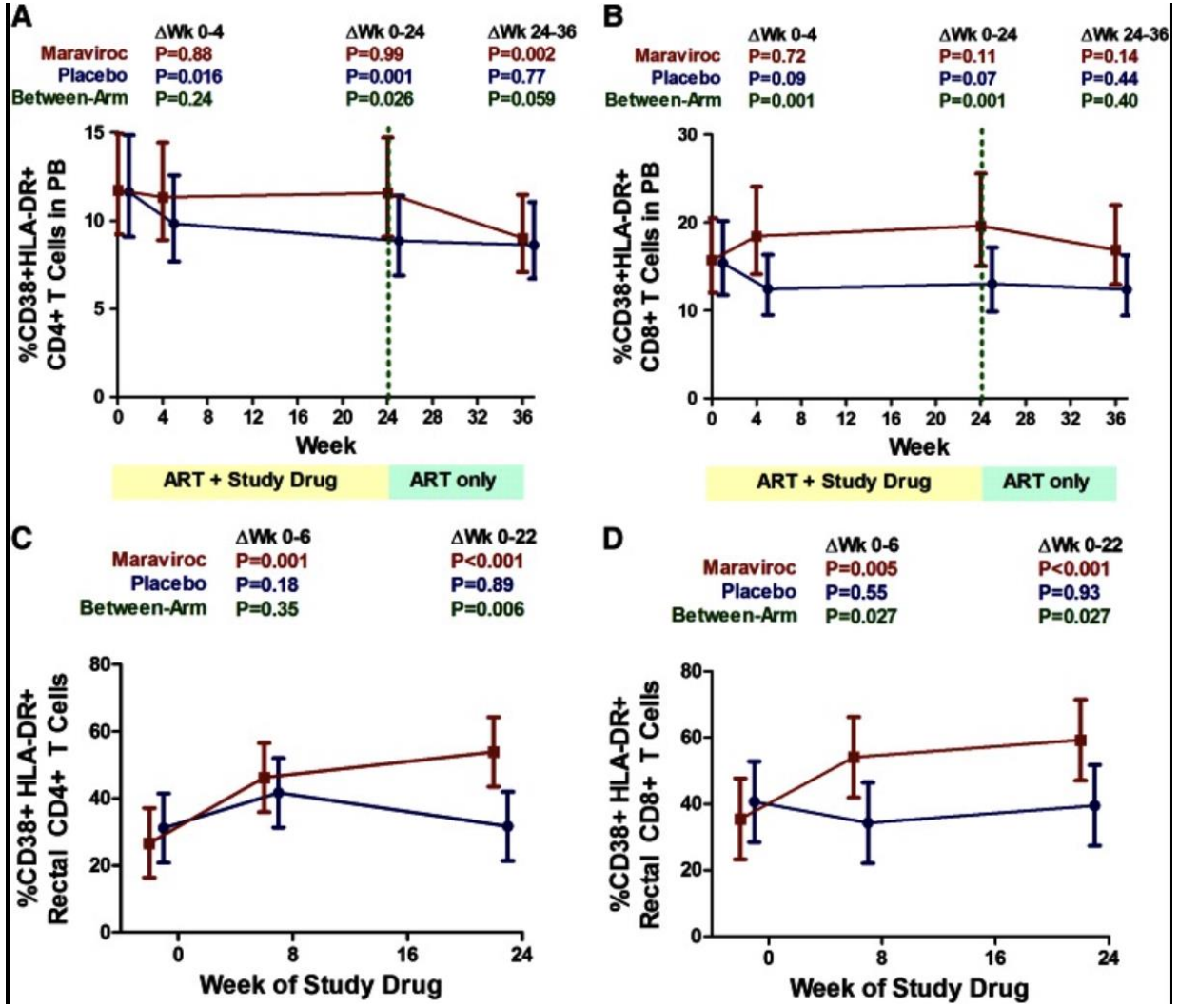
We randomized 45 HIV-infected subjects with CD4 counts <350/uL and plasma HIV RNA levels <48 copies/mL on cART to add maraviroc vs placebo to their regimen for 24 weeks followed by 12 weeks on ART alone





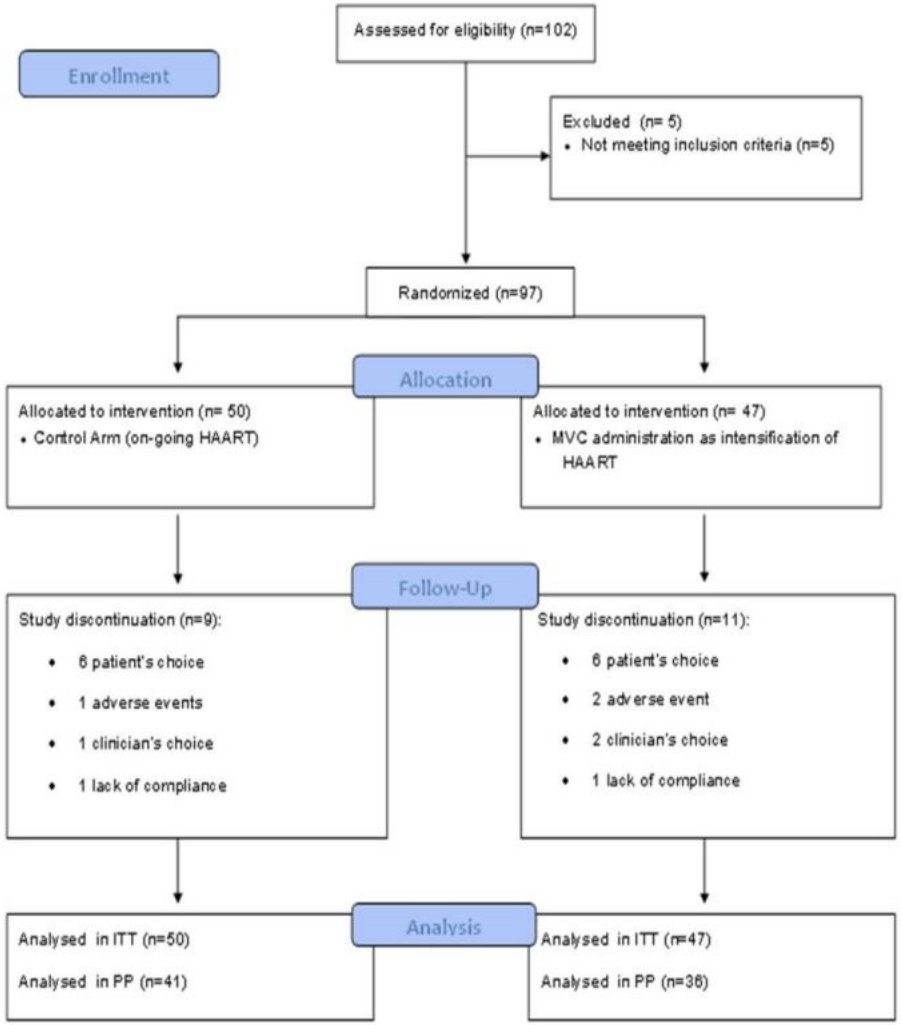
MVC intensification in INR: increased T cell activation in blood and gut

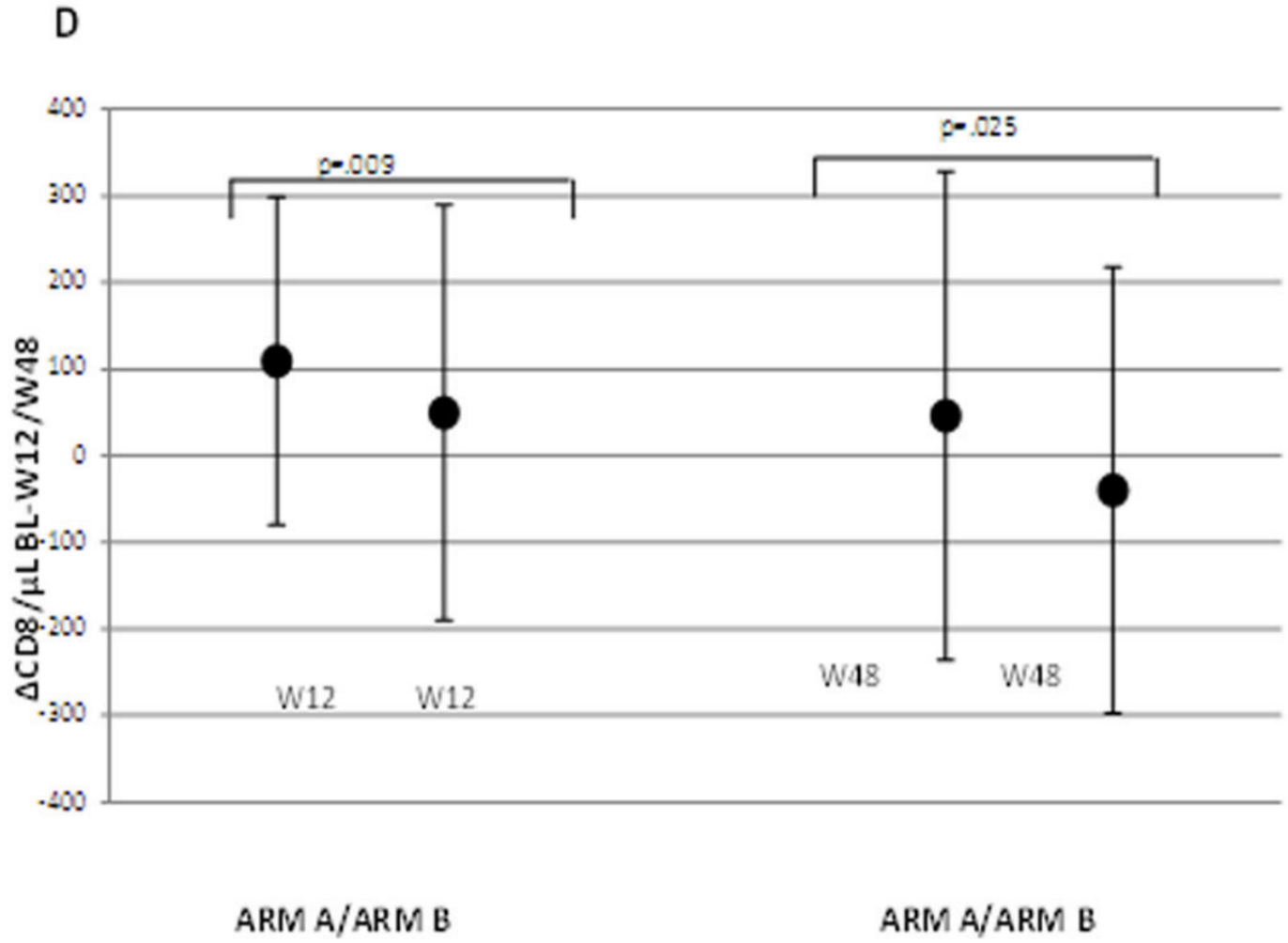




Hunt et al. Blood, 2013

MVC intensification in INR: increased CD8+ T cells

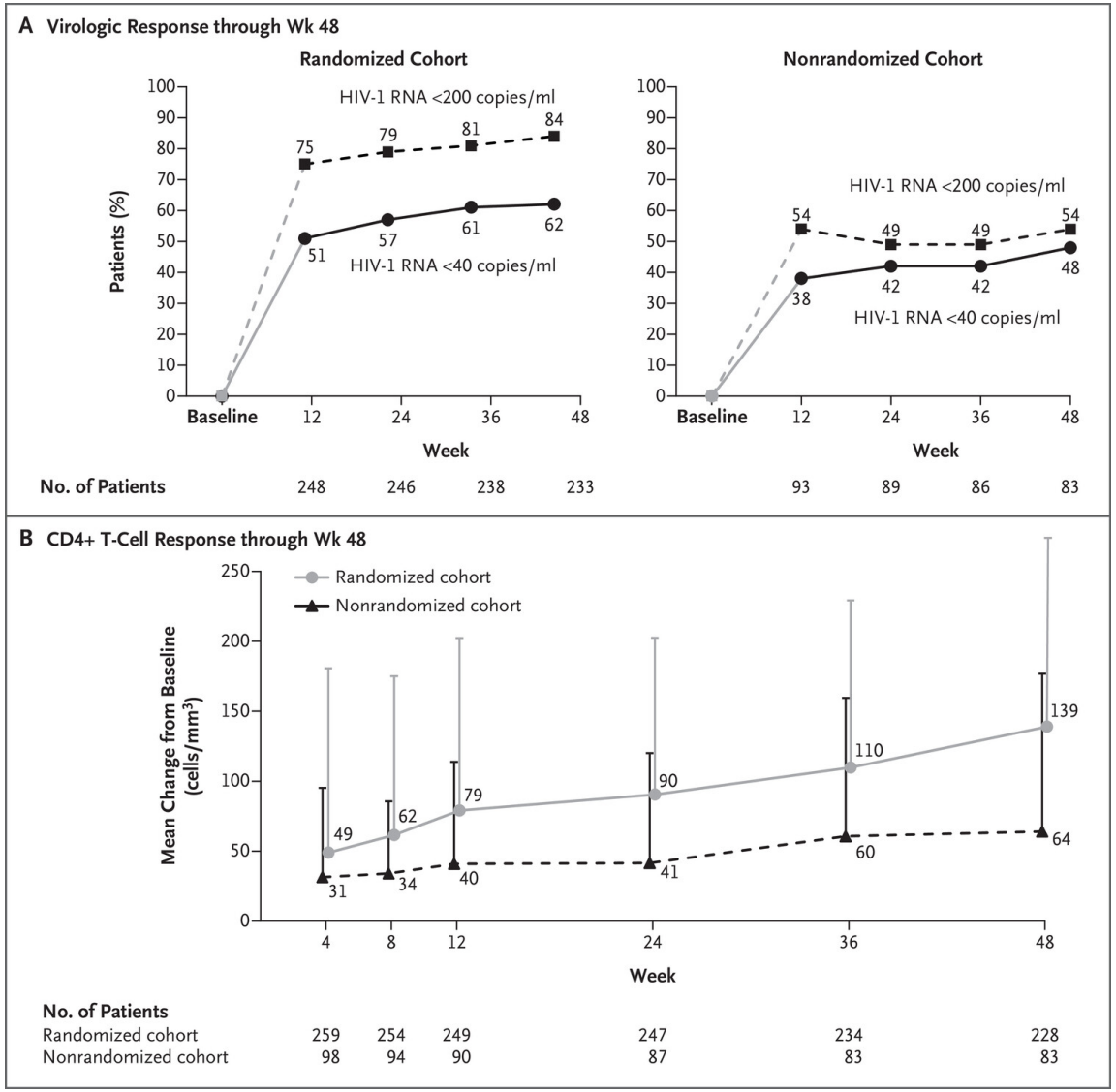




Rusconi, PlosOne, 201

Fostemsavir

- Fostemsavir is the prodrug of temsavir, a first-in-class investigational HIV-1 **attachment inhibitor**.
- Temsavir binds the viral envelope protein gp120 on HIV-1, adjacent to the gp120-CD4+ binding site. In doing so, it prevents the conformational change required for attachment of HIV-1 to the host cell.



Kozal, NEJM, 2020

U.S. National Library of Medicin

ClinicalTrials.gov

Previous Study | Return to List | Next Study

Changes in Immunologic Parameters Following the Addition of Fostemsavir in Virologically Suppressed Immunologic Non-responders Living With HIV-the RECOVER Study

Brief Summary:

The RECOVER study is a self-controlled case series to evaluate whether the addition of **Fostemsavir** (Rukobia) to a stable HIV regimen in virologically suppressed patients living with HIV who never experience optimal CD4 T-cell count recovery can result in meaningful increases in different immunologic parameters such as CD4 T-cell count, CD4 T-cell percentage and CD4/CD8 ratio

Condition or disease	Intervention/treatment	Phase
HIV-1-infection	Drug: **Fostemsavir** 600 MG [Rukobia]	Phase 4

- Documented plasma HIV-1 RNA < 50 c/mL x 2 within the last year prior to screening
- Must be on a stable ARV regimen for ≥6 months prior to screening
- CD4+T-cell count<350 cells/mm3 while on ARVs for at least 2 years
- Must be willing to add FTR 600 mg twice daily to their current antiretroviral regimen

Impact of Anti-CD4 Autoantibodies on Immune Reconstitution in People with Advanced HIV

Epling et al, 2024 | *Clinical Infectious Diseases*

IDSA
Infectious Diseases Society of America

Retrospective Cohort Study

1. Characterize the relative frequency of anti-CD4 autoantibodies in a wide variety of cohorts of people with and without HIV.
2. Assess the impact of these autoantibodies on the rate and extent of CD4 recovery in people with advanced HIV starting ART.

ART-naive people with advanced HIV (pre-ART CD4 ≤100 cells/μL, N=210):

Anti-CD4 autoantibody positive at ART initiation

N = 61 (29%)

Anti-CD4 autoantibody negative at ART initiation

N = 149 (71%)

These AAb were not detected in any people without HIV (N=104)

Rate of CD4 Recovery

5.8 cells/μL per month

6.6 cells/μL per month

P = .007

CD4 Count after 192 weeks of ART

268 cells/μL

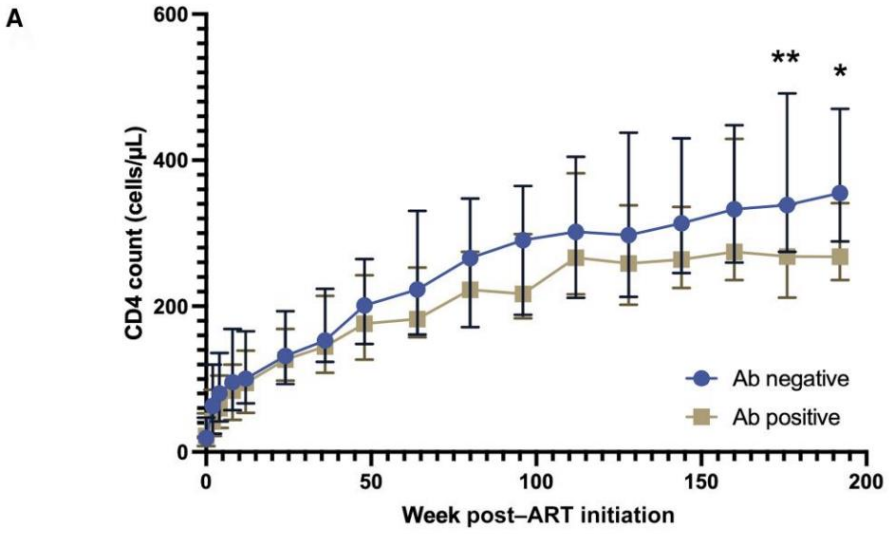
355 cells/μL

P = .019

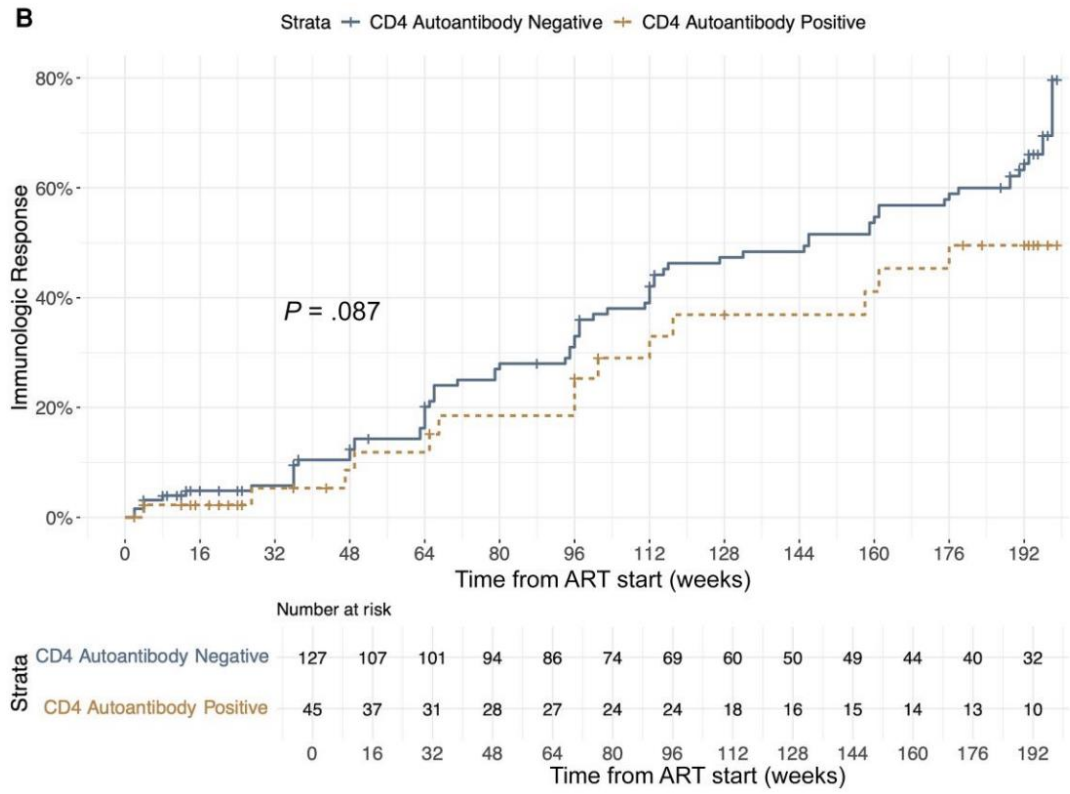
1. 29% of people with advanced HIV starting ART had autoantibodies against the CD4 receptor. These autoantibodies were not isolated from any cohort of people without HIV.
2. The presence of anti-CD4 autoantibodies at ART initiation was associated with an impaired rate and extent of CD4 recovery. Conversely, incidental immunosuppressive therapy was associated with increased CD4 counts in these participants.

Clinical Infectious Diseases https://doi.org/10.1093/cid/ciae562

Anti CD4 Autoantibodies and Immune Reconstitution



Week	0	2	4	8	12	24	36	48	64	80	96	112	128	144	160	176	192
N (AAb neg)	149	133	125	112	114	112	104	98	98	100	94	95	90	88	85	82	84
N (AAb pos)	61	51	45	37	42	37	33	29	28	24	26	26	22	21	20	20	16
P value	.673	.136	.106	.107	.185	.981	.369	.399	.307	.06	.084	.748	.217	.076	.114	**.008**	**.018**



Incidental, clinically indicated immunosuppressive therapy in these participants was associated with an improved rate of CD4 reconstitution (P = .0019) and higher week 192 CD4 count (551 vs 268 cells/μL, P = .019).

Epling, CID, 2025

Role of ibalizumab in INR?

D3–D4 domains contain the epitope(s) for the generation and binding of anti-CD4 autoantibody

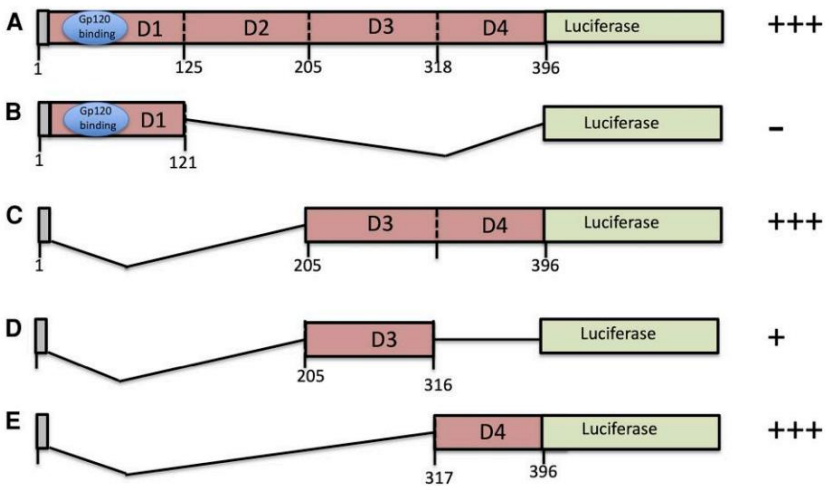
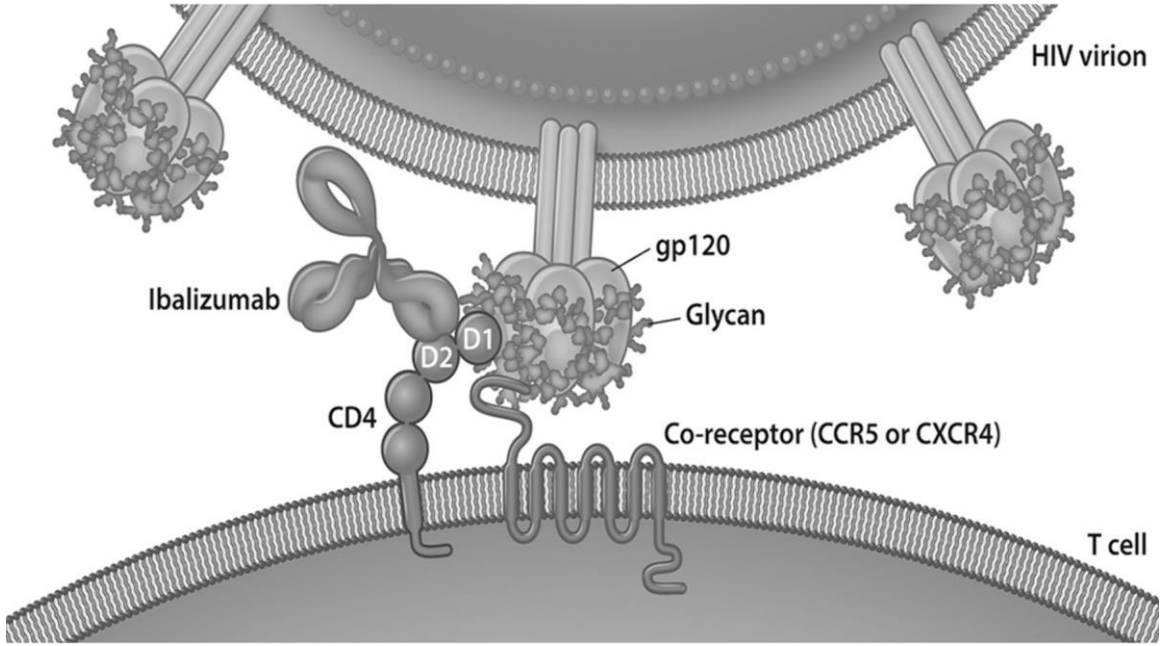


Figure 2. Mapping of autoantibody binding to different regions of the CD4 receptor. Relative autoantibody binding to different regions of the CD4 receptor determined by serological testing are summarized (–, negative, +; weak and +++; strong). The extracellular region of the CD4 receptor consisting of the D1–D4 protein domains showed strong immunoreactivity (*A*). A deletion mutant of CD4 containing only the D1 domain (*B*) was seronegative for CD4 autoantibody binding. Antibody binding was strongly retained with deletion mutants of CD4 maintaining the integrity of the D3–D4 domains (*C*), weakly with the D3 domain (*D*), and strongly with the D4 domain (*E*).



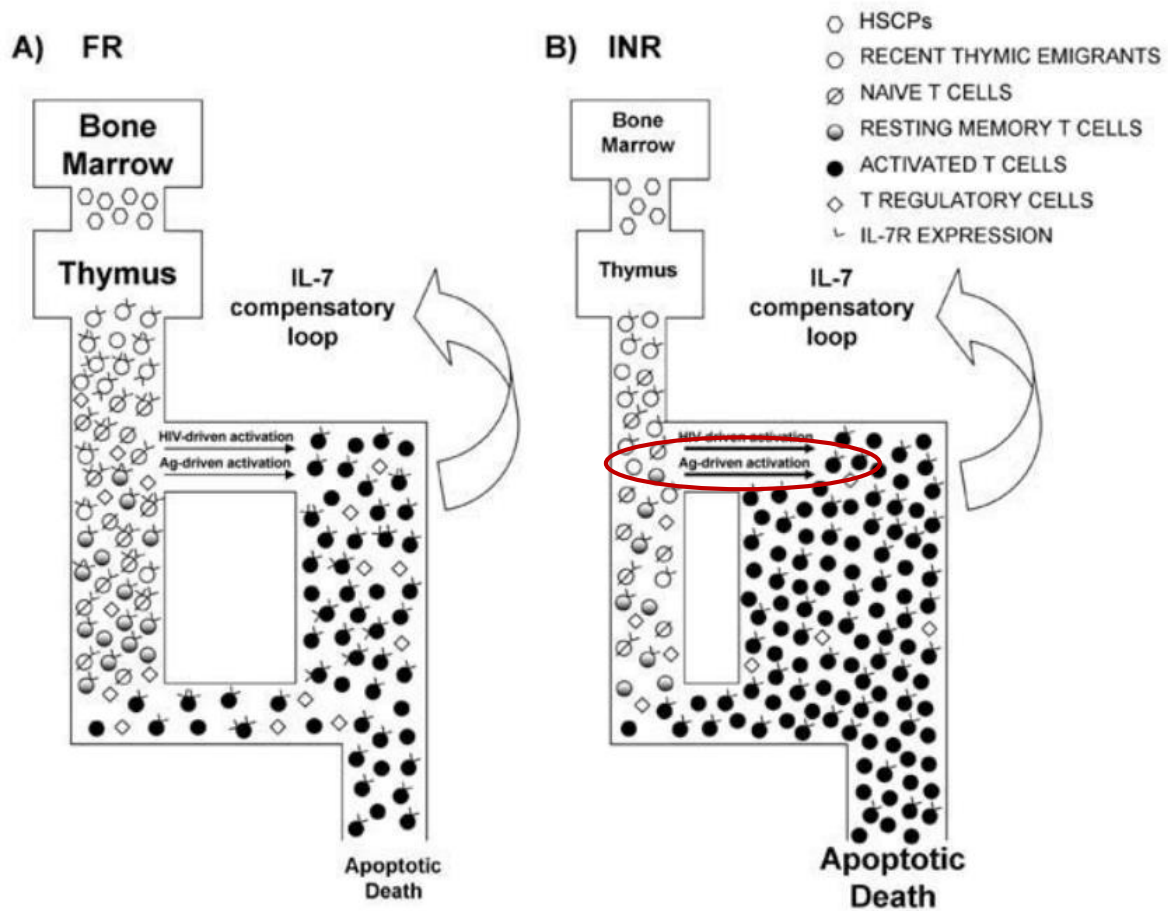
Epling, CID, 2025

Beccari, AAC, 201

The Absence of CD4$^+$ T Cell Count Recovery Despite Receipt of Virologically Suppressive Highly Active Antiretroviral Therapy: Clinical Risk, Immunological Gaps, and Therapeutic Options

Lidia Gazzola, Camilla Tincati, Giusi Maria Bellistrì, Antonella d'Arminio Monforte, and Giulia Marchetti

Department of Medicine, Surgery, and Dentistry, Clinic of Infectious Diseases, "San Paolo" Hospital, University of Milan, Milan, Italy



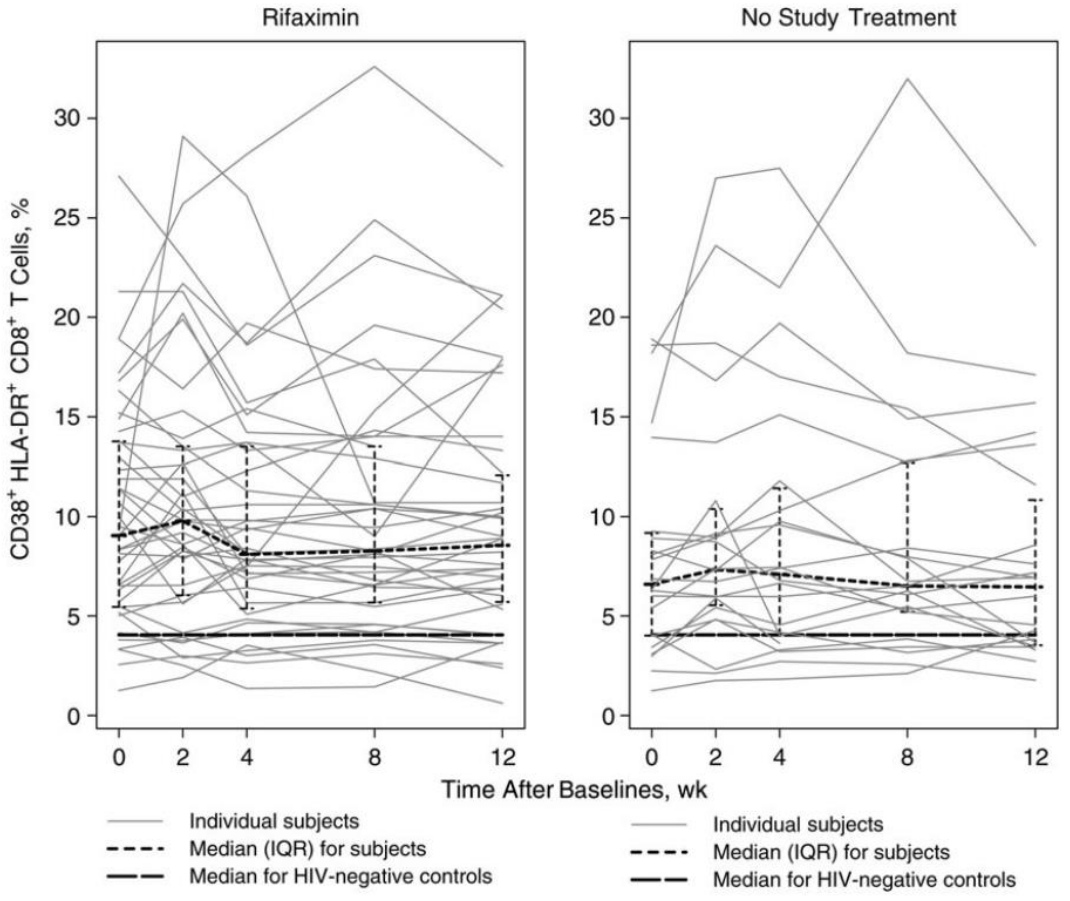
Adjuvant therapeutic strategy #4: reduce immune activation by counteracting microbial translocation/correcting dysbiosis

No effect of rifaximin in INR

- Non-absorbable antibiotic that decreases lipopolysaccharide (LPS) in cirrhotics
- HIV-positive adults receiving ART for ≥96 weeks with undetectable viremia for ≥48 weeks and CD4(+) T-cell counts <350 cells/mm(3) were randomized 2:1 to rifaximin versus no study treatment for 4 weeks

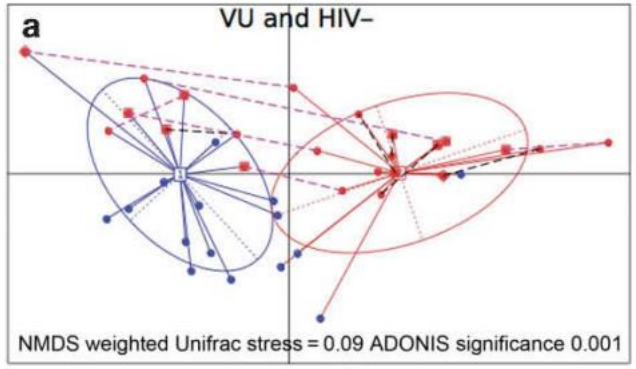
Table 1. Baseline Demographic, Immunologic, and Virologic Characteristics of the 65 Subjects Included in the As-Treated Analyses

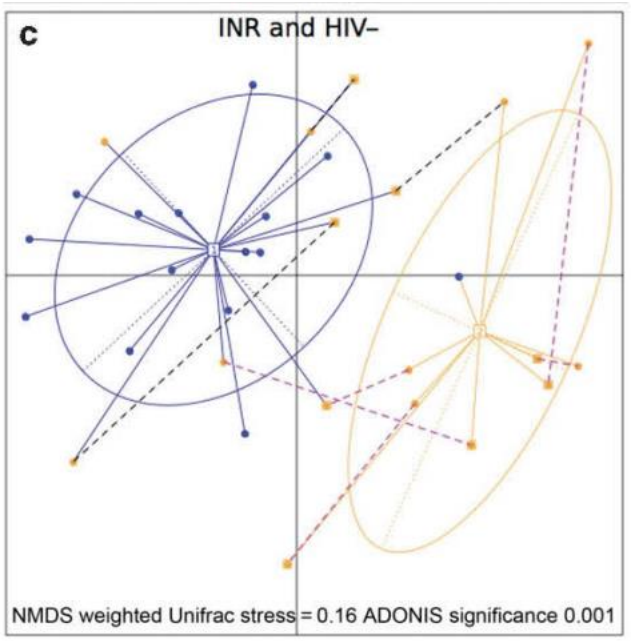
Baseline Characteristic	All Subjects (N = 65)	Rifaximin Arm (n = 43)	No-Treatment Arm (n = 22)
Age, median (IQR), y	50 (44–55)	48 (43–56)	51 (45–55)
Age ≥60 y, No. (%)	7 (11)	4 (9)	3 (14)
Race/ethnicity, No. (%)			
White non-Hispanic	31 (48)	19 (44)	12 (55)
Black non-Hispanic	20 (31)	17 (40)	3 (14)
Hispanic	13 (20)	7 (16)	6 (27)
Other	1 (2)	0 (0)	1 (5)
Sex, No. (%)			
Male	59 (91)	39 (91)	20 (91)
Female	6 (9)	4 (9)	2 (9)
Cotrimoxazole use, No. (%)	29 (45)	21 (49)	8 (36)
Baseline $CD4^+$ T-cell count[a]			
Median (IQR), cells/mm^3	236 (179–284)	251 (179–286)	223 (167–280)
≥350 cells/mm^3, No. (%)	1 (2)	0 (0)	1 (5)
Nadir $CD4^+$ T-cell count, median (IQR), cells/mm^3	41 (15–88)	50 (22–71)	40 (10–88)
Entry HIV-1 RNA level below lower limit of assay, No. (%)	65 (100)	43 (100)	22 (100)
Interval since 1st undetectable HIV-1 RNA level, median (IQR), y	3.8 (2.4–7.3)	3.3 (2.2–7.3)	3.9 (2.8–8.8)



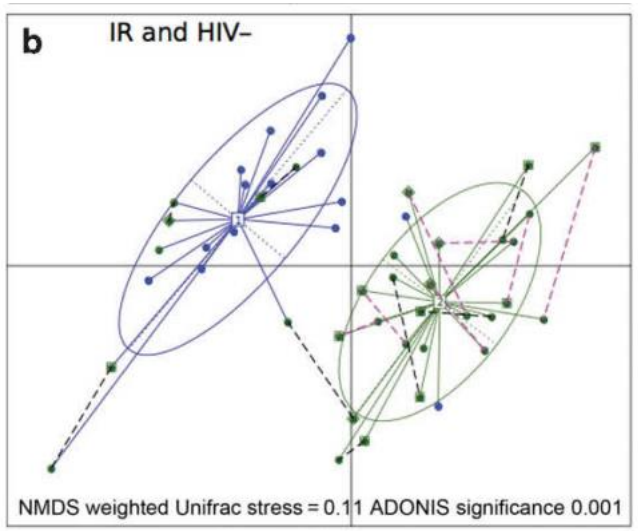
Tenorio, JID, 2015

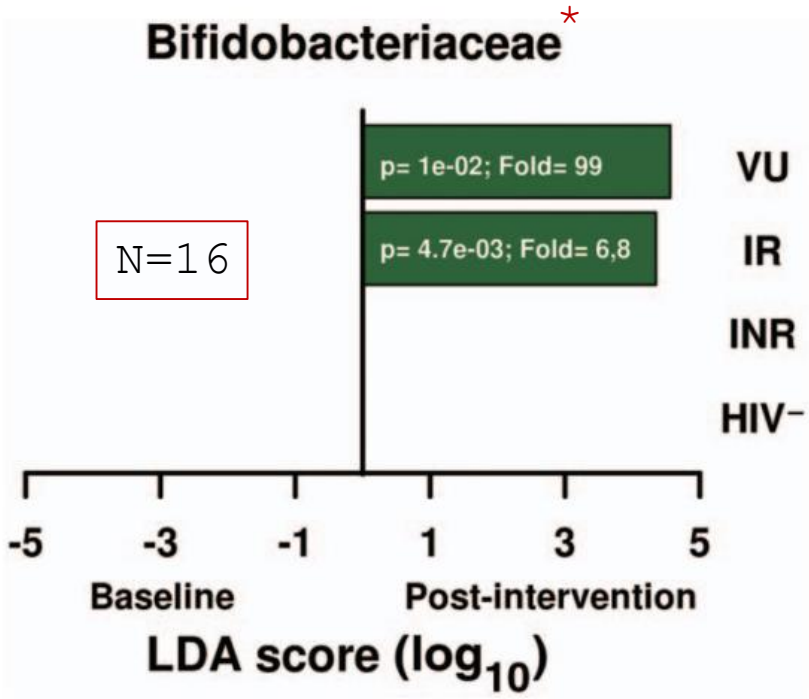
Scant effect of prebiotics (scGOS/lcFOS/glutamine) in INR





Gut bacterial communities



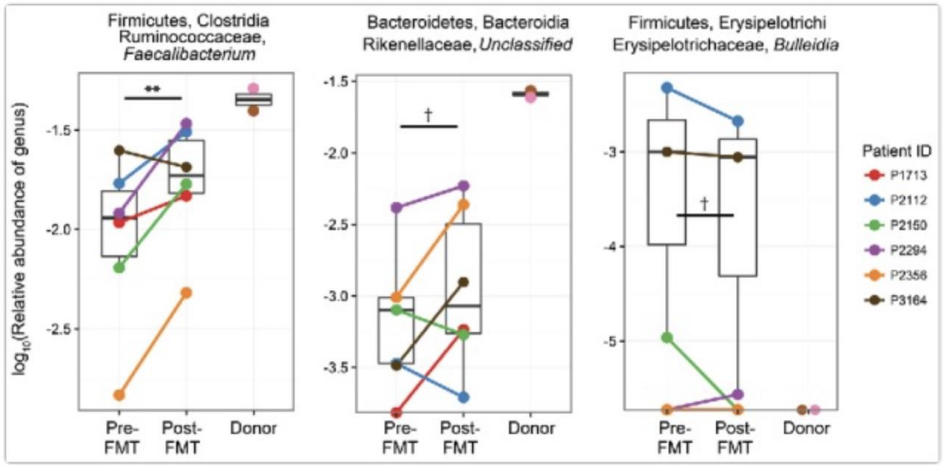


*immunomodulatory properties and amino acids metabolism

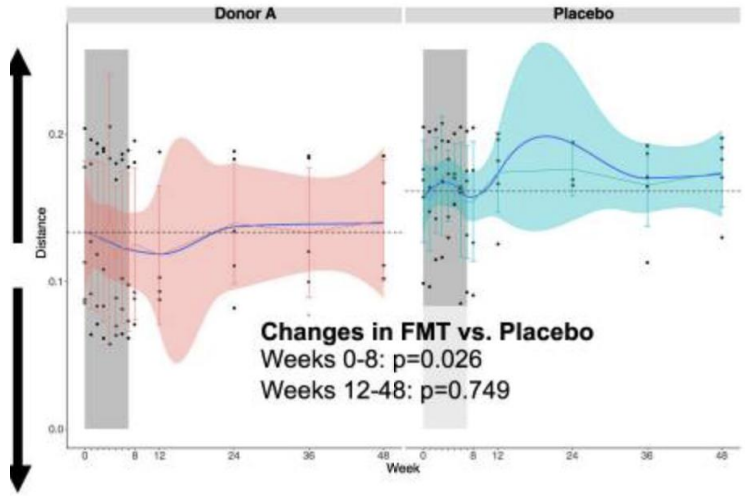
Serrano-Villar, Mucosal Immunology, 2017

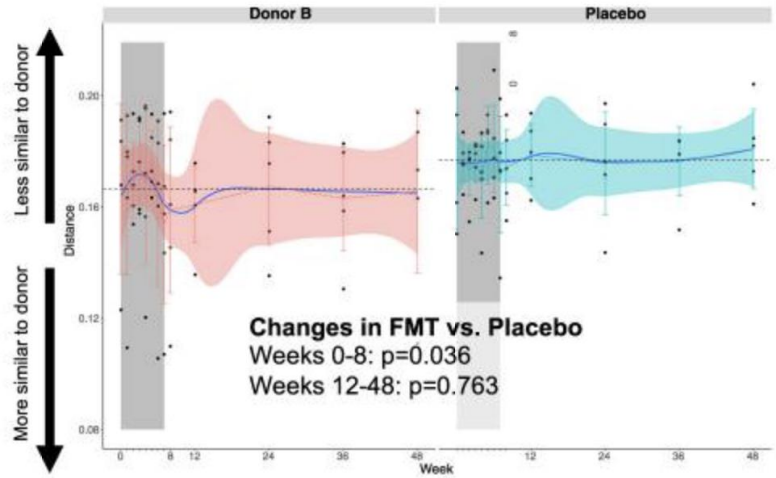
Deusch, AIDS, 2018

Limited engrafment of donor FMT in HIV



FMT via colonoscopy (one-time)





Capsulized FMT (8 weeks)

Vujkovic-Cvijin, Gut Microbes 2017

Serrano-Villar, Nat Commun 20

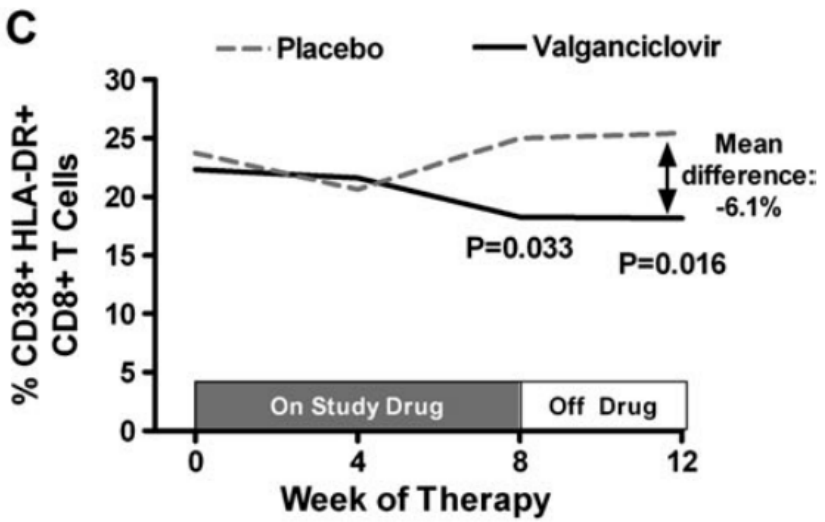
Adjuvant therapuetic strategy #5: reduce immune activation by treating co-infections

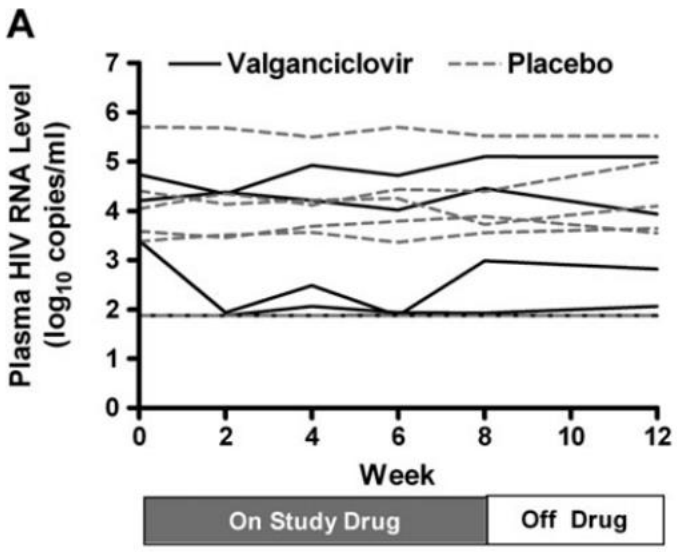
Valganciclovir Reduces T Cell Activation in HIV-infected Individuals With Incomplete $CD4^+$ T Cell Recovery on Antiretroviral Therapy

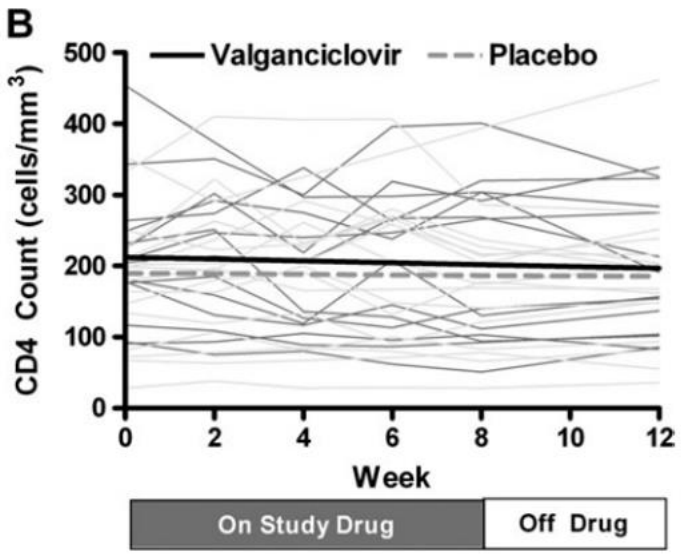
Peter W. Hunt,[1] Jeffrey N. Martin,[1] Elizabeth Sinclair,[1] Lorrie Epling,[1] Juli Teague,[1] Mark A. Jacobson,[1] Russell P. Tracy,[2] Lawrence Corey,[3] and Steven G. Deeks[1]

[1]Departments of Medicine, Epidemiology, and Biostatistics, University of California, San Francisco; [2]Departments of Pathology and Biochemisty, University of Vermont College of Medicine, Burlington; [3]Departments of Laboratory Medicine, Medicine and Microbiology, University of Washington, Fred Hutchison Cancer Research Center, Seattle

- 30 cART-treated, CMV-seropositive participants
- CD4 counts <350 cells/mm^3
- randomized to receive valganciclovir 900 mg daily or placebo for 8 weeks, followed by an additional 4-week observation period
- The primary outcome was the week 8 change in percentage of activated







Letermovir reduces immunologic and cardiometabolic biomarkers in PLWH

Figure 1. Futility Analysis: Letermovir unexpectedly increased sTNFR2 and had little effect on sCD163

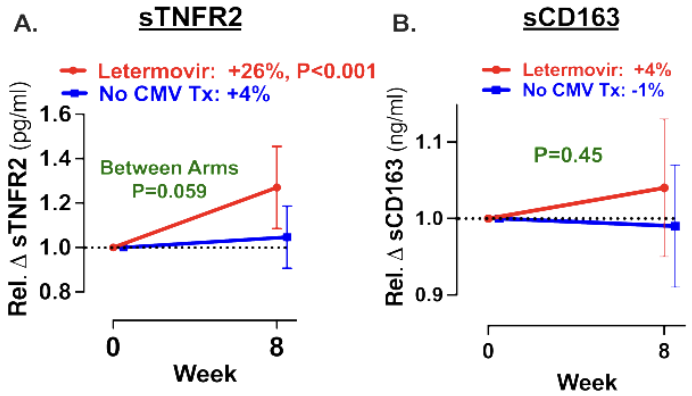


Figure 2. Suppression of CMV viral IL-10 may have contributed to the increase in plasma sTNFR2.

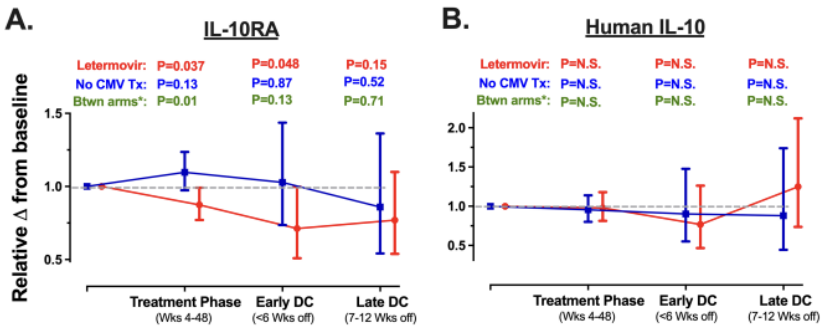
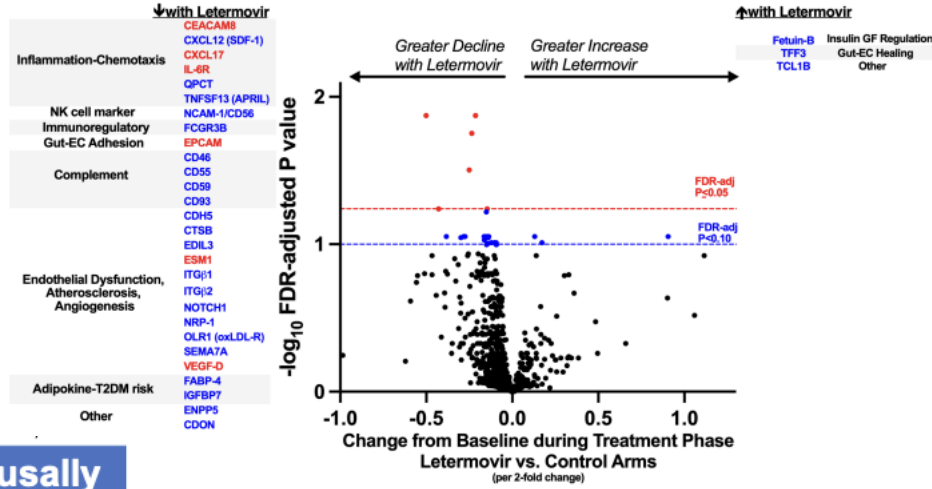


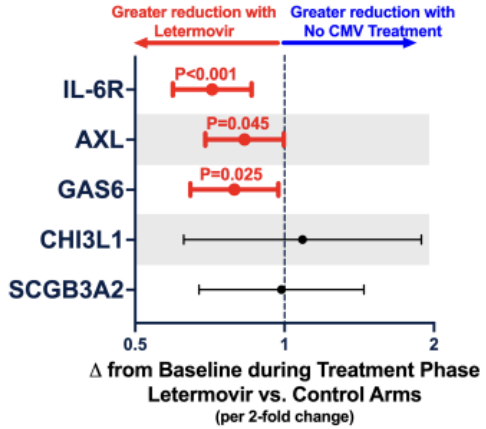
Figure 3. Letermovir broadly impacts immunologic and cardiometabolic biomarkers in people with HIV.



Evaluate the antiinflammatory efficacy of letermovir 480 mg once daily for 48 weeks in PWH and asymptomatic CMV with ART-mediated suppression

Letermovir, n=18
No treatment, n=21

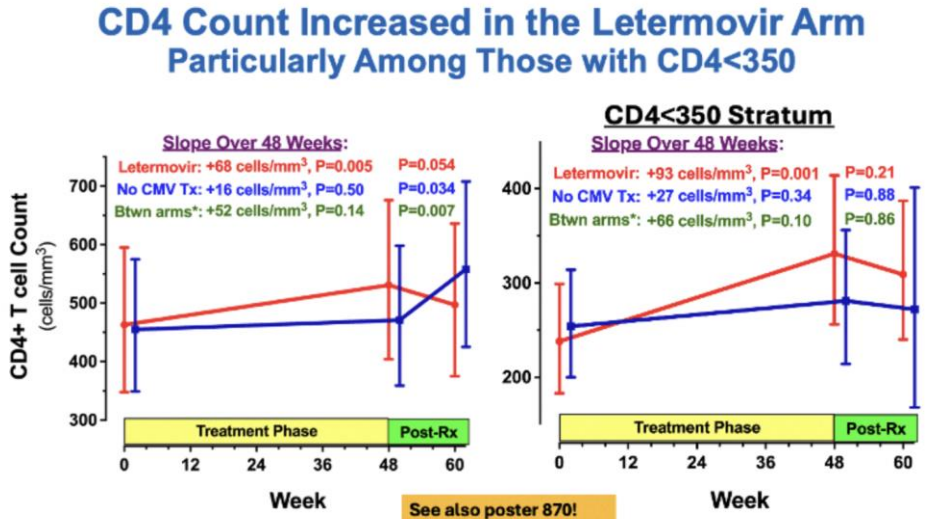
Figure 4. Letermovir suppresses 3/5 proteins causally linked to CVD Events by Mendelian Randomization

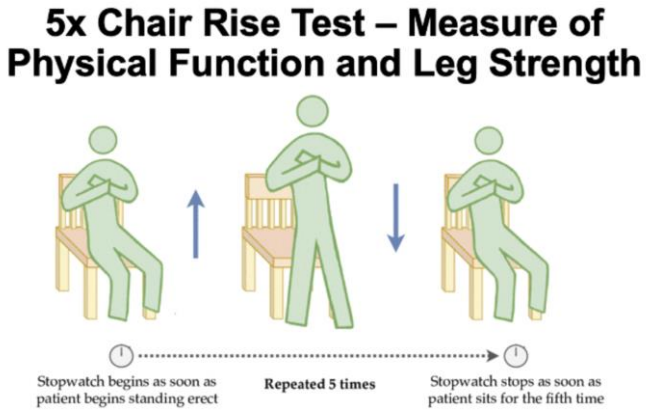


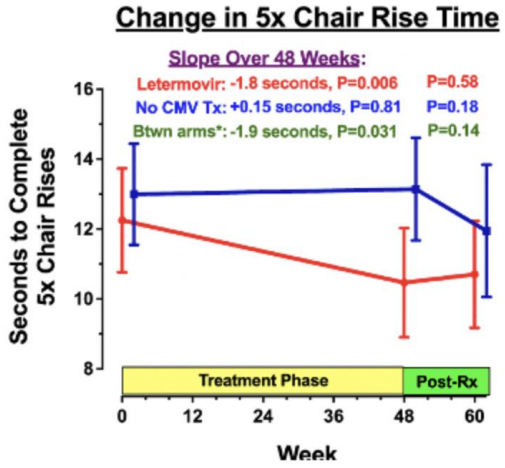
- Reilly et al conducted the first Mendelian Randomization study of causal determinants of CVD events in treated HIV. (Reilly et al, JID, 2023)
- These 5 proteins were the only ones causally linked to CVD events.
- Letermovir decreased three of them (IL-6R, AXL, GAS6) to a greater degree than in the control arm.
- AXL and GAS6 are unique causal predictors of CVD in HIV.
- AXL/GAS6 also linked to transplant vasculopathy (Glinton, J Heart Lung Transpl, 2021)

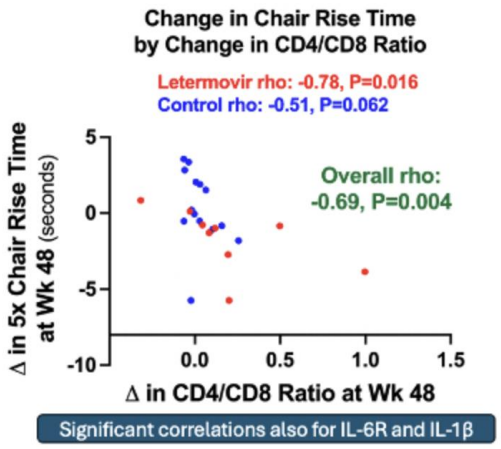
Weibel #354 CROI 2024

Immune and aging benefits following letermovir?









Weibel CROI 2025

Tincati *et al. BMC Infectious Diseases* (2018) 18:8
DOI 10.1186/s12879-017-2942-3

BMC Infectious Diseases

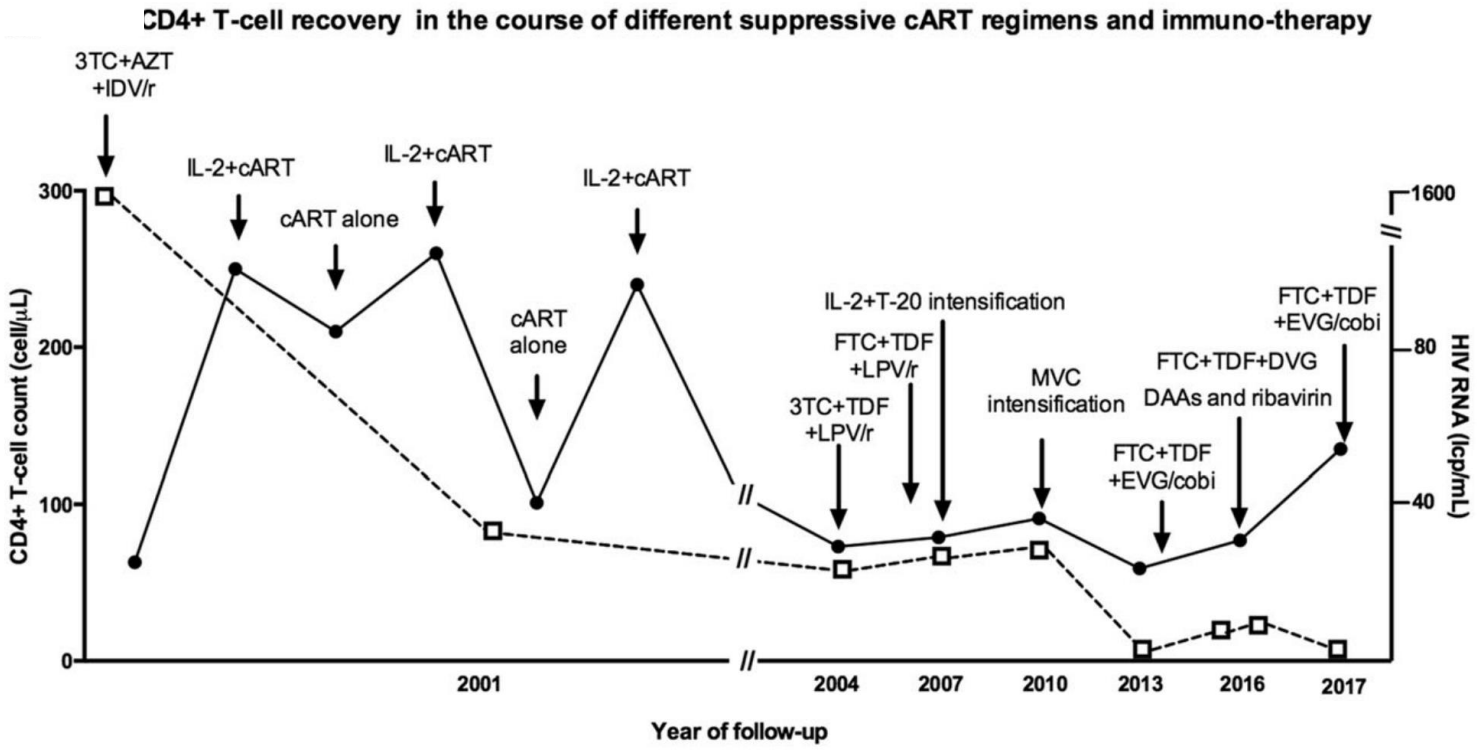
CASE REPORT Open Access

Is weak CD4+ gain in the course of suppressive combination antiretroviral therapy for HIV infection a current clinical challenge? A case report and brief review of the literature

Camilla Tincati*, Esther Merlini, Antonella d'Arminio Monforte and Giulia Marchetti

April 2025 (BIC/FTC/TAF):

- CD4+ T cell count: 89/uL (7%)
- HIV RNA: undetectable



Poor CD4 Cell Recovery and Persistent Inflammation Despite Viral Suppression

Updated: May 26, 2021
Reviewed: May 26, 2021

Key Considerations and Recommendations
• Persistently low CD4 T lymphocyte (CD4) cell counts and immune activation are each associated with increased AIDS- and non-AIDS-related morbidity and mortality among individuals with antiretroviral therapy (ART)-mediated viral suppression. • Adding antiretroviral (ARV) drugs to a suppressive ARV regimen (ART intensification) does not improve CD4 cell recovery or reduce immune activation and, therefore, **is not recommended (AI).** • In individuals with viral suppression, switching ARV drug classes does not consistently improve CD4 cell recovery or reduce all relevant markers of immune activation and **is not recommended (BIII).** • Interleukin-2 **is not recommended (AI)** to increase CD4 cell counts and/or decrease immune activation, because clinical trial data demonstrated no clinical benefit. • Other interventions designed to increase CD4 cell counts and/or decrease immune activation **are not recommended** outside of a clinical trial, because no current interventions have been proven to decrease morbidity or mortality during ART-mediated viral suppression **(AII).** • Efforts to decrease morbidity and mortality during ART-mediated viral suppression should focus on addressing modifiable risk factors for chronic disease (e.g., encouraging smoking cessation, a healthy diet, and regular exercise; treating hypertension and hyperlipidemia). • Monitoring markers of immune activation and inflammation is not recommended, because no intervention targeting immune pathways has proven to improve the health of individuals with HIV, and many blood markers that predict morbidity and mortality fluctuate within individuals **(AII).**
Rating of Recommendations: *A = Strong; B = Moderate; C = Weak* ***Rating of Evidence:*** *I = Data from randomized controlled trials; II = Data from well-designed nonrandomized trials or observational cohort studies with long-term clinical outcomes; III = Expert opinion*

Conclusions

- Poor immune recovery is multifactorial

-cART class/strategy di not appear to impact immune recovery

-adjuvant strategies are ineffective

- Poor immune recovery is linked to disease progression

-need for clinical endpoints, not (only) CD4+ T-cell restoration (IL-2)

- **Prevention of poor immune recovery through early cART introduction (avoiding Late Presentation)**

Acknowledgments

Clinic and Laboratory of Infectious Diseases, Dept of Health Sciences, San Paolo Hospital, University of Milan

- Matteo Augello
- Valeria Bono
- Valentina Sala
- Claudia Acampora
- Marta Limonta
- Andrea Santoro
- Roberta Rovito
- Giulia Marchetti*

Patholgy Unit, Dept of Health Sciences, San Paolo Hospital, University of Milan

- Delfina Tosi
- Carlo Pescia
- Monica Falleni
- Umberto Gianelli

INACTION
ITALIAN NETWORK ACUTE HIV INFECTION

VIROMARKERS
Virus related biomarkers to improve management of chronic conditions

***Funding**

Giovani Ricercatori- Regione Lombardia: GR-2009-1592029

Ministero della Salute-Progetto di Rete: NET-2013-02355333

MIUR-PRIN 2022

Italian Cohort I. C O. N A. Naive Antiretrovirals

innovative health initiative

Co-funded by the European Union