La terapia a lungo termine della infezione da HIV

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Domande nel 1995

- **Quanti sono in CD 4 ?**
- **Quanto mi resta da vivere ?**
- **Quando uscirà una cura ?**

Domande nel 2025

- **Quanto è la carica virale ?**
- **Quanto sono colesterolo e vitamina D ?**
- **Quando uscirà una cura definitiva?**

FDA Approval of HIV Medicines

1981: First AIDS cases are reported in the United States.

1985-89

1987
Zidovudine (NRTI)

1990-94

1991
Didanosine* (NRTI)

1992
Zalcitabine* (NRTI)

1994
Stavudine* (NRTI)

1995-99

1995
Lamivudine (NRTI)
Saquinavir Mesylate* (PI)

1996
Indinavir* (PI)
Nevirapine (NNRTI)
Ritonavir (PI)

1997
Combivir† (FDC)
Delavirdine* (NNRTI)
Nelfinavir* (PI)
Saquinavir* (PI)

1998
Abacavir (NRTI)
Efavirenz (NNRTI)

1999
Amprenavir* (PI)

2000-04

2000
Didanosine EC* (NRTI)
Kaletra (FDC)
Trizivir* (FDC)

2001
Tenofovir DF (NRTI)

2002
Stavudine XR* (NRTI)

2003
Atazanavir (PI)
Emtricitabine (NRTI)
Enfuvirtide* (FI)
Fosamprenavir* (PI)

2004
Epzicom† (FDC)
Truvada (FDC)

2005-09

2005
Tipranavir* (PI)

2006
Atripla† (FDC)
Darunavir (PI)

2007
Maraviroc (CA)
Raltegravir (INSTI)

2008
Etravirine (NNRTI)

2010-14

2011
Complera (FDC)
Nevirapine XR (NNRTI)
Rilpivirine (NNRTI)

2012
Stribild (FDC)
Truvada (PrEP)

2013
Dolutegravir (INSTI)

2014
Cobicistat (PE)
Elvitegravir* (INSTI)
Triumeq (FDC)

2015-19

2015
Evotaz (FDC)
Genvoya (FDC)
Prezcobix (FDC)

2016
Descovy (FDC)
Odefsey (FDC)

2017
Juluca (FDC)
Raltegravir HD (INSTI)

2018
Biktarvy (FDC)
Cimduo (FDC)
Delstrigo (FDC)
Doravirine (NNRTI)
Ibalizumab-uiyk (PAI)
Symfi (FDC)
Symfi Lo† (FDC)
Symtuza (FDC)
Temixys* (FDC)

2019
Dovato (FDC)
Descovy (PrEP)

2020-24

2020
Fostemsavir* (AI)
Tivicay PD (INSTI)

2021
Cabenuva (FDC)
Cabotegravir (INSTI)
Cabotegravir (PrEP)

2022
Triumeq PD (FDC)
Lenacapavir (CI)

2024
Rilpivirine PED (NNRTI)

2025
Lenacapavir (PrEP)

Drug Class Abbreviations:
AI: Attachment Inhibitor; CA: CCR5 Antagonist; CI: Capsid Inhibitors; FDC: Fixed-Dose Combination; FI: Fusion Inhibitor; INSTI: Integrase Inhibitor; NNRTI: Non-Nucleoside Reverse Transcriptase Inhibitor; NRTI: Nucleoside Reverse Transcriptase Inhibitor; PE: Pharmacokinetic Enhancer; PI: Protease Inhibitor; PAI: Post-Attachment Inhibitor; PrEP: Pre-exposure prophylaxis

Note: Approvals are for HIV treatment, unless otherwise indicated.
*Drugs in gray are no longer available and/or are no longer recommended for use in the United States by the HHS HIV/AIDS medical practice guidelines. These drugs may still be used in fixed-dose combination formulations.
†Fixed-dose combination brand products that are available as generic only.

Life expectancy after 2015 of adults with HIV on long-term antiretroviral therapy in Europe and North America: a collaborative analysis of cohort studies

Adam Trickey, Caroline A Sabin, Greer Burkholder, Heidi Crane, Antonella d'Arminio Monforte, Matthias Egger, M John Gill, Sophie Grabar, Jodie L Guest, Inma Jarrin, Fiona C Lampe, Niels Obel, Juliana M Reyes, Christoph Stephan, Timothy R Sterling, Ramon Teira, Giota Touloumi, Jan-Christian Wasmuth, Ferdinand Wit, Linda Wittkop, Robert Zangerle, Michael J Silverberg, Amy Justice, Jonathan A C Sterne

206.891 persone con HIV prese in considerazione, a partire dal 2015

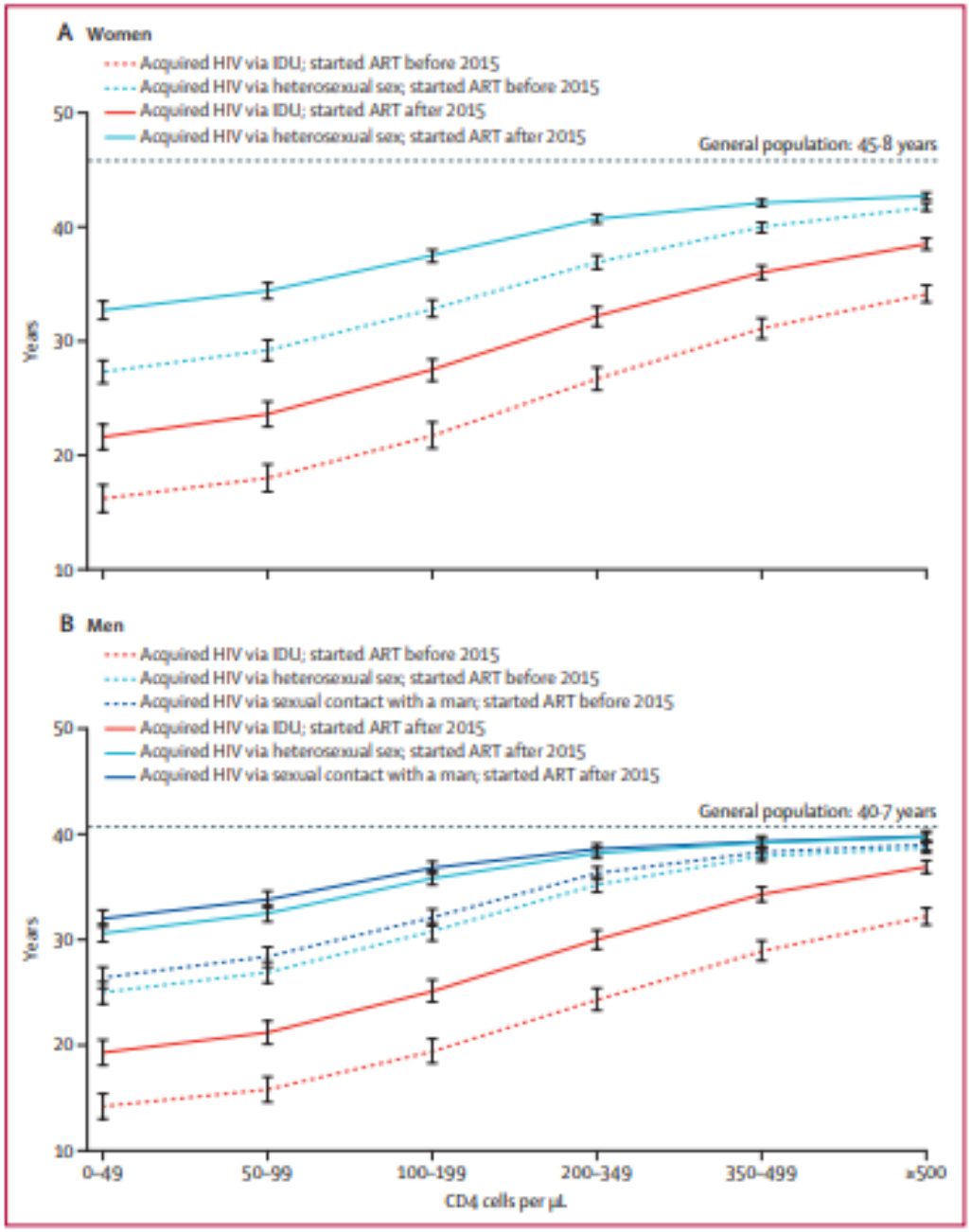


Figure: **Estimated years of life left at age 40 years for women (A) and men (B) with HIV on ART who had suppressed viral loads and did not have AIDS at the start of follow-up**

Data are stratified by CD4 cell count, HIV acquisition route, and ART start year. Error bars show 95% CIs. ART=antiretroviral therapy. IDU=injecting drug use.

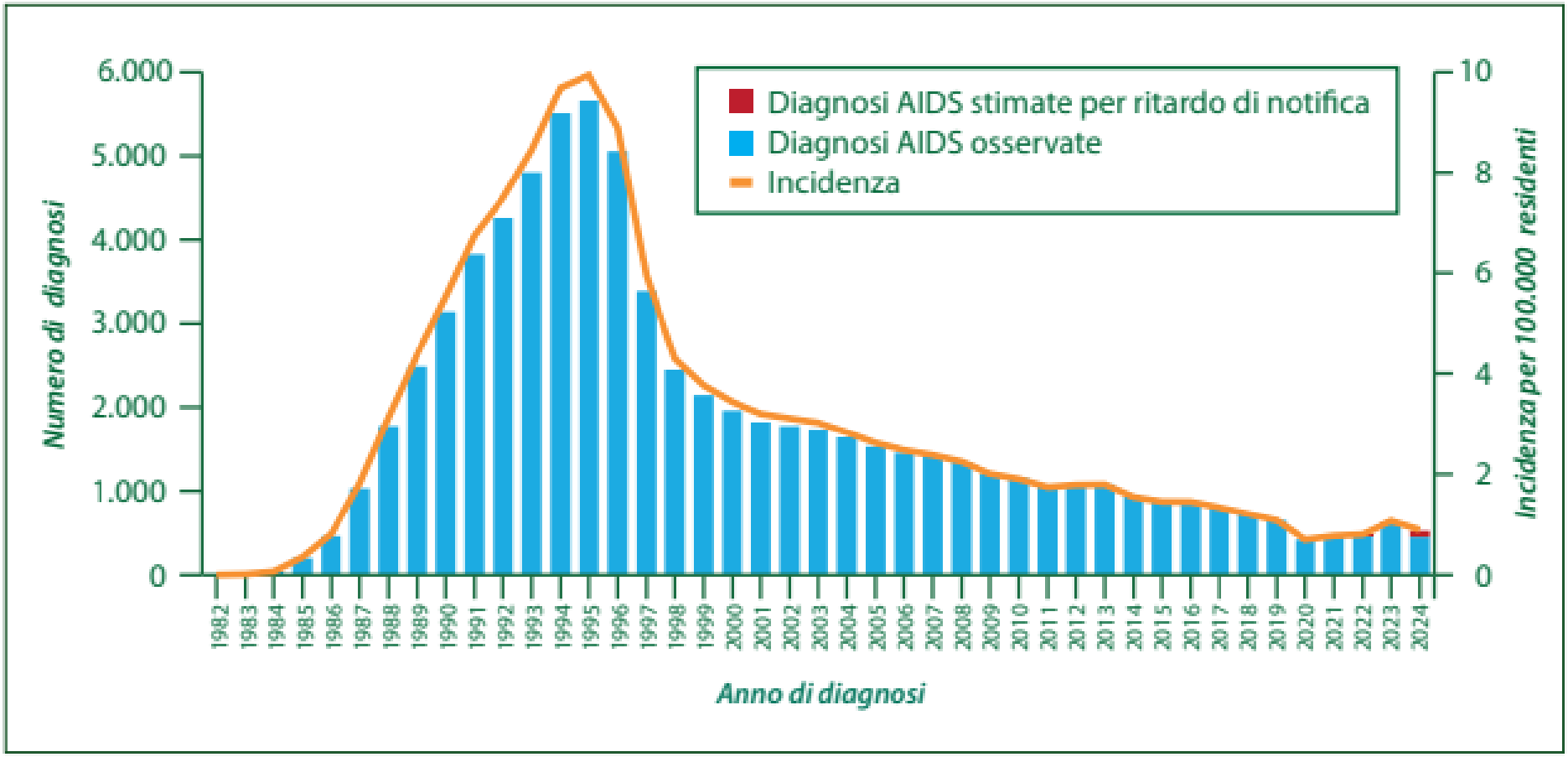
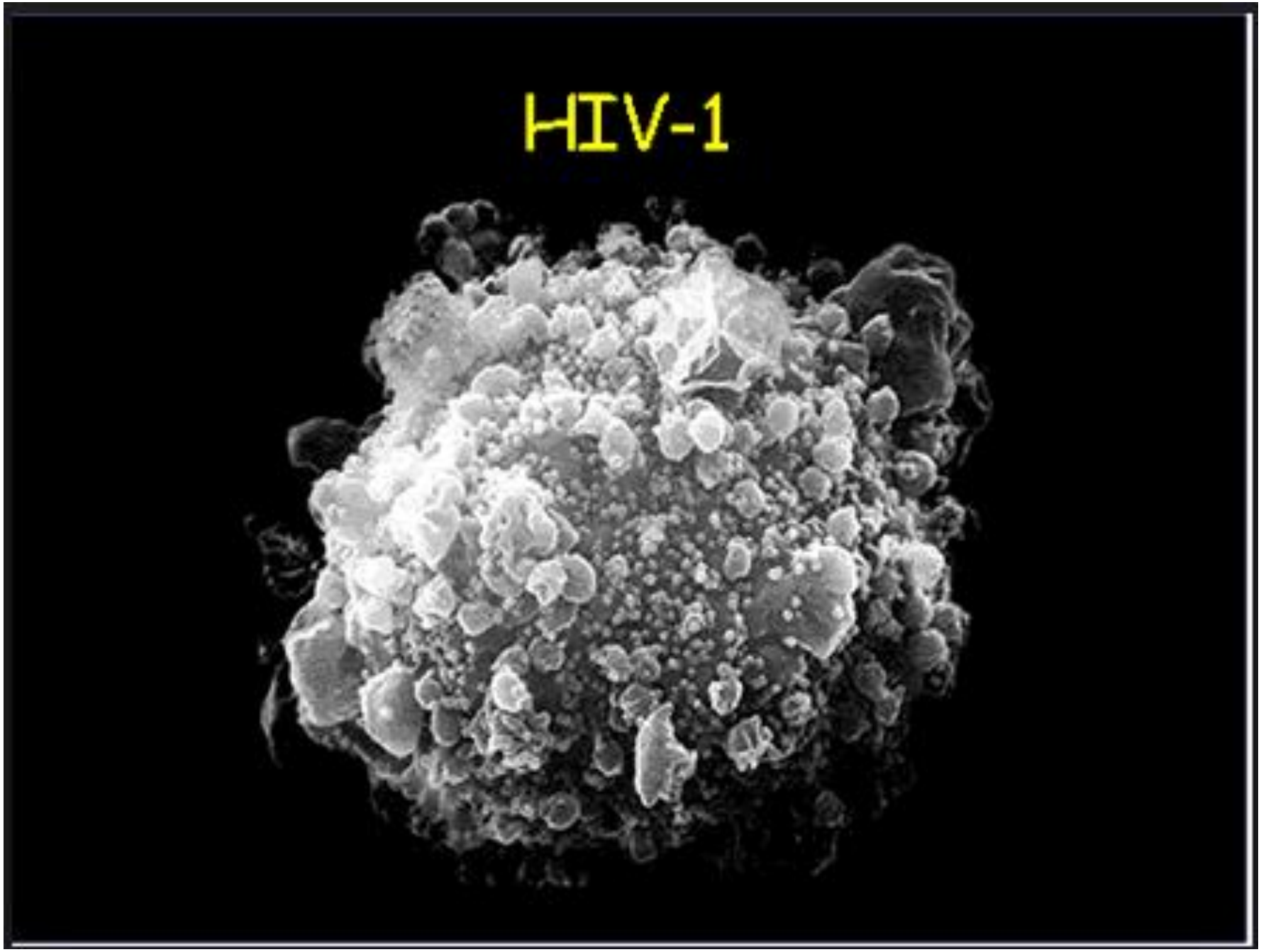
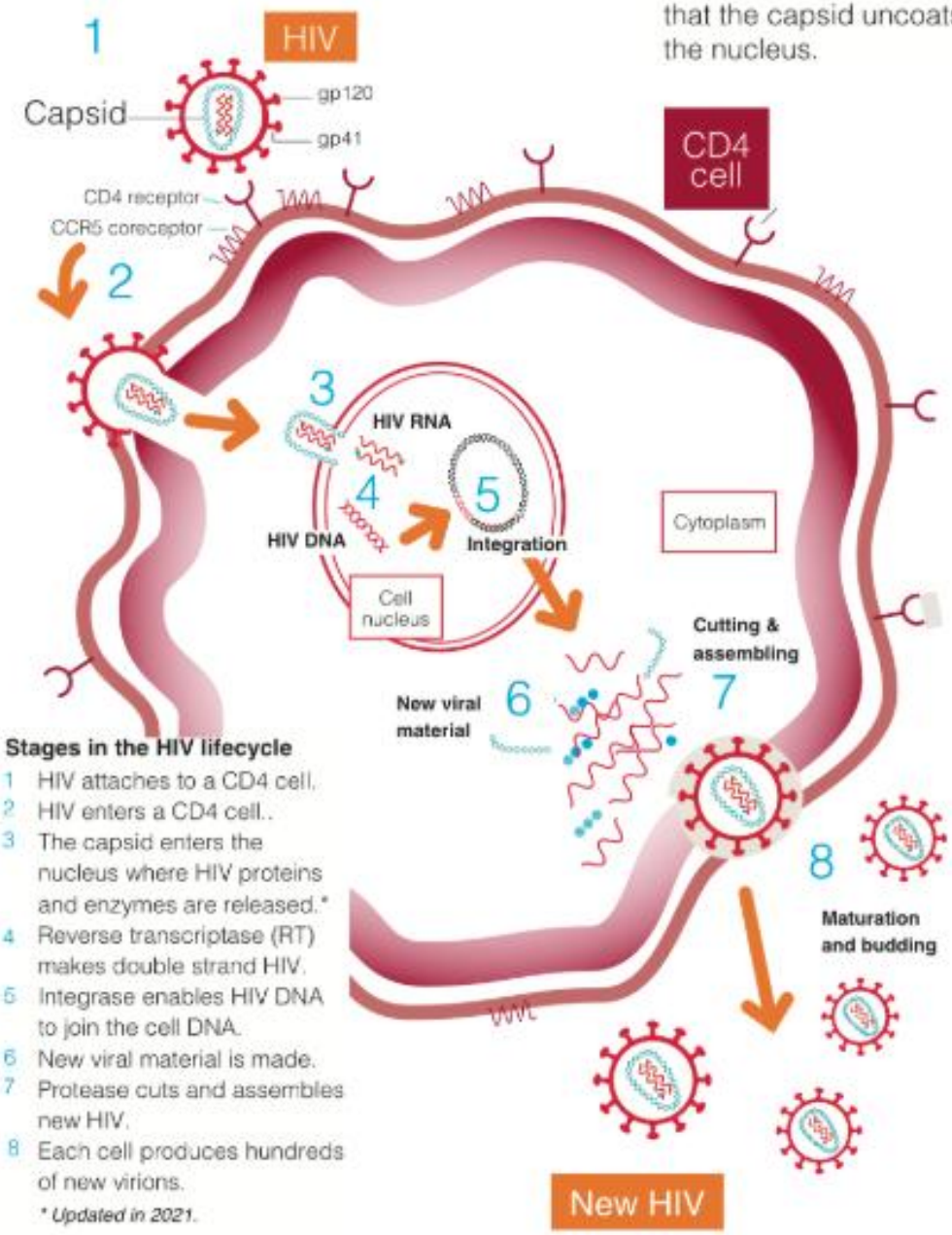


Figura 16 - Nuove diagnosi AIDS e incidenze corrette per ritardo di notifica (1982-2024)


HIV-1

HIV lifecycle (2021)

Note: In March 2021, researchers accepted that the capsid uncoats in the nucleus.



Stages in the HIV lifecycle

1. HIV attaches to a CD4 cell.
2. HIV enters a CD4 cell..
3. The capsid enters the nucleus where HIV proteins and enzymes are released.*
4. Reverse transcriptase (RT) makes double strand HIV.
5. Integrase enables HIV DNA to join the cell DNA.
6. New viral material is made.
7. Protease cuts and assembles new HIV.
8. Each cell produces hundreds of new virions.

** Updated in 2021.*

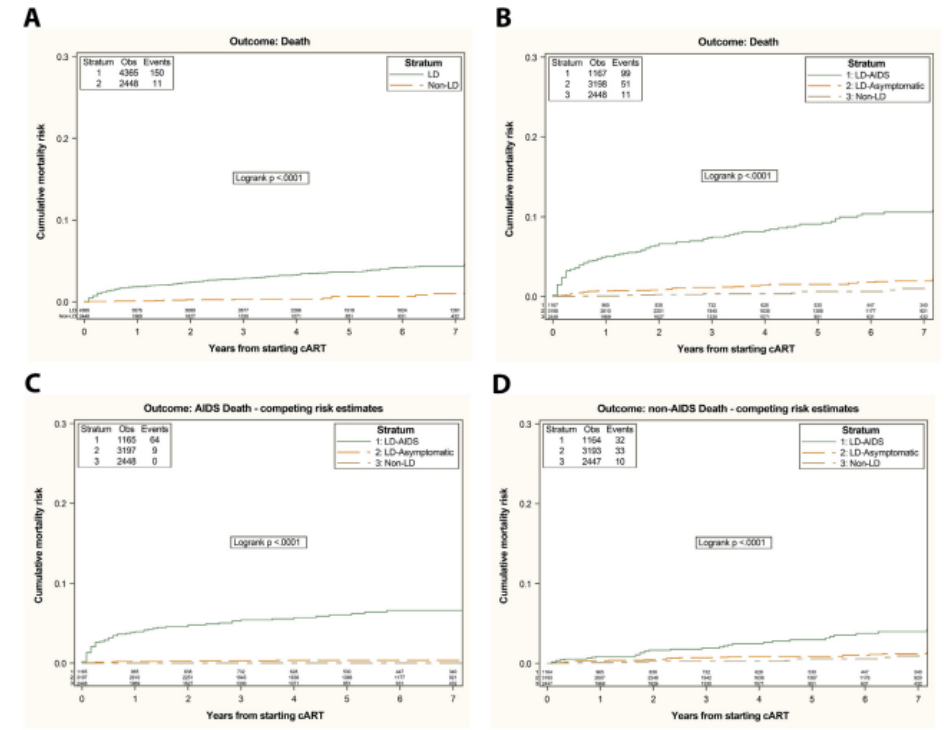
Di più

- Puo' essere che le PLWH arrivino a vivere più a lungo della popolazione non contagiata :
- Controlli ematici ogni 6 mesi
- Cambiamenti stili di vita (sedentarietà , fumo, cibo)
- Cura delle altre patologie,
- Vaccinazioni

Persistent poor clinical outcomes of people living with HIV presenting with AIDS and late HIV diagnosis – results from the ICONA cohort in Italy, 2009-2022

Annalisa Mondi[1], Alessandro Cozzi-Lepri[2], Alessandro Tavelli[3,*], Antonella Cingolani[4], Andrea Giacomelli[5], Giancarlo Orofino[6], Gabriella De Girolamo[7], Carmela Pinnetti[1], Andrea Gori[8], Annalisa Saracino[9], Alessandra Bandera[10], Giulia Marchetti[11], Enrico Girardi[12], Cristina Mussini[13], Antonella d'Arminio Monforte[3], Andrea Antinori[1], for the ICONA Foundation Study Group[§]

International Journal of Infectious Diseases 142 (2024) 106995



ure 1. Kaplan–Meier curves for all-cause mortality (non-LD vs LD [a] and non-LD vs LD-asymptomatic vs LD-AIDS [b]) and cause-specific mortality[a] (AIDS-related deaths and non-AIDS–related deaths [d]) according to the exposure group. [a]Competing risk Kaplan–Meier curves. cART, combined antiretroviral therapy; LD, late diagnosis; -LD, non-late diagnosis.

- **La chiave del successo, in termini di sopravvivenza della persona, passa per la capacità che hanno questi farmaci di praticamente azzerare la replicazione virale e spegnere la malattia , se assunti fedelmente**
- **Può, una persona, ragionevolmente pensare di assumere una compressa (o più compresse) per tutta la vita, senza saltare mai ?**

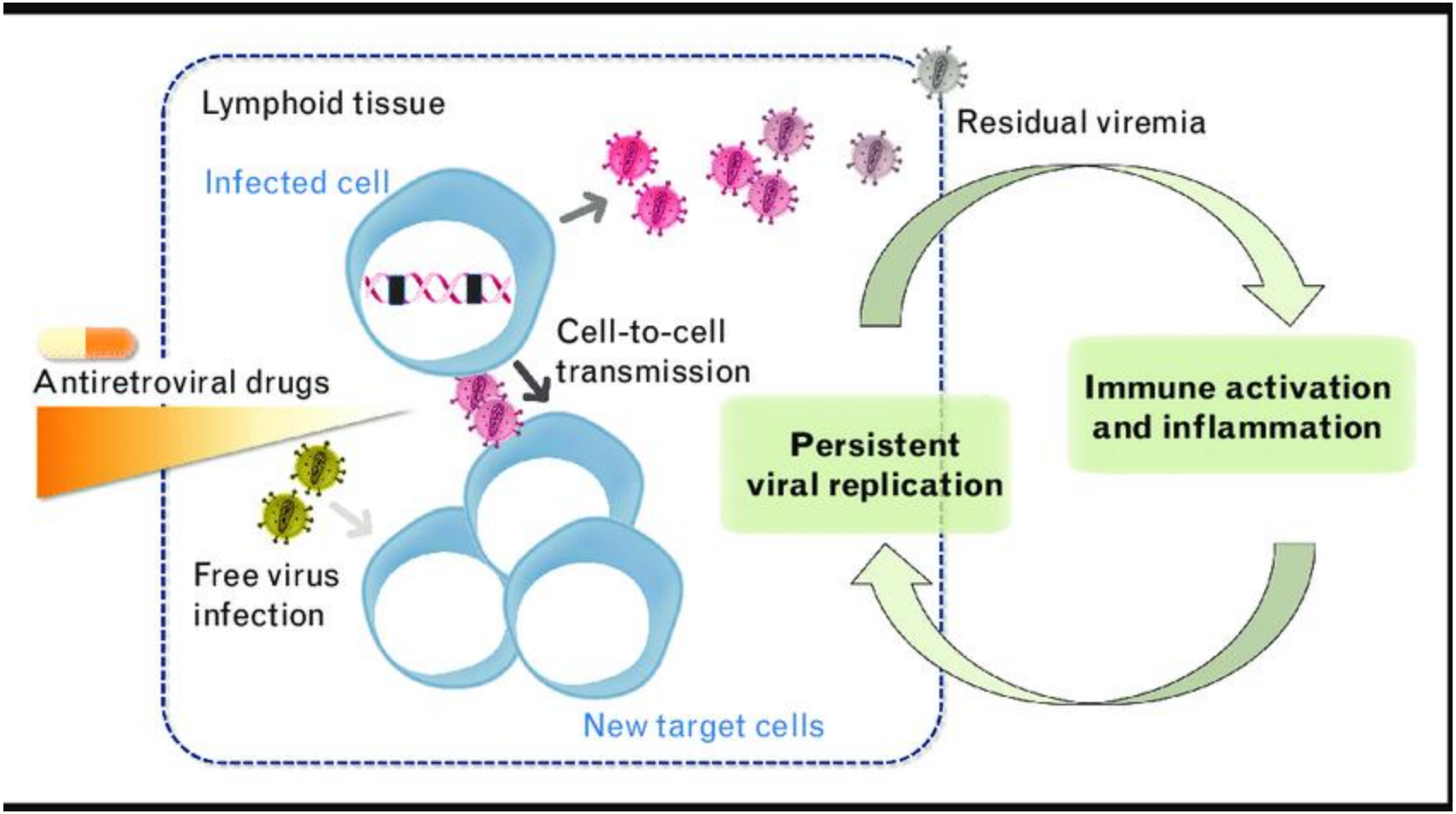
La sfida della aderenza terapeutica a lungo termine

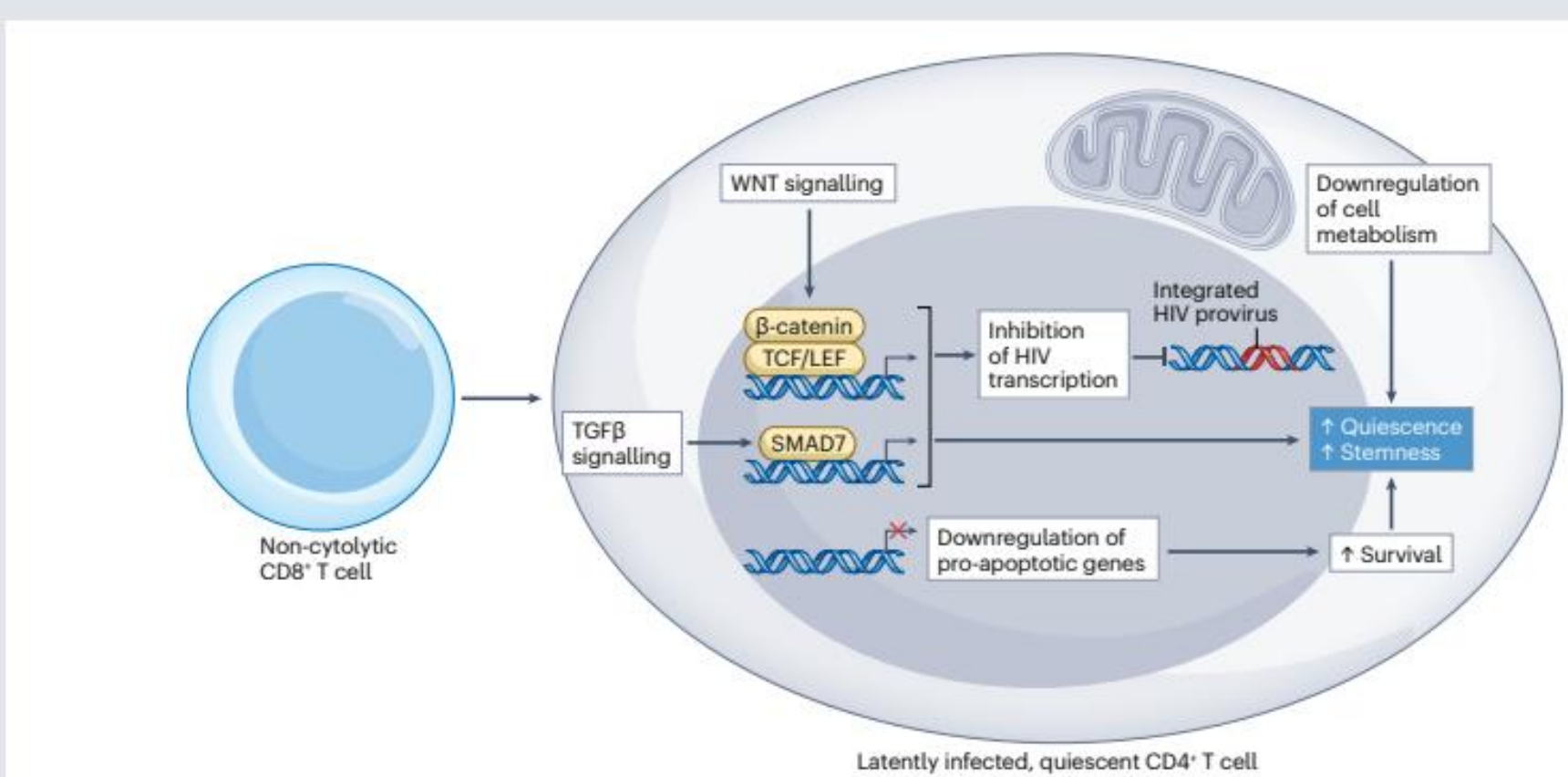

Long-Acting Antiretrovirals

Si può dire che i primi L.A sono solo dei prototipi, per quanto altamente efficaci
La persona delega la sua cura ad altri (iniezioni) e si “ libera ” dalla schiavitù delle compresse
Altre strategie L.A. seguiranno, anche con farmaci per os (ma con meno assunzioni)
La strada ormai aperta e non si torna indietro

Che cosa significa U = U

- È una formula, una equivalenza , che si può utilizzare anche sotto forma di slogan, che sintetizza un dato scientifico : **una persona con infezione da HIV e con viremia soppressa (la prima U) nel plasma da almeno 6 mesi ed in trattamento antiretrovirale efficace e correttamente assunto ha un rischio pari a 0 di trasmettere (la seconda U) la infezione da HIV ad un partner , attraverso rapporti sessuali non protetti dal condom**


Lymphoid tissue
Infected cell
Residual viremia
Cell-to-cell transmission
Antiretroviral drugs
Immune activation and inflammation
Persistent viral replication
Free virus infection
New target cells



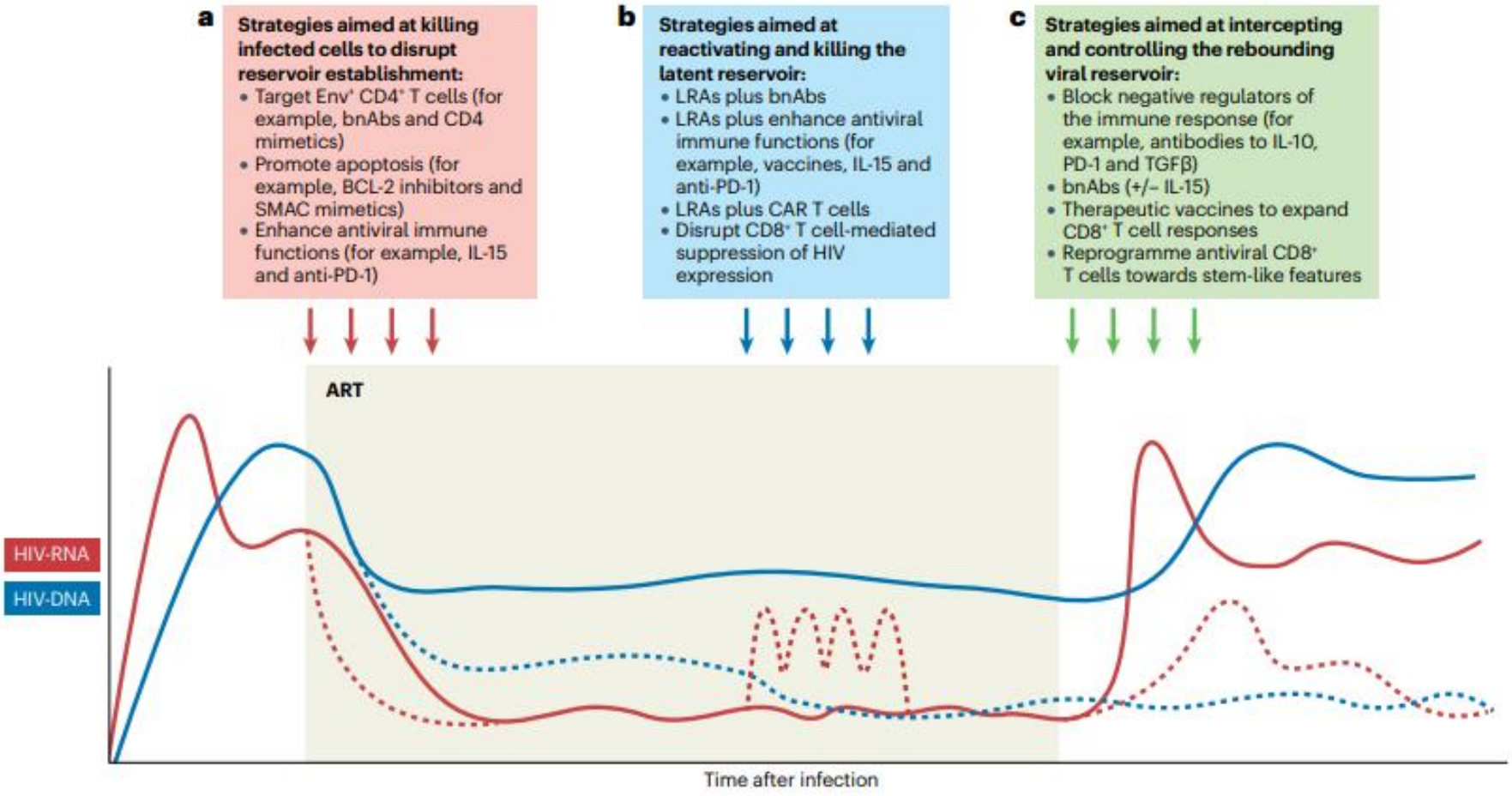
Perspective

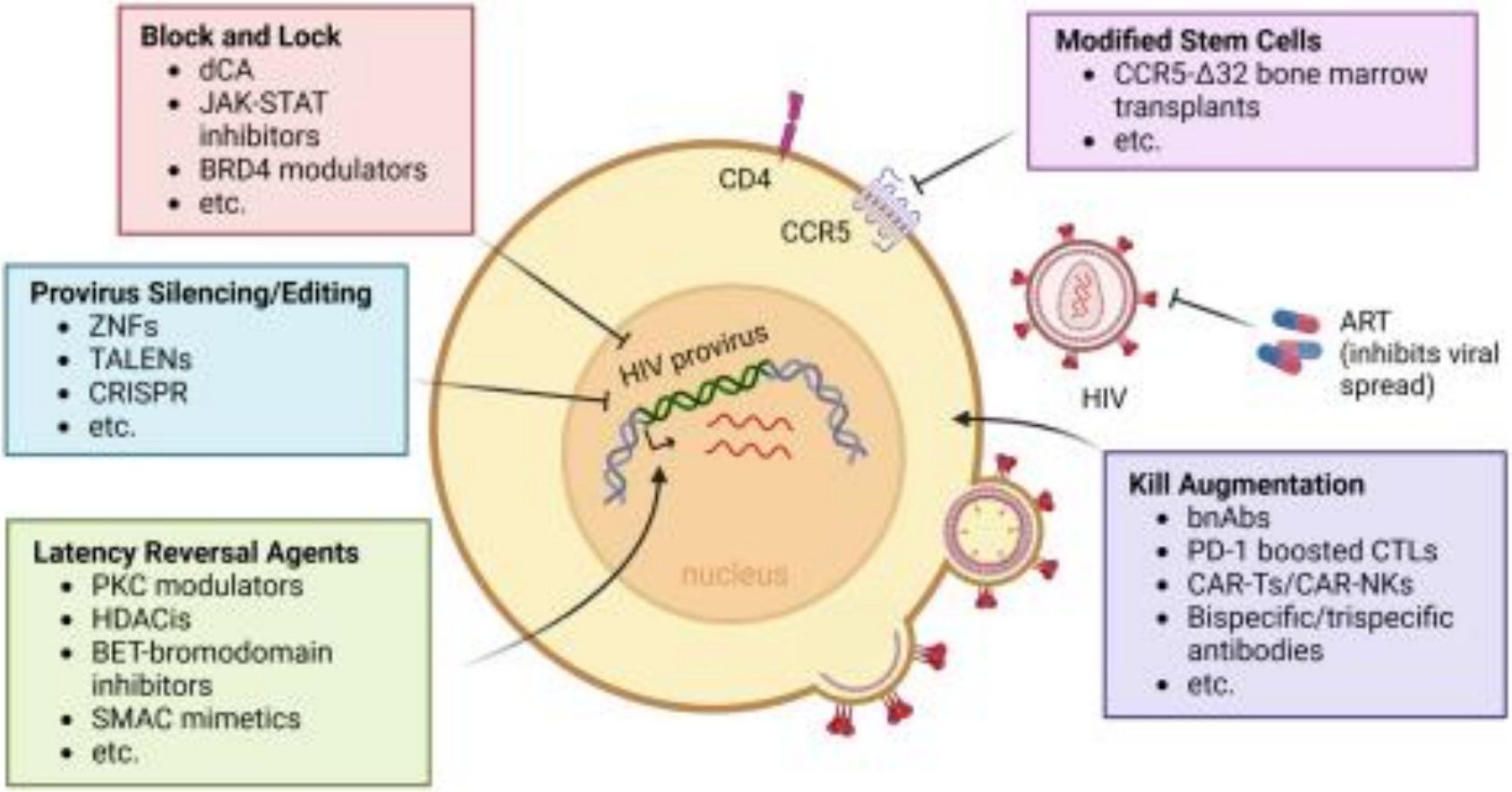
Check for updates

Immune-mediated strategies to solving the HIV reservoir problem

Deanna A. Kulpa[1,2], Mirko Paiardini[1,2] & Guido Silvestri[1,2]

Nature Reviews Immunology | Volume 25 | July 2025 | 542–553


a
Strategies aimed at killing infected cells to disrupt reservoir establishment:
• Target Env+ CD4+ T cells (for example, bnAbs and CD4 mimetics)
• Promote apoptosis (for example, BCL-2 inhibitors and SMAC mimetics)
• Enhance antiviral immune functions (for example, IL-15 and anti-PD-1)
b
Strategies aimed at reactivating and killing the latent reservoir:
• LRAs plus bnAbs
• LRAs plus enhance antiviral immune functions (for example, vaccines, IL-15 and anti-PD-1)
• LRAs plus CAR T cells
• Disrupt CD8+ T cell-mediated suppression of HIV expression
c
Strategies aimed at intercepting and controlling the rebounding viral reservoir:
• Block negative regulators of the immune response (for example, antibodies to IL-10, PD-1 and TGFβ)
• bnAbs (+/– IL-15)
• Therapeutic vaccines to expand CD8+ T cell responses
• Reprogramme antiviral CD8+ T cells towards stem-like features
ART
HIV-RNA
HIV-DNA
Time after infection



Review

HIV Persistence, Latency, and Cure Approaches: Where Are We Now?

Viruses **2024**, *16*, 1163

Tessa C. Chou [1], Nishad S. Maggirwar [1] and Matthew D. Marsden [1,2,*]