European AIDS Treatment Group

ageing with HIV

# Ageing with HIV Conference
# NEW CHALLENGES AND UNMET NEEDS OF PEOPLE LIVING AND AGEING WITH HIV/AIDS AGED 18 - 50
## Quality of Life and Preventive Healthcare

3-6 May 2018 Alfavito Hotel, Kyiv, Ukraine

Session: **HIV CURE - managing expectations**

# Overview

*Giulio Maria Corbelli, European AIDS Treatment Group (EATG)*

European AIDS Treatment Group

ageing with HIV

# Outline

- What is a cure for HIV infection?
- Which strategies are being explored?
- Managing community concerns and expectations

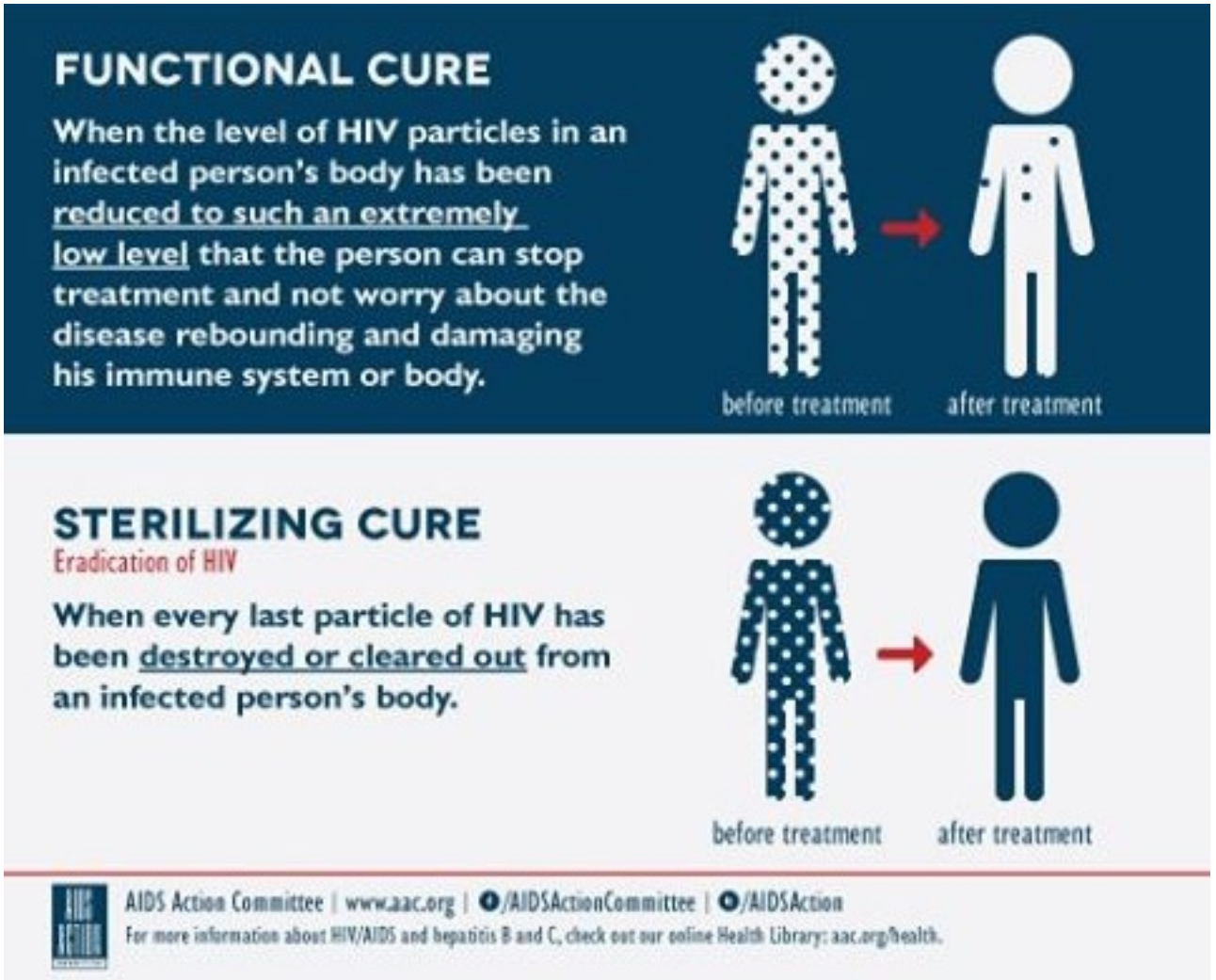
European AIDS Treatment Group

ageing with HIV

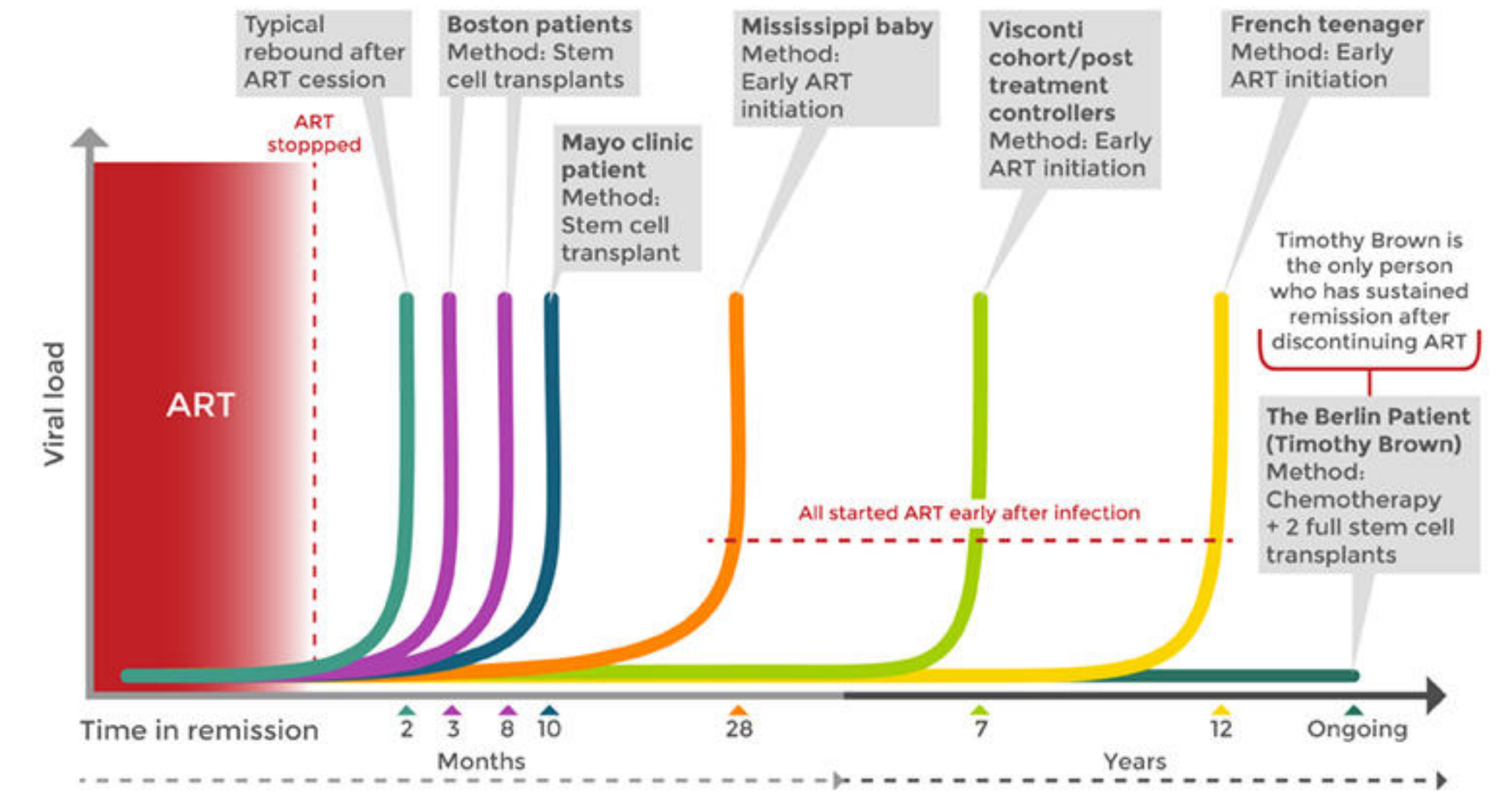
# What does ‘cure’ mean?

- No need for on-going medication (ARV treatment)
- No symptoms (clinical progression)
- No viral progression/immune damage
- No risk of transmission

# Two different ‘curative’ approaches



# HIV cure trials: Time in remission and viral rebound after ART cessation

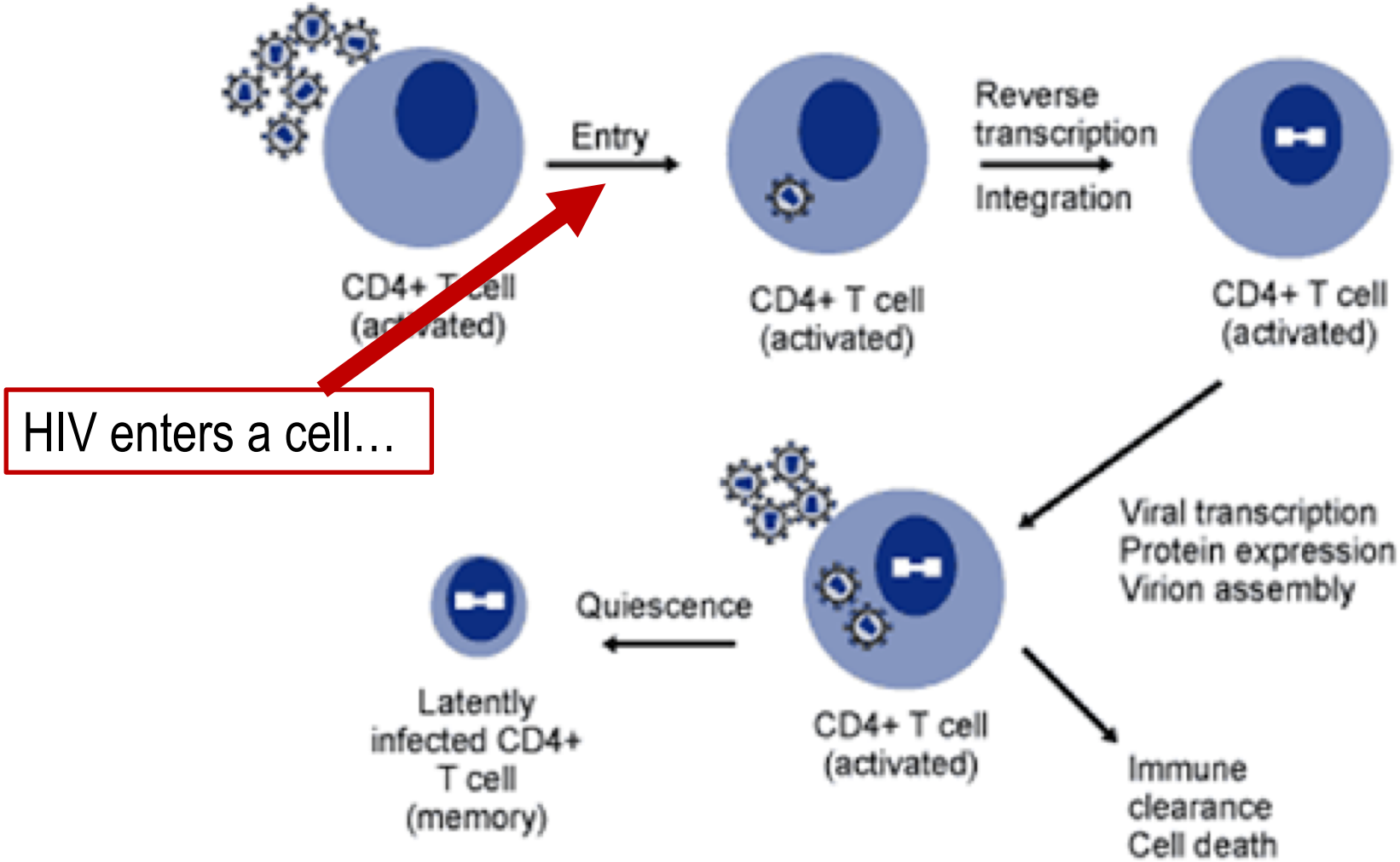



AVERT.org Source: IAS Society 'Full recommendations: Towards an HIV cure 2016'

European AIDS Treatment Group

# Why is it so hard to 'cure' HIV infection?

ageing with HIV




Schematic representation of the establishment of a latent HIV reservoir in quiescent memory CD4 T cells

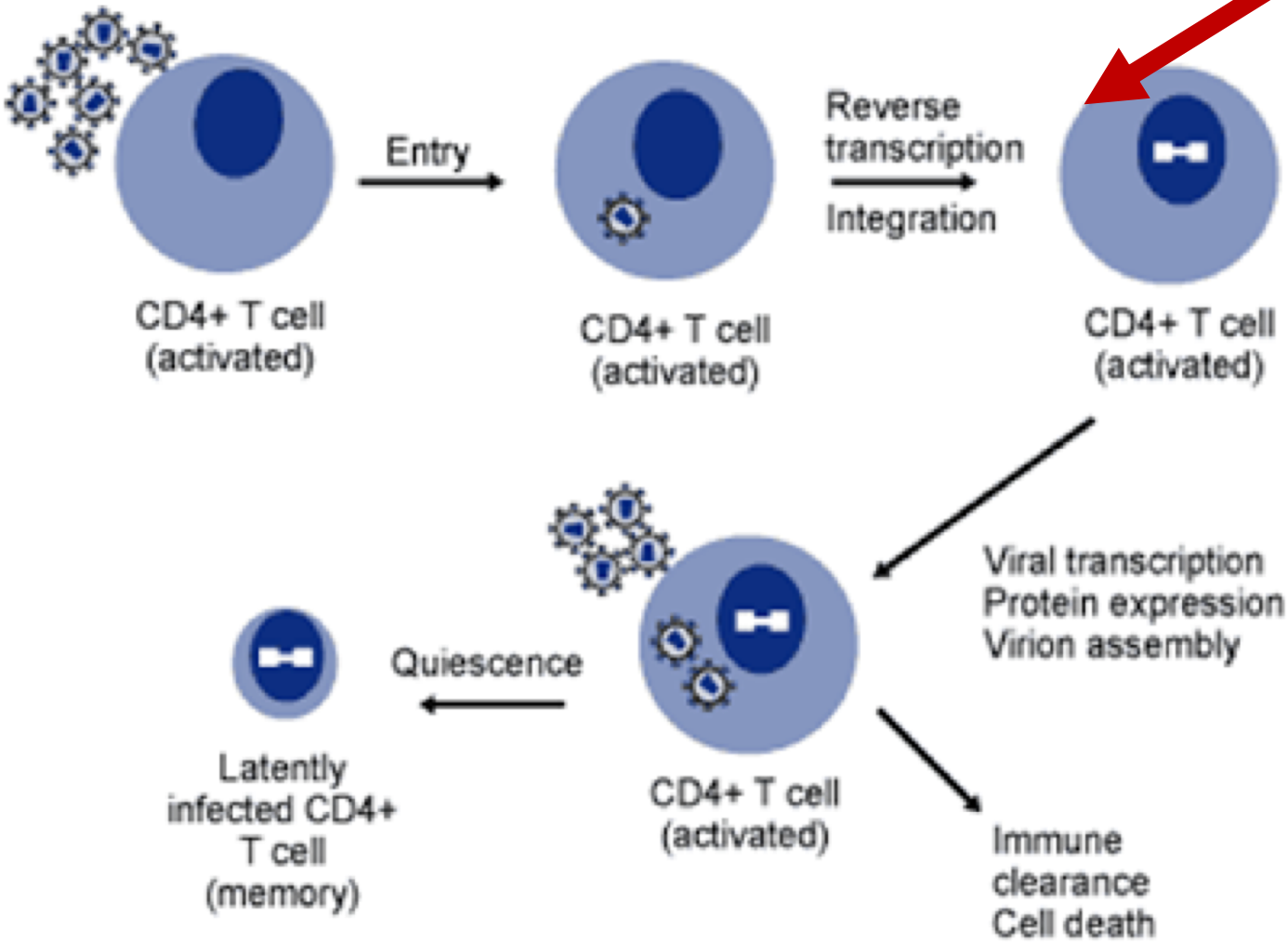
Source: The GW Research Center for the Eradication of HIV. https://smhs.gwu.edu/timetoendhiv/hiv-aids/finding-a-cure

European AIDS Treatment Group

# Why is it so hard to 'cure' HIV infection?

ageing with HIV

and integrates into the cell's DNA



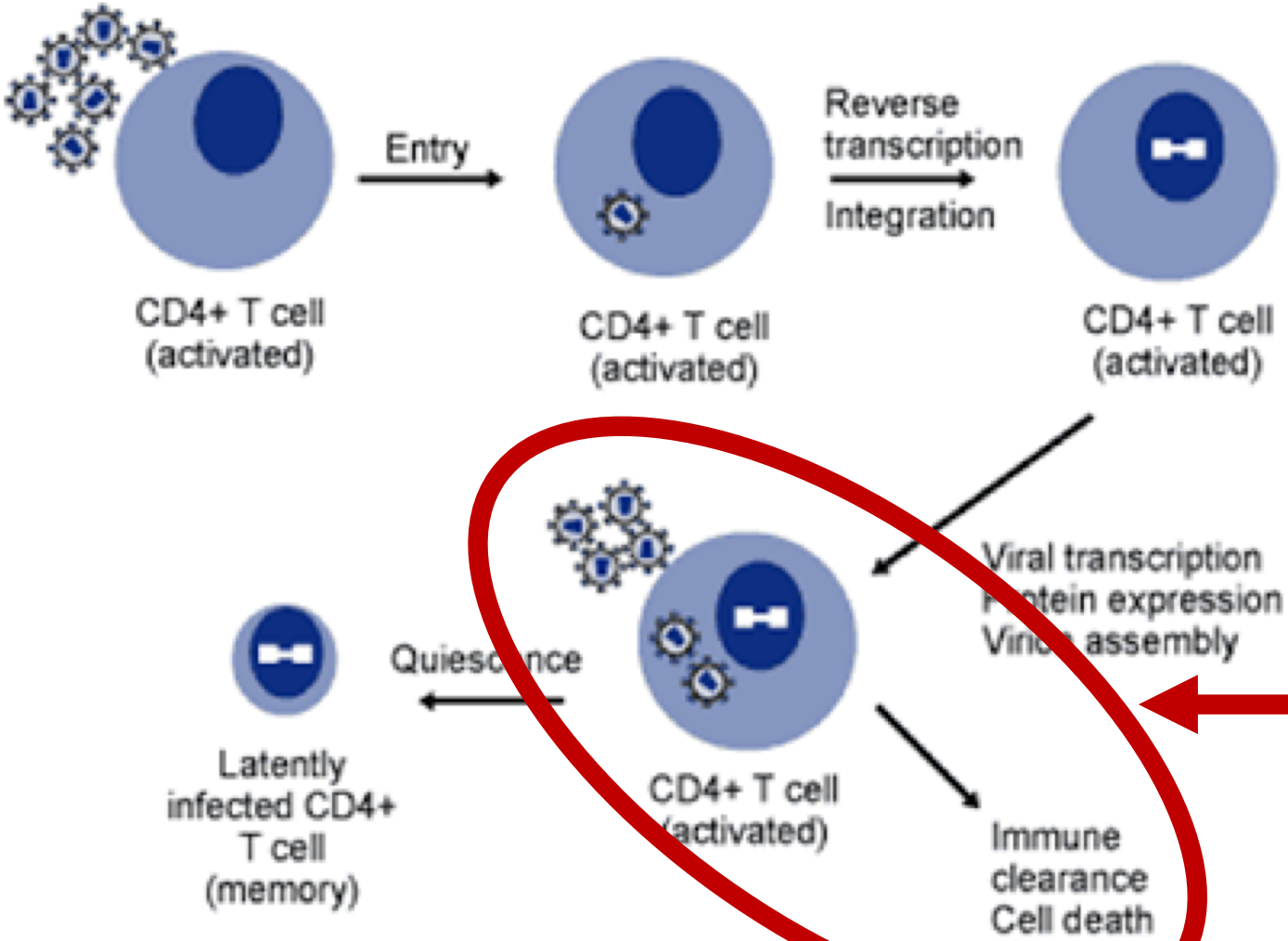

Schematic representation of the establishment of a latent HIV reservoir in quiescent memory CD4 T cells

Source: The GW Research Center for the Eradication of HIV. https://smhs.gwu.edu/timetoendhiv/hiv-aids/finding-a-cure

European AIDS Treatment Group

# Why is it so hard to 'cure' HIV infection?

ageing with HIV




Schematic representation of the establishment of a latent HIV reservoir in quiescent memory CD4 T cells

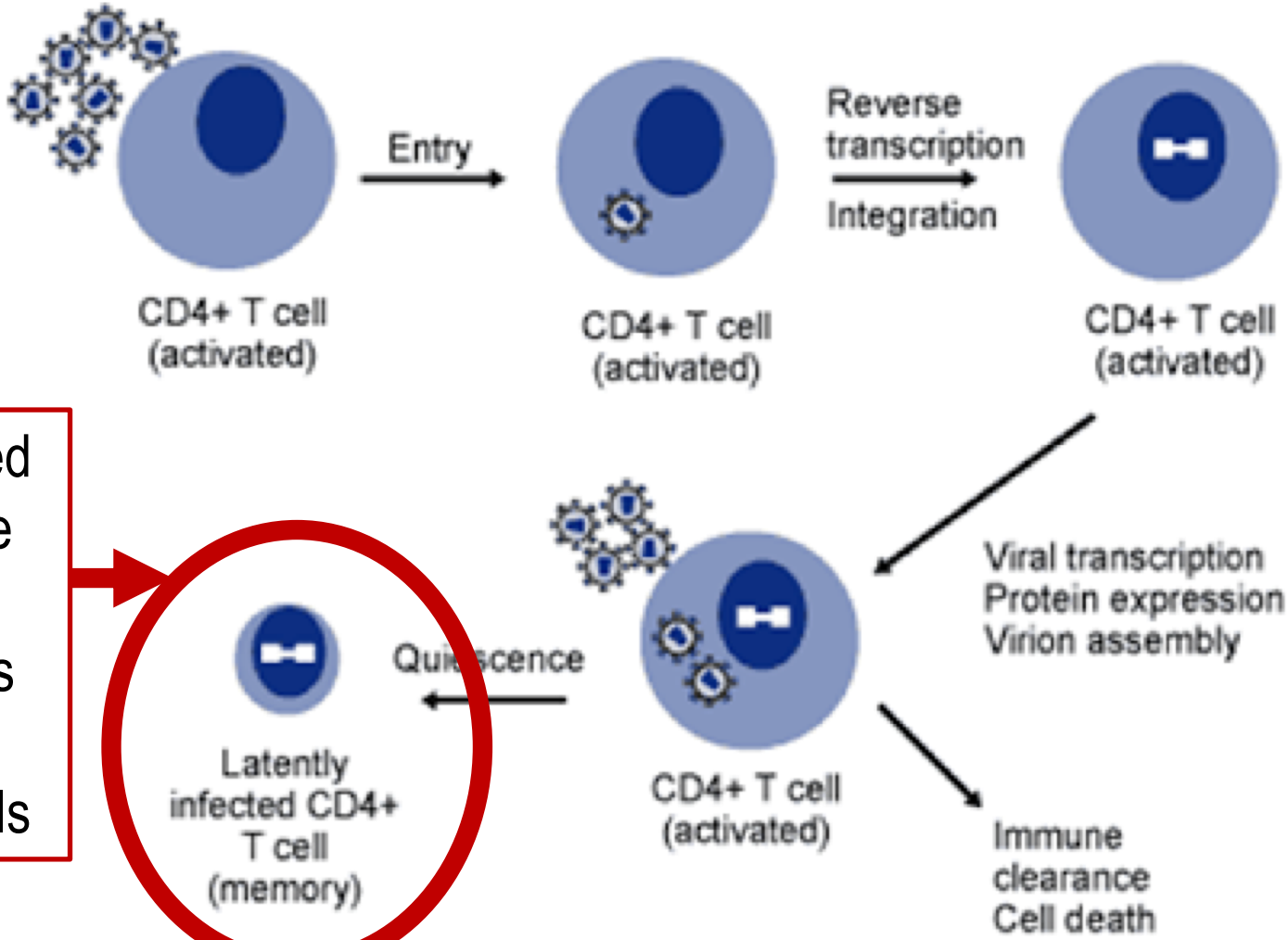
Most cells recognize infection, causing cell death

Source: The GW Research Center for the Eradication of HIV. https://smhs.gwu.edu/timetoendhiv/hiv-aids/finding-a-cure

European AIDS Treatment Group

# Why is it so hard to 'cure' HIV infection?

ageing with HIV




A few infected cells become "long-lived" memory cells or "resting memory" cells

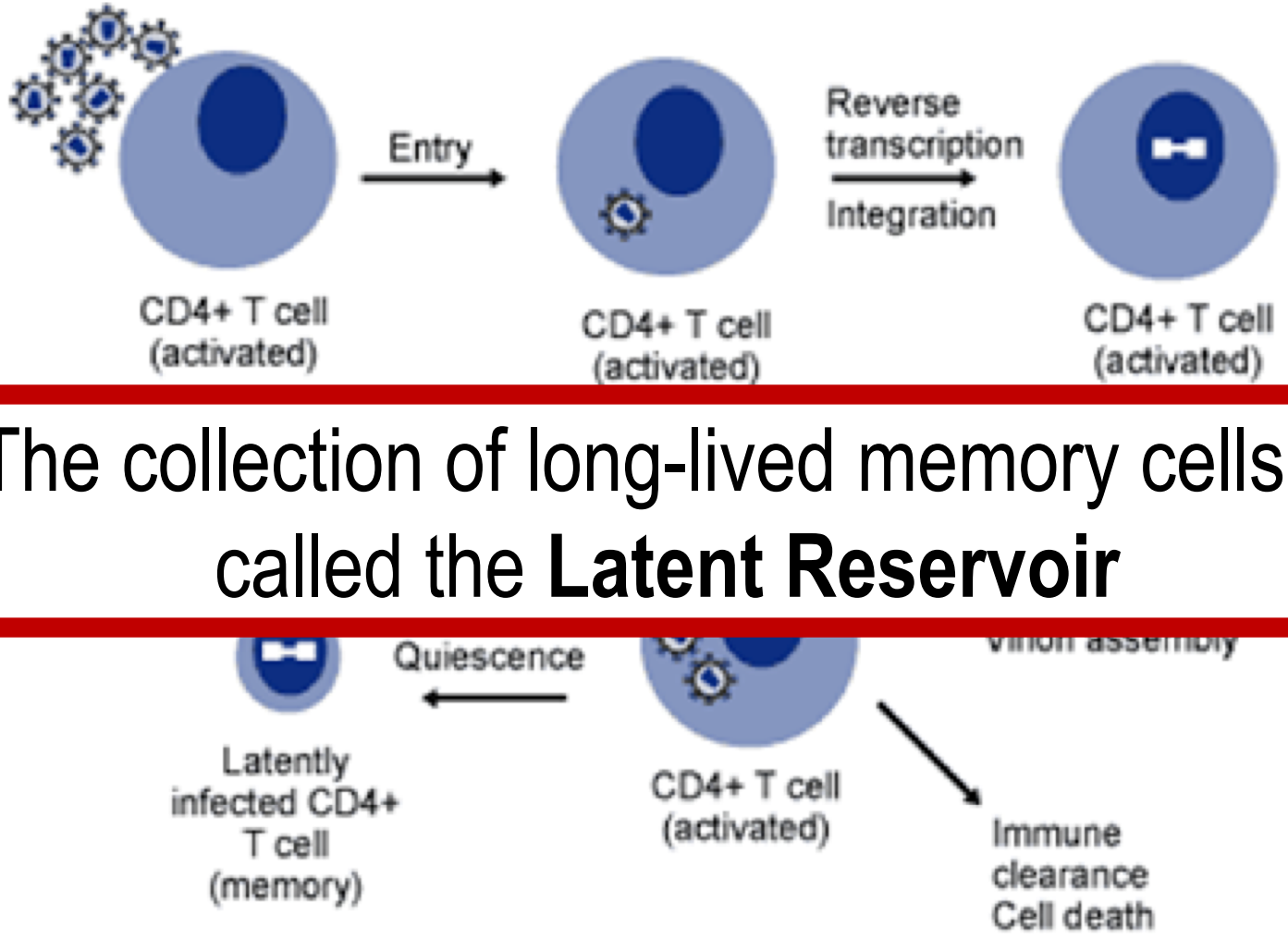
Schematic representation of the establishment of a latent HIV reservoir in quiescent memory CD4 T cells

Source: The GW Research Center for the Eradication of HIV. https://smhs.gwu.edu/timetoendhiv/hiv-aids/finding-a-cure

European AIDS Treatment Group

# Why is it so hard to 'cure' HIV infection?

ageing with HIV



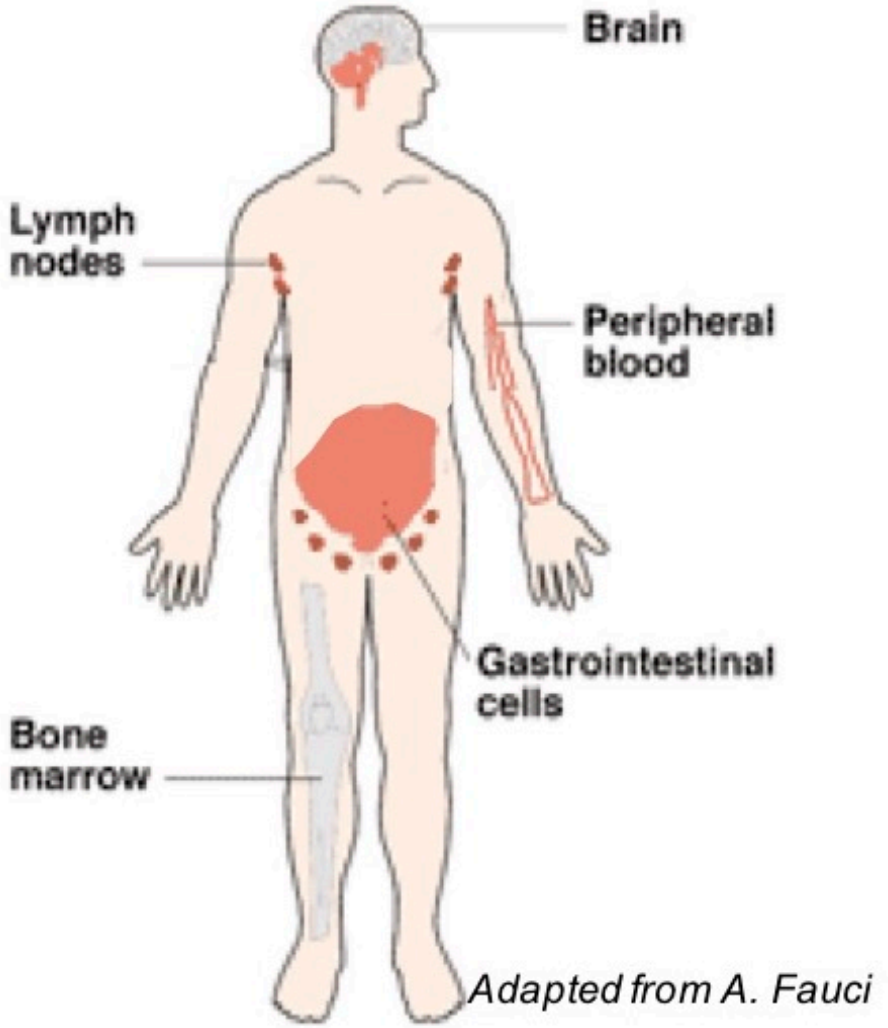

The collection of long-lived memory cells is called the **Latent Reservoir**

Schematic representation of the establishment of a latent HIV reservoir in quiescent memory CD4 T cells

Source: The GW Research Center for the Eradication of HIV. https://smhs.gwu.edu/timetoendhiv/hiv-aids/finding-a-cure

# Where is the reservoir

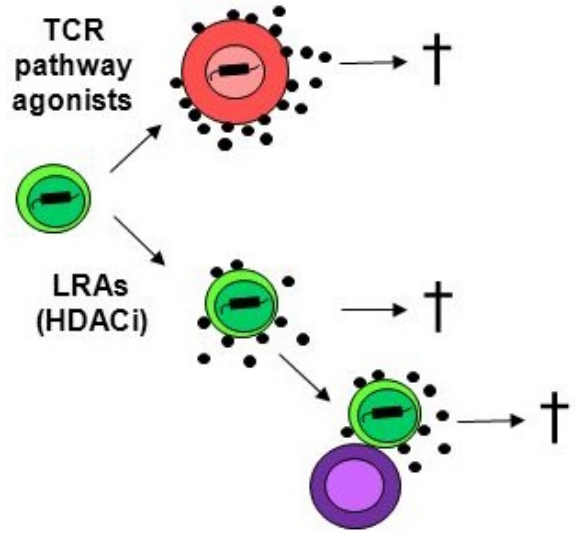
- Brain
- Lymph nodes
- Peripheral blood
- Gut
- Bone marrow
- Genital tract



European AIDS Treatment Group

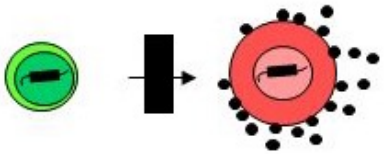
ageing with HIV

# Approaches to HIV cure

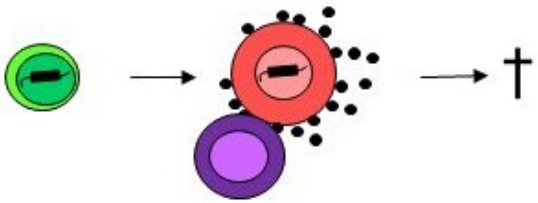



Shock and kill
Or Activate and Eliminate

Gene Rx



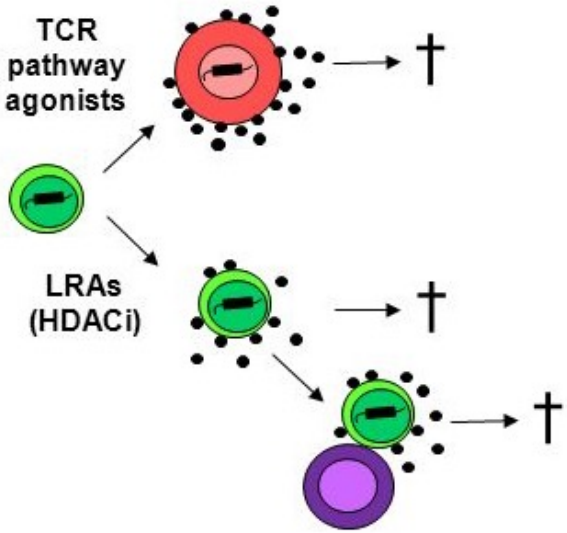
Prevent reactivation




Induce elite control

From JM Siliciano, PhD, at Washington, DC; April 2016, IAS-USA

# Activate and eliminate




- Latency Reversing Agents (LRAs) have been studied to reactivate resting infected cells
- ART treatment and other interventions (vaccines, monoclonal antibodies, immunotherapies) are studied to eliminate reactivated infected cells

Barriers:

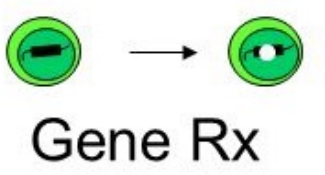
- No decrease in reservoir size so far
- LRAs can pose safety issues

From JM Siliciano, PhD, at Washington, DC; April 2016, IAS-USA

European AIDS Treatment Group

ageing with HIV

# Gene Therapy




- Manipulate genome to make the cells resistant to HIV
- Zinc Finger Nucleases (ZFN) and CRISPR/Cas9 are the most promising techniques

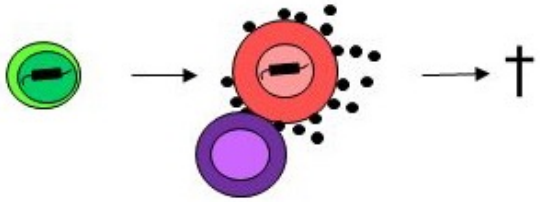
Barriers:

- No way to deliver interventions to every cell
- Risk for off-target effects

From JM Siliciano, PhD, at Washington, DC; April 2016, IAS-USA

# Immunotherapy

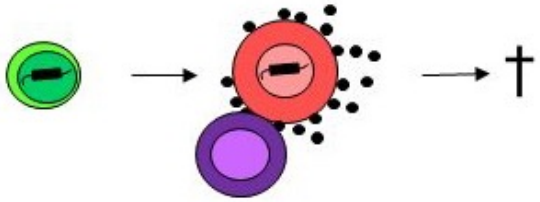
- Stimulate the immune system so to make it able to overcome HIV infection
- Therapeutic vaccines or monoclonal antibodies some of the strategies studied so far



Induce elite control

From JM Siliciano, PhD, at Washington, DC; April 2016, IAS-USA

# Immunotherapy




Induce elite control

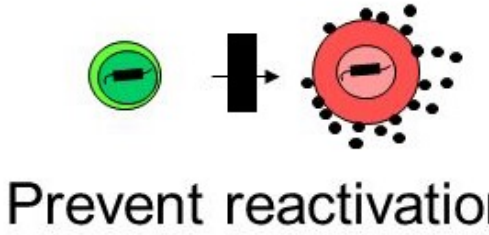
Barriers:

- Great viral variability makes it difficult to engineer an intervention which is effective against any virus
- Complex regulatory issues because each vaccine component will need to be evaluated separately and in combination
- Animal models do not always translate to humans
- Proving that strict immune control of HIV is clinically equivalent or better than ART

From JM Siliciano, PhD, at Washington, DC; April 2016, IAS-USA

# Prevent reactivation

- Very few studies so far




Barriers:

- Infected cells will remain in the body, although in a latent state
- How to be sure no reactivation will occur?

From JM Siliciano, PhD, at Washington, DC; April 2016, IAS-USA

# What Are the Social & Ethical Challenges

- Balancing resources
- Risk versus reward
- Participant selection
- Trial design
- Cost
- Scalability

European AIDS Treatment Group

ageing with HIV

# Analytical Treatment Interruptions (ATIs)

DRAFT CIRCULATED FOR COMMENTS ONLY

## Community recommendations for clinical research involving antiretroviral treatment interruptions

### Introduction

This brief review provides community recommendations for research that requires HIV-positive people to interrupt antiretroviral treatment (ART).

We recognize that there are important scientific questions that can only be answered by stopping ART. Examples can include research to either cure HIV or to induce a long-term immune response capable of suppressing HIV in the absence of ongoing ART. Experimental approaches include immune-based therapies, therapeutic vaccines and treatments intended to reduce or clear HIV reservoirs.

http://i-base.info/htb/wp-content/uploads/2014/07/Community-TI-draft-for-comment-210714.pdf

European AIDS Treatment Group

ageing with HIV

# Conclusions

- Despite the fact that few results have been obtained so far, HIV cure research must go on
- Community should be involved in any research project
- Awareness and education about cure research must be promoted in the community
- Ethical issues (informed consent, treatment interruption, risky interventions) should be addressed with community involvement
- Social research about HIV cure should be promoted

European AIDS Treatment Group

ageing with HIV

# Thank you for your attention

Giulio Maria Corbelli

giuliomaria.corbelli@eatg.org