

Allogeneic stem cell transplant in HIV-1-infected individuals

Javier Martinez-Picado



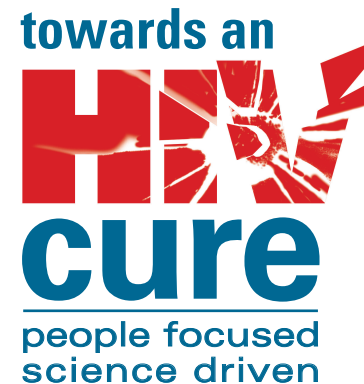
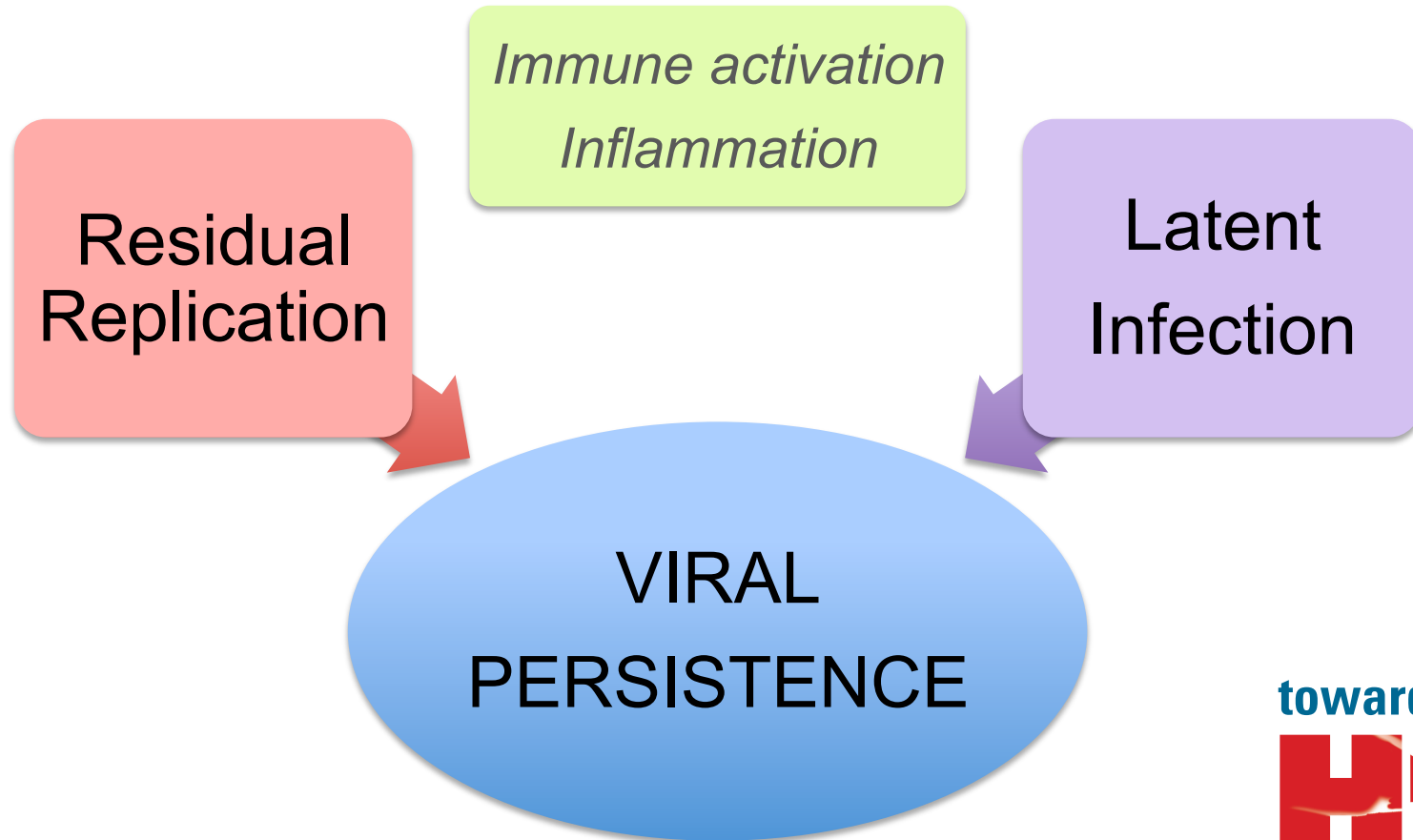
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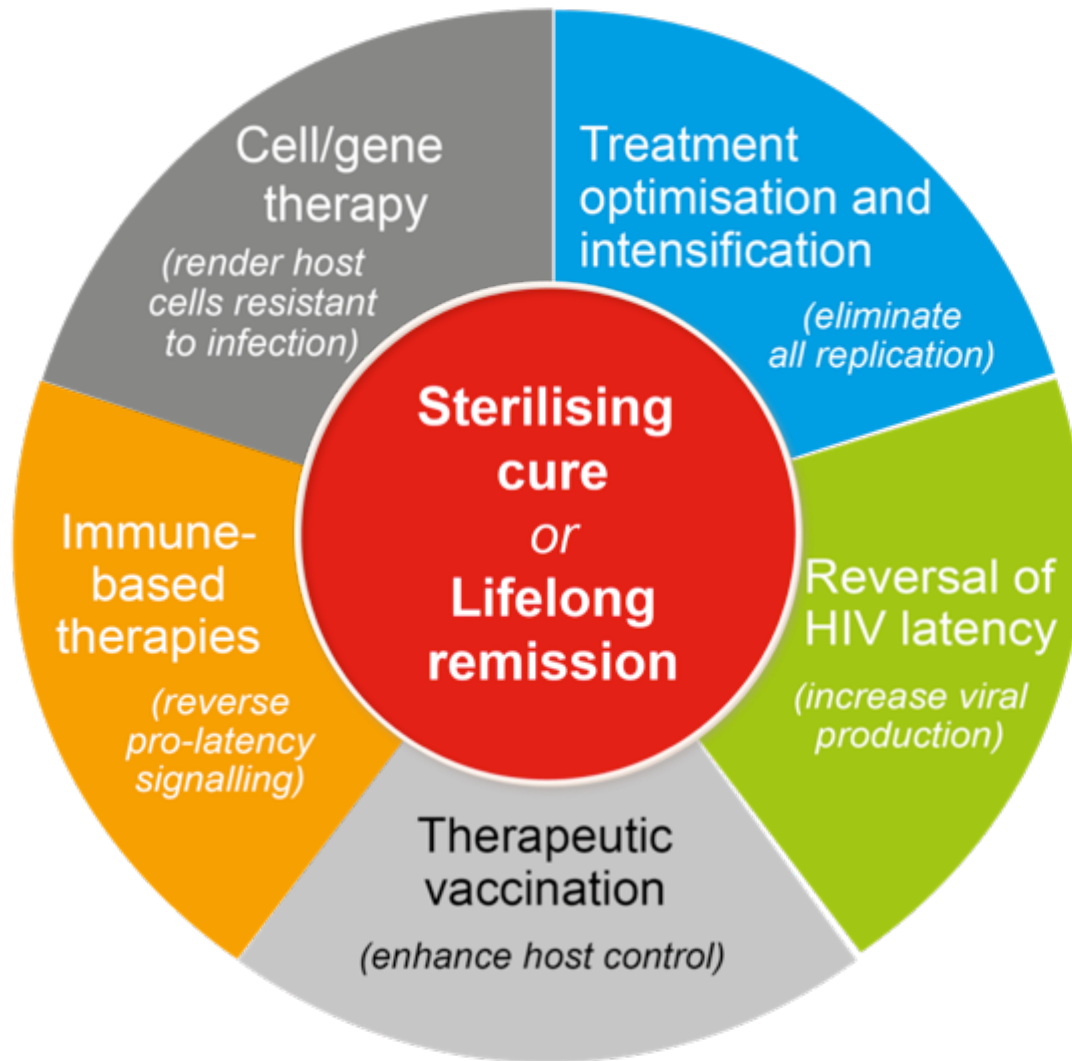
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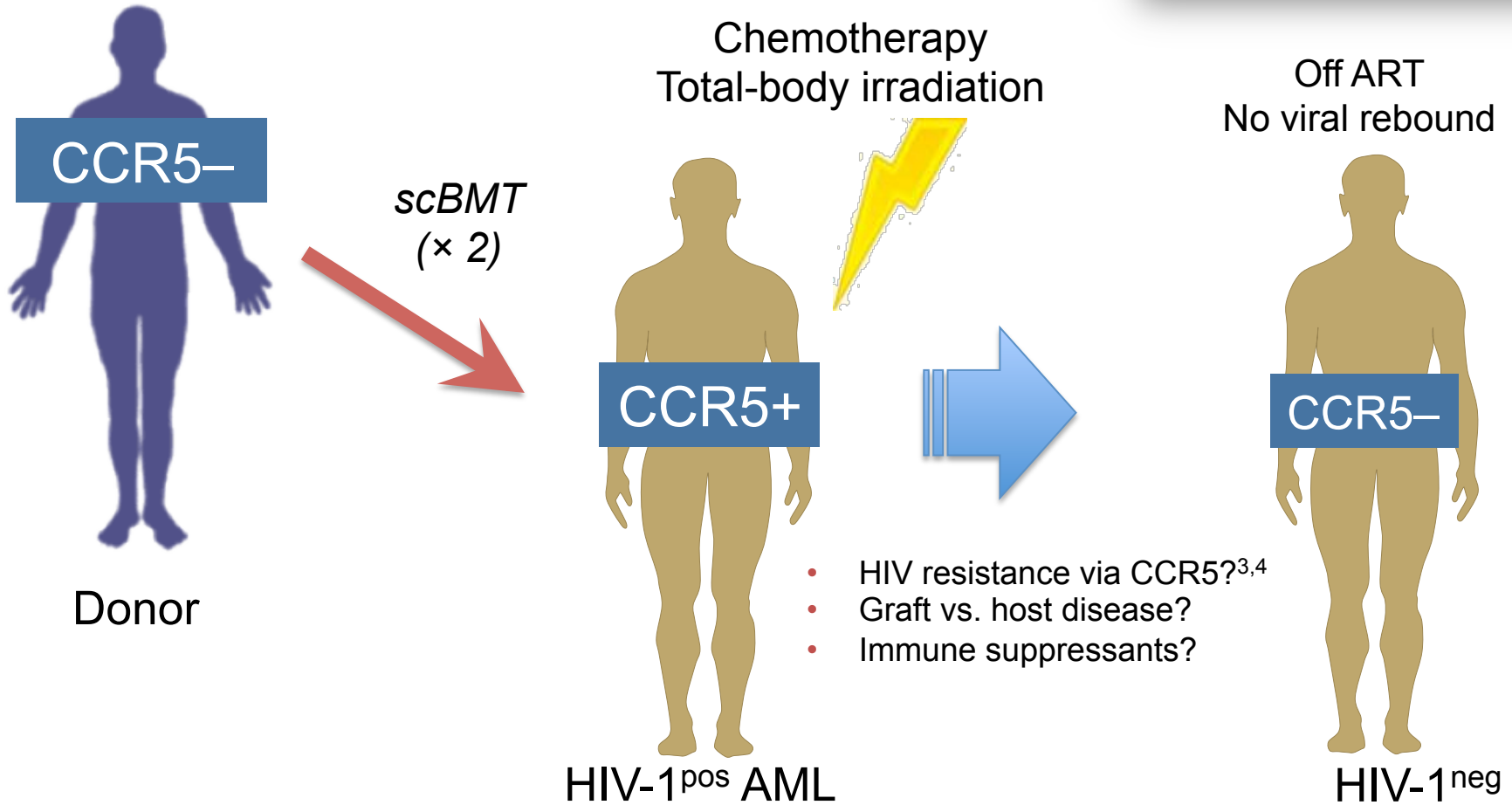
Barriers to cure HIV infection



Strategies to cure HIV



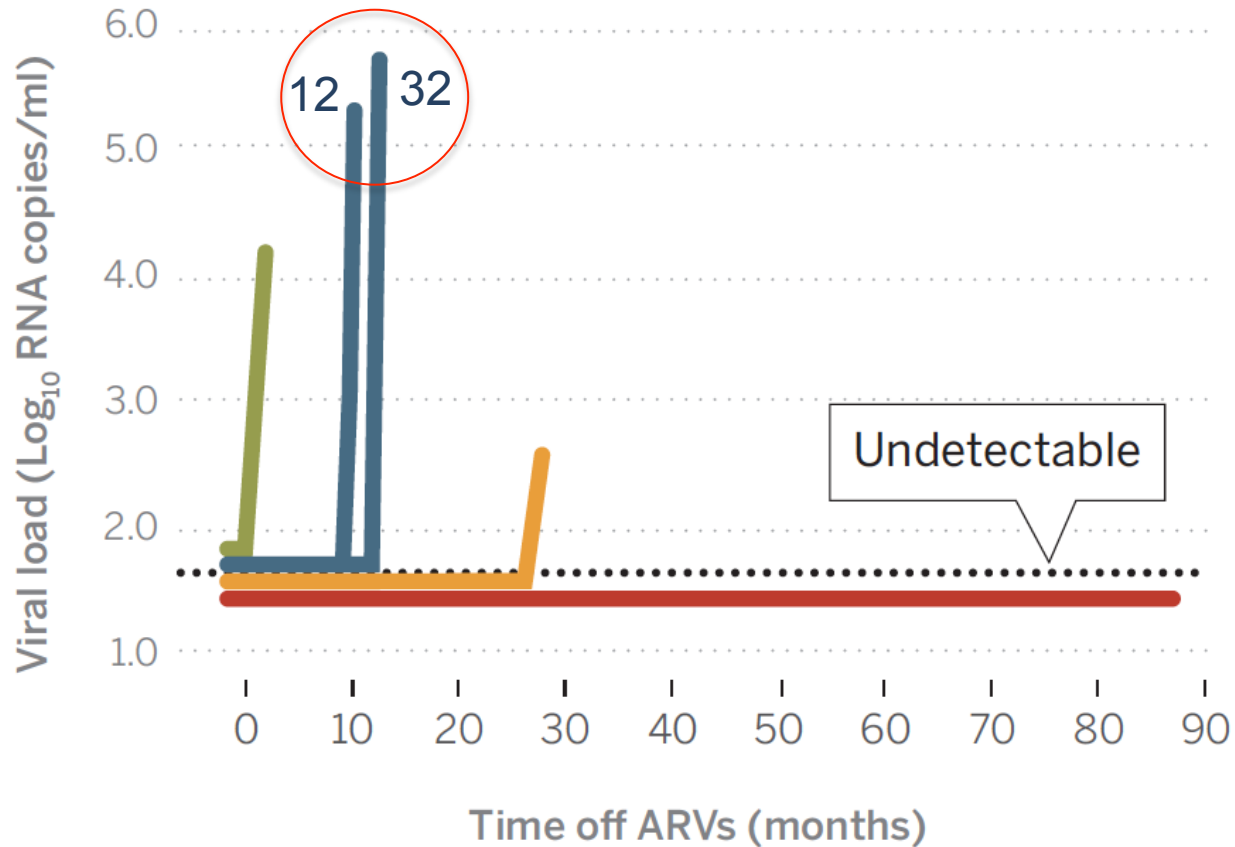
Long-term control of HIV by CCR5 Δ 32/ Δ 32 stem cell transplant¹⁻²



scBMT, allogenic transplant with peripheral blood stem cells

Created from 1. Hütter G, et al. New Eng J Med 2009;360:692–8; 2. Allers K, et al. Blood 2011;117:2791–9; 3. Henrich TJ, et al. IAS 2013; Abstract WELBA05. Available at <http://pag.ias2013.org/session.aspx?s=75>. Accessed August 2013; 4. Henrich TJ, et al. J Infect Dis 2013;207:1694–702.

ARVs stopped, HIV rebounds



- Timothy Ray Brown
- Mississippi child
- Boston bone marrow transplants
- Typical person suppressed 1 year

Adapted from Diana Finzi, U.S. National Institute of Allergy and Infectious Diseases
J Cohen, 2014 Science

**Why only one person
has been “cured” of HIV**



Stem cells sources for allogeneic transplant



*HLA-matched
Sibling Donor
(10/10)*



$\geq 9/10$
*HLA-matched
Unrelated Donor*



Cord Blood
(single/double)*



$\geq 4/6$

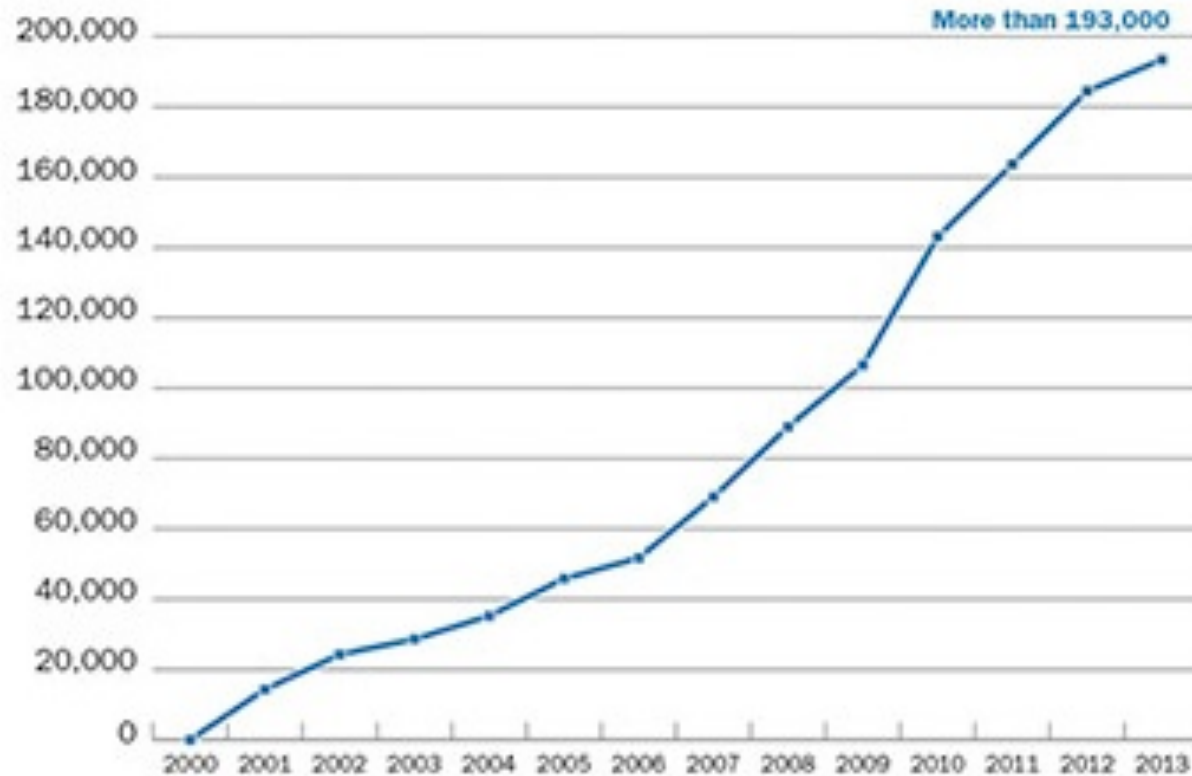
** Potential problem:
Limited CBU Cell Dose*

$\geq 5/10$

*Haploidentical
Family Donor*



Growth of Cord Blood Units on the BE THE MATCH registry



Source: National Marrow Donor Program/Be The Match FY 2013



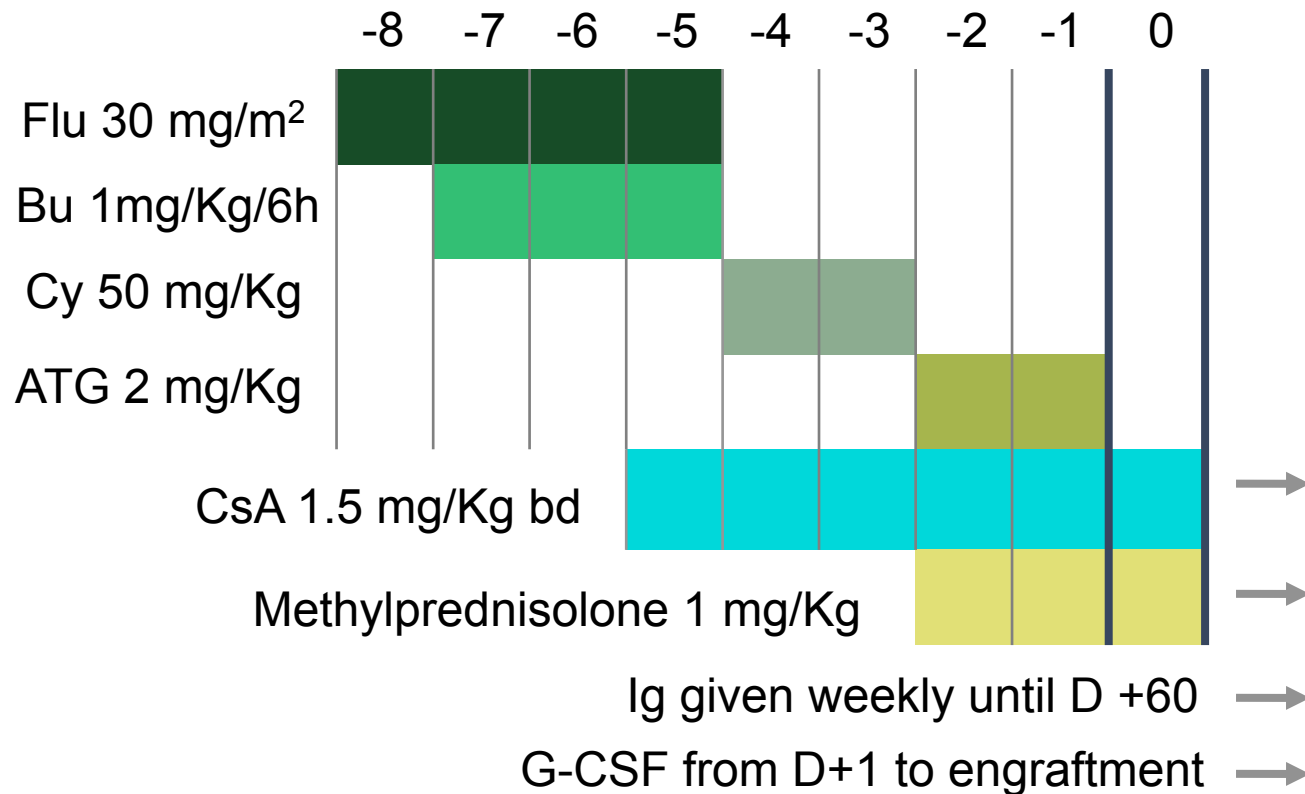
**Allogeneic HCT using CB (CCR5 Δ 32/ Δ 32)
in a patient with a HIV infection and a
diffuse large B-cell lymphoma (DLBCL)**

Allogeneic CBT in HIV-1+ patient with DLBCL

Abstract 432

- ♂ 37 years-old
- HIV diagnosed in 09/2009
 - CD4+: 272/mm³; pVL= 79,298 copies/ml
 - Initiates ART: Truvada (FTC+ TDF) + Viramune (NVP)
- Follow up shows good treatment adherence
 - CD4+ 300-500/mm³; pVL <50 copies/ml
- Diffuse large B-cell Lymphoma (II-A) diagnosed in 11/2011
 - Great hemiabdomen tumour (23 cm, left kidney to lower inferior quadrant)
- Chemotherapy + Autologous SCT
 - No persistent response
 - Allogeneic SCT

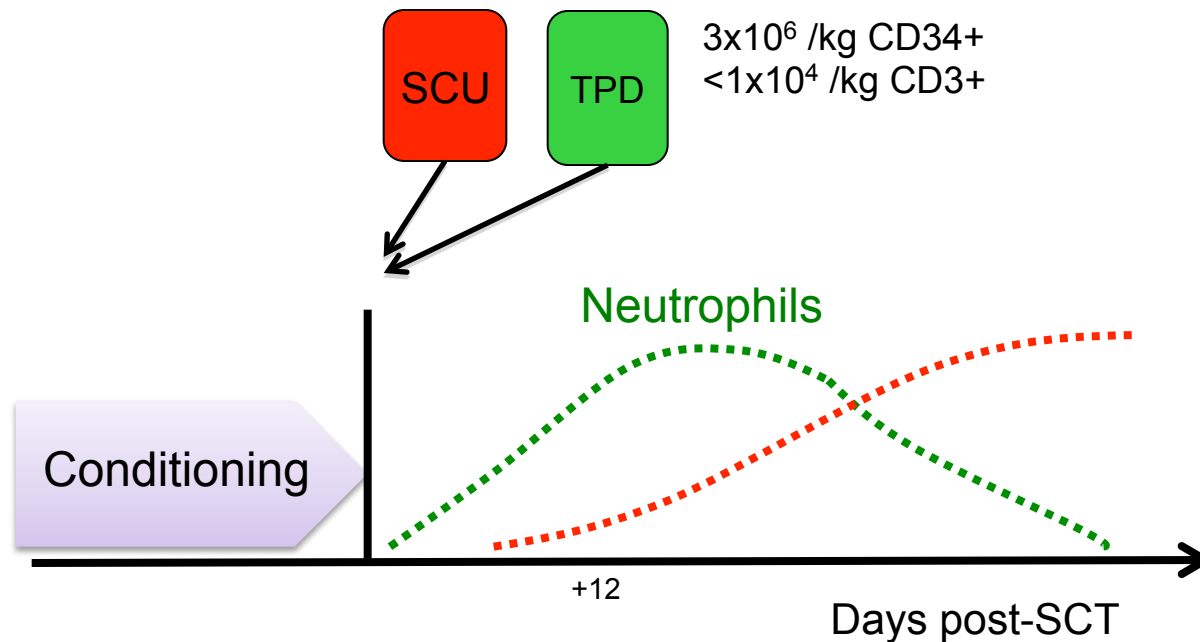
Conditioning Regimen



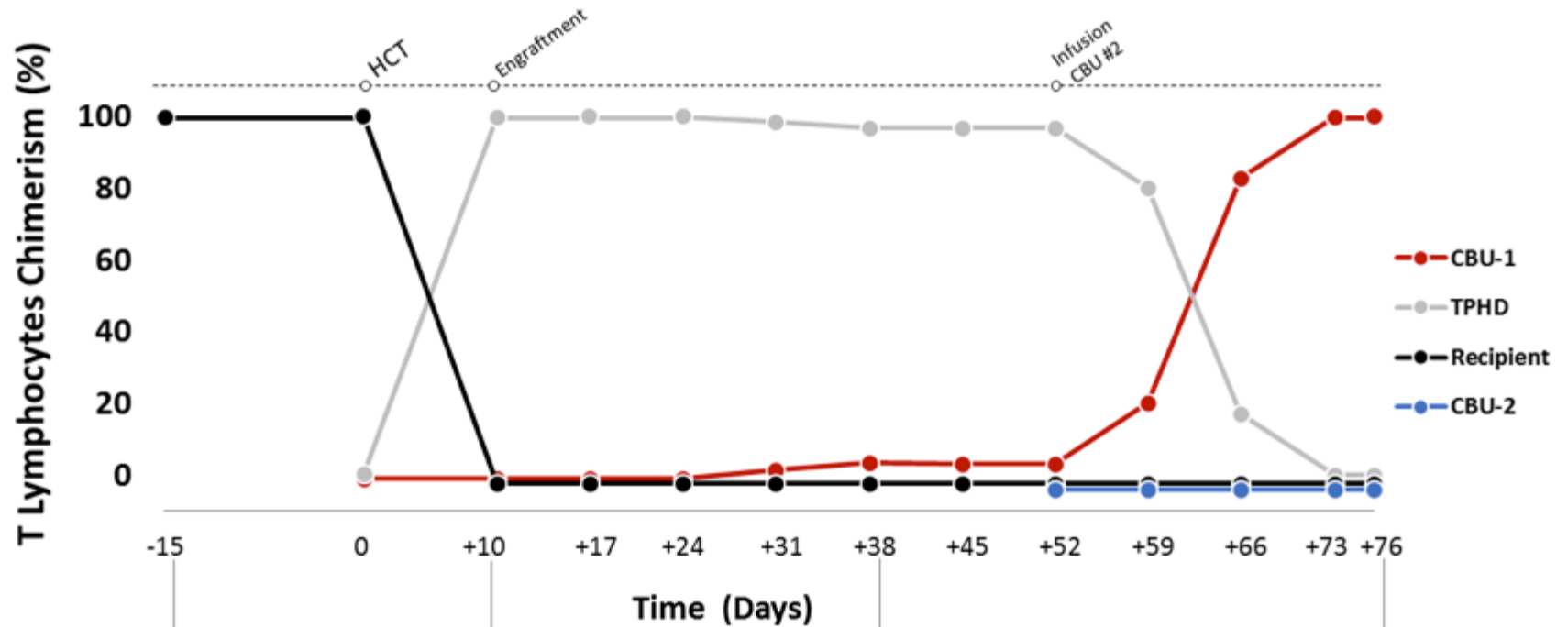
Infectious prophylaxis: Pentamidine/TMP-SMX, Posaconazole
Acyclovir, Ciprofloxacin

“Haplo-cord transplant”

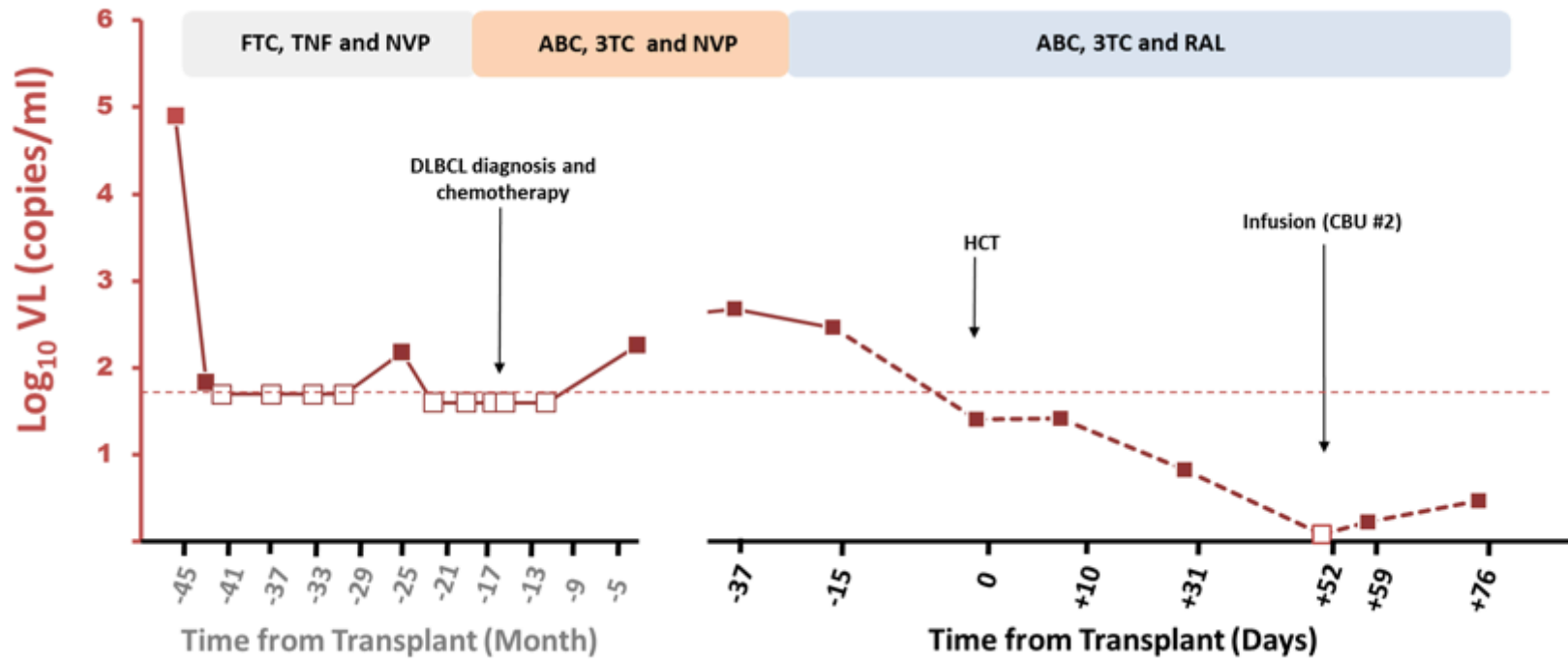
Single CB transplantation with the co-infusion of a T-cell depleted CD34+ graft from a third party HLA-mismatched donor (TPD), to accelerate PMN recovery



CB(CCR5 Δ 32/ Δ 32)+TPHD(CCR5 Δ 32/wt) microchimerism



CB(CCR5 Δ 32/ Δ 32)+TPHD(CCR5 Δ 32/wt)





Scientific Project to Investigate...

***“Allogeneic stem cell transplant in
HIV-1-infected individuals”***



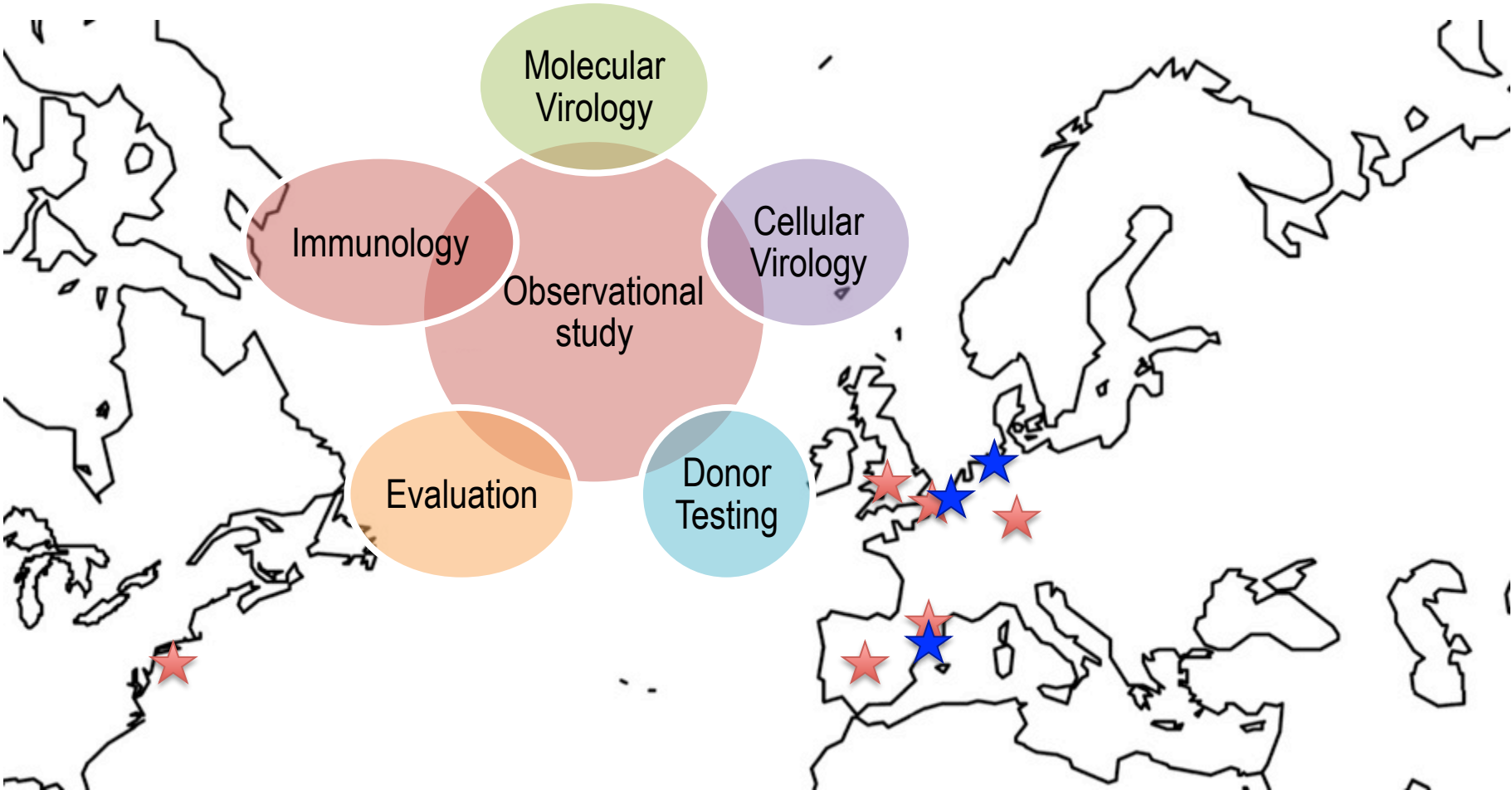
ARCHE

amfAR Research Consortium
on HIV Eradication

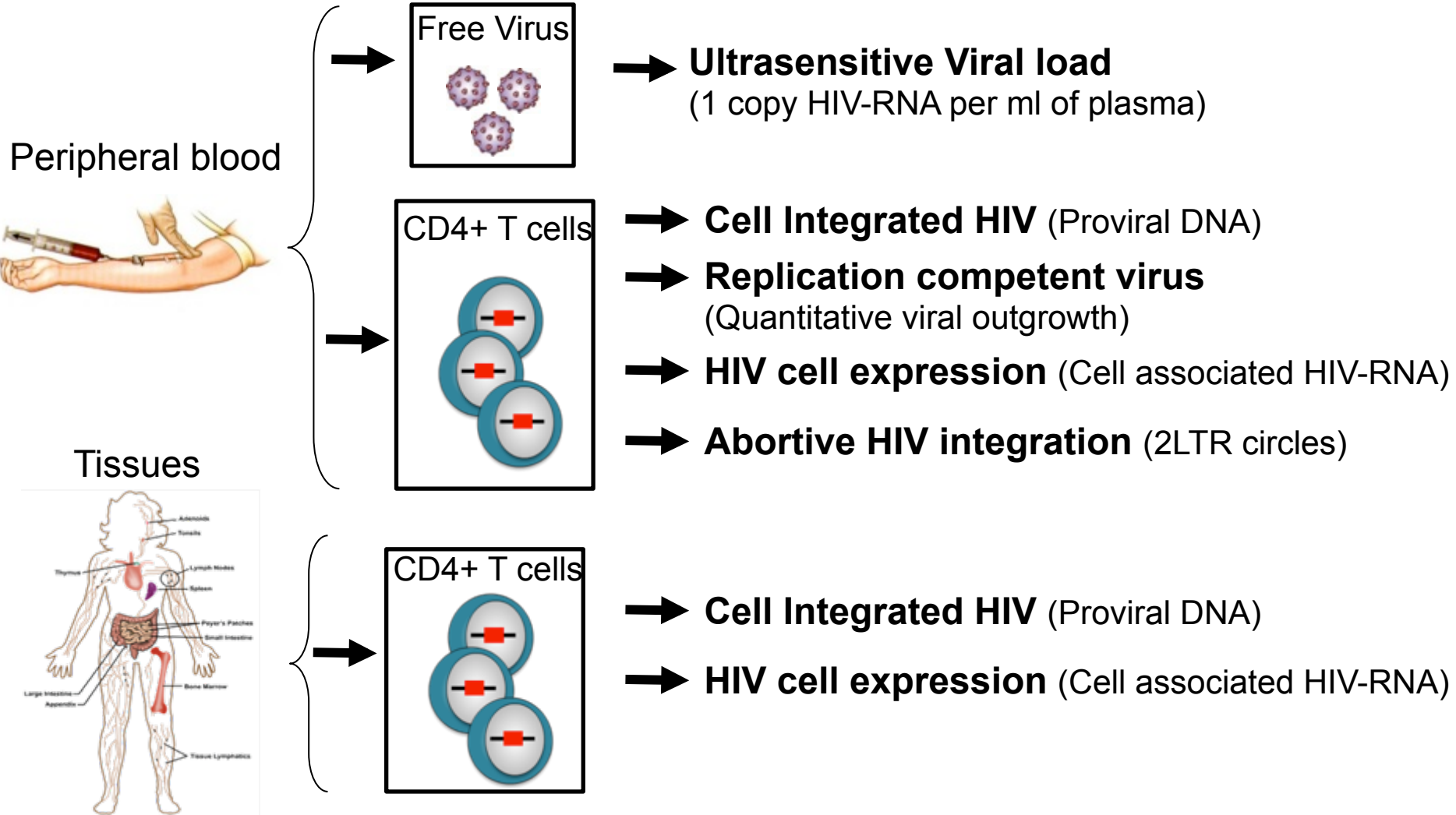
amfAR

MAKING AIDS HISTORY

EpiStem



How viral persistence is measured?



Focusing on CCR5 Δ 32/ Δ 32

OPEN  ACCESS Freely available online

 PLOS | ONE

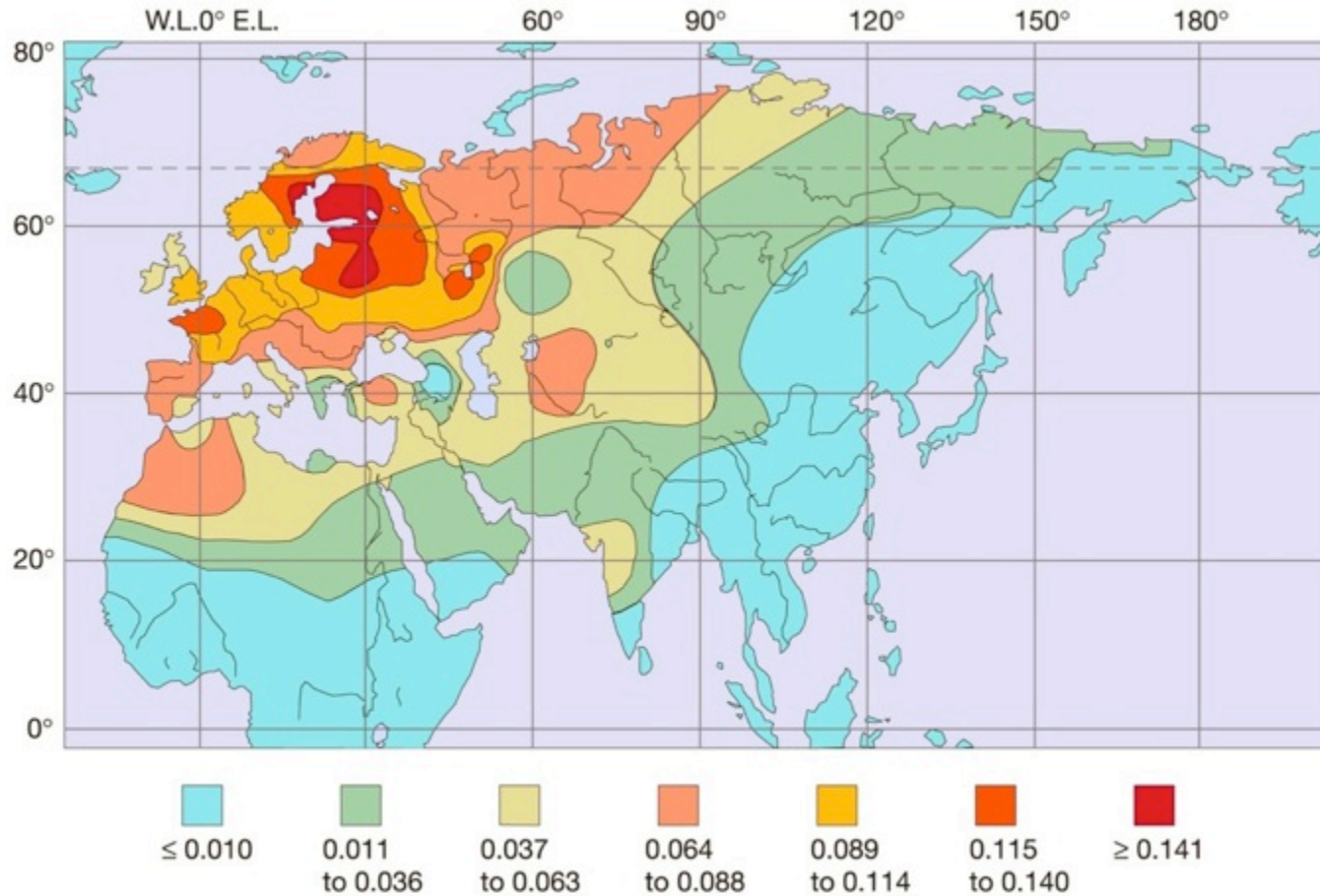
Impact of Chemotherapy for HIV-1 Related Lymphoma on Residual Viremia and Cellular HIV-1 DNA in Patients on Suppressive Antiretroviral Therapy

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 PLOS | PATHOGENS

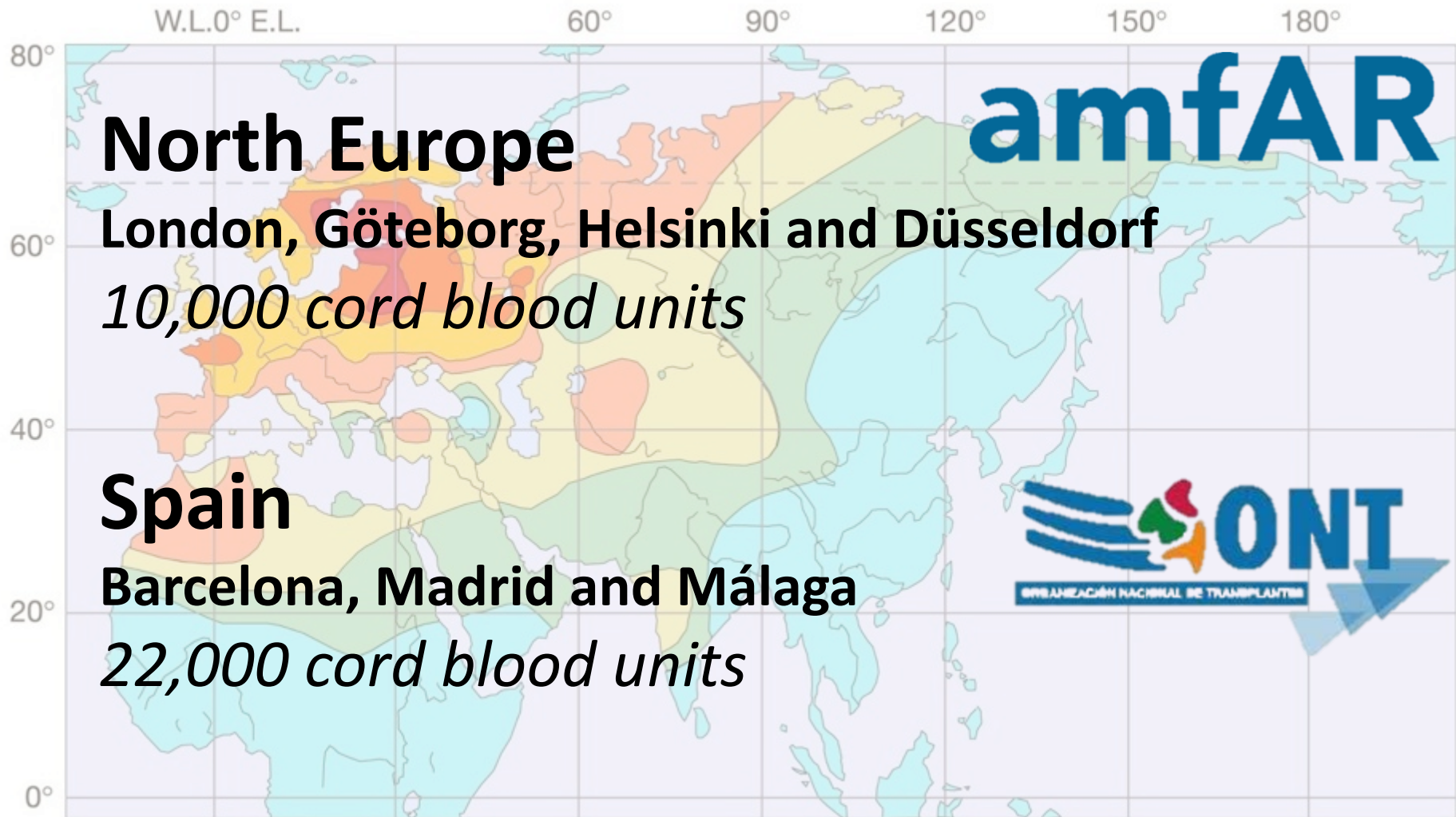
Persistence of Virus Reservoirs in ART-Treated SHIV-Infected Rhesus Macaques after Autologous Hematopoietic Stem Cell Transplant

CCR5 Δ 32/ Δ 32 geographical distribution

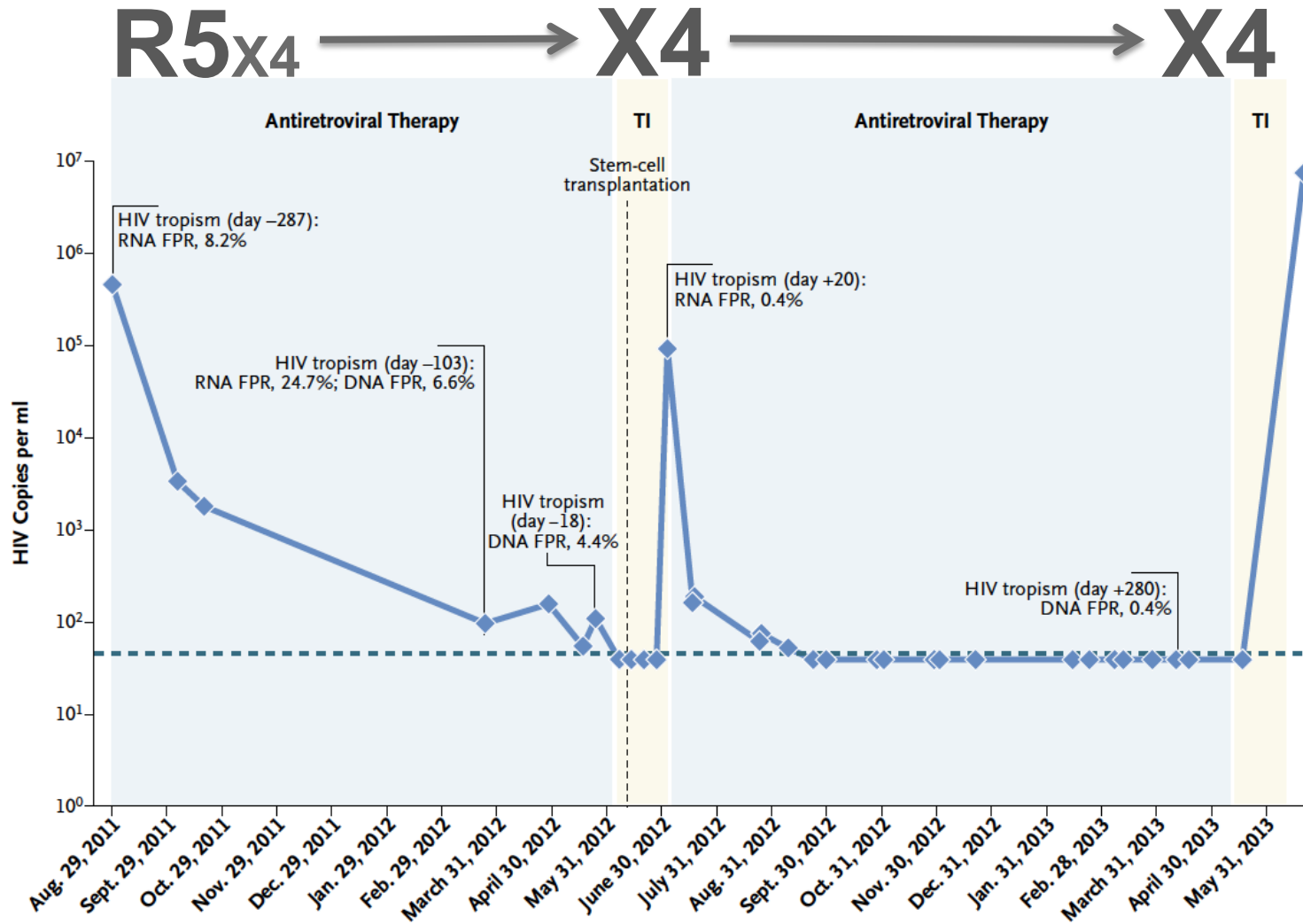


Frequency of CCR5- Δ 32 allele
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Registry of CCR5 Δ 32/ Δ 32 donors



Shift of HIV Tropism in Stem-Cell Transplantation with CCR5 Δ 32/ Δ 32



Open Considerations

- Haplo/cord vs. classical allo-Tx.?
- Which conditioning is best?
- Conditioning of patients without malignancies feasible?
- What is the best ART?
- How much immunosuppression is needed?
- How much GvH/GvD is necessary?
- What is the best ATI strategy?
- Ethical considerations



How to contact:

<http://www.epistem-project.org>



EPiSTEM

- AIDS Research Institute *IrsiCaixa, Barcelona*
- *Univ Medical Center Utrecht*
- *Univ Medical Center Hamburg*
- *Catalan Institute of Oncology, Barcelona*
- *Hosp Gral Univ Gregorio Marañón, Madrid*
- *Oxford Univ*
- *Cellex GmbH, Dresden*



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