



# HTI-vaccine-induced, broad and polyfunctional CD4 and CD8 T cell responses are associated with prolonged time off ART and lower pVL at the end of ATI in the AELIX-002 therapeutic vaccine trial

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on behalf of the **AELIX-002 Study Group**

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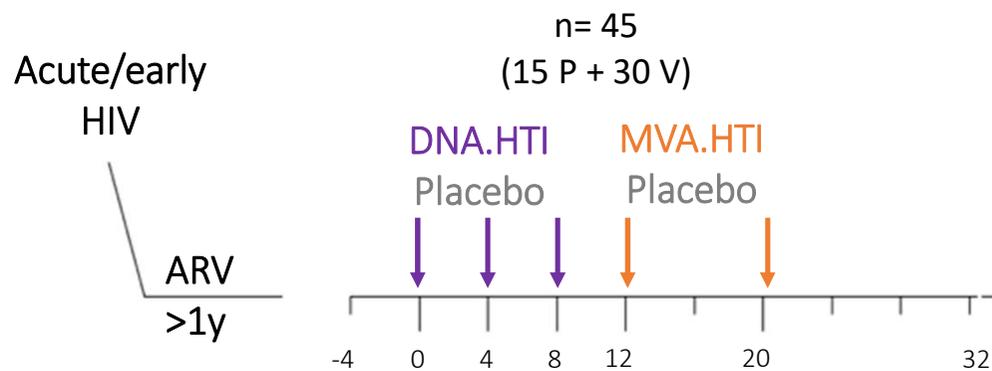


**C O N F L I C T S   O F   I N T E R E S T**

Co-inventor of the HTI immunogen with Christian Brander & Anuska Llano (patent application PCT/EP2013/051596),  
Consultant for AELIX Therapeutics SL and  
Speakers' fees from Gilead, Janssen and ViiV Healthcare, outside this work

# Introduction

- HTI vaccines are designed to induce HIV-specific T cell responses associated with better viral control in humans<sup>1,2</sup>
- AELIX-002 was a FIH Phase 1/2 study to evaluate safety, immunogenicity and efficacy of HTI vaccines in early-treated people with HIV (PWH) NCT03204617<sup>3</sup>



nature medicine

Article

<https://doi.org/10.1038/s41591-022-02060-2>

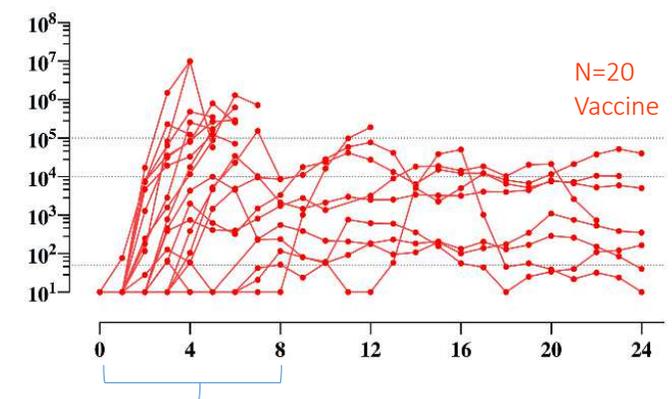
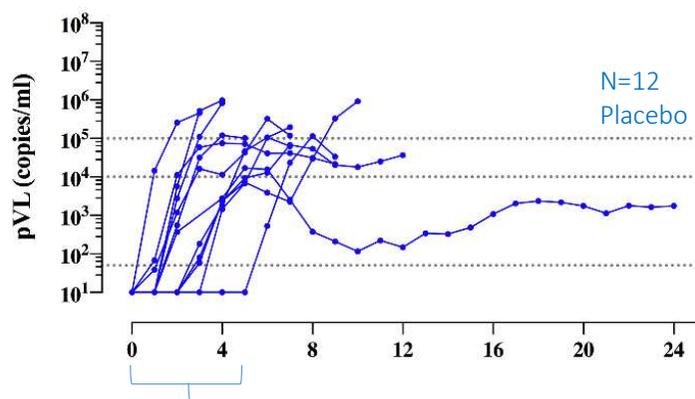
**Safety, immunogenicity and effect on viral rebound of HTI vaccines in early treated HIV-1 infection: a randomized, placebo-controlled phase 1 trial**

3 <sup>1</sup>Mothe JTM 2011; <sup>2</sup>Mothe JTM 2015; <sup>3</sup>Bailon Nat Med 2022

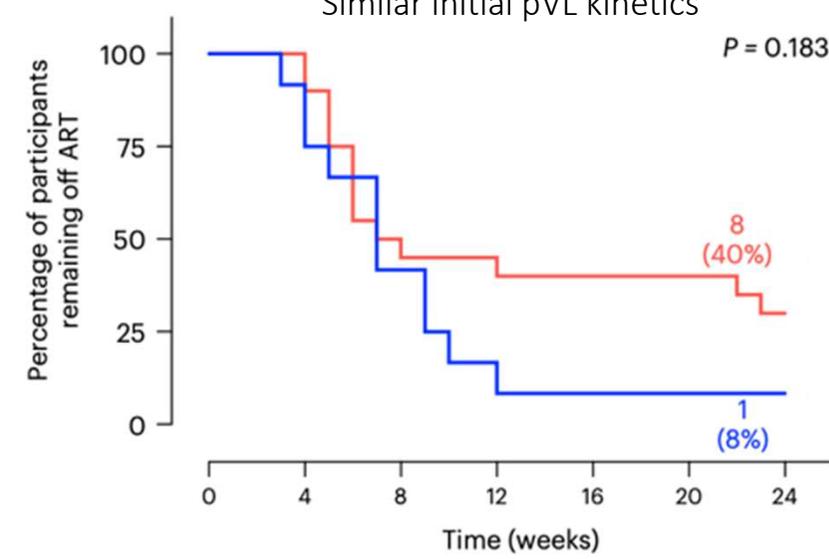


# AELIX-002 RCT

## Participants Without Beneficial HLA class I alleles



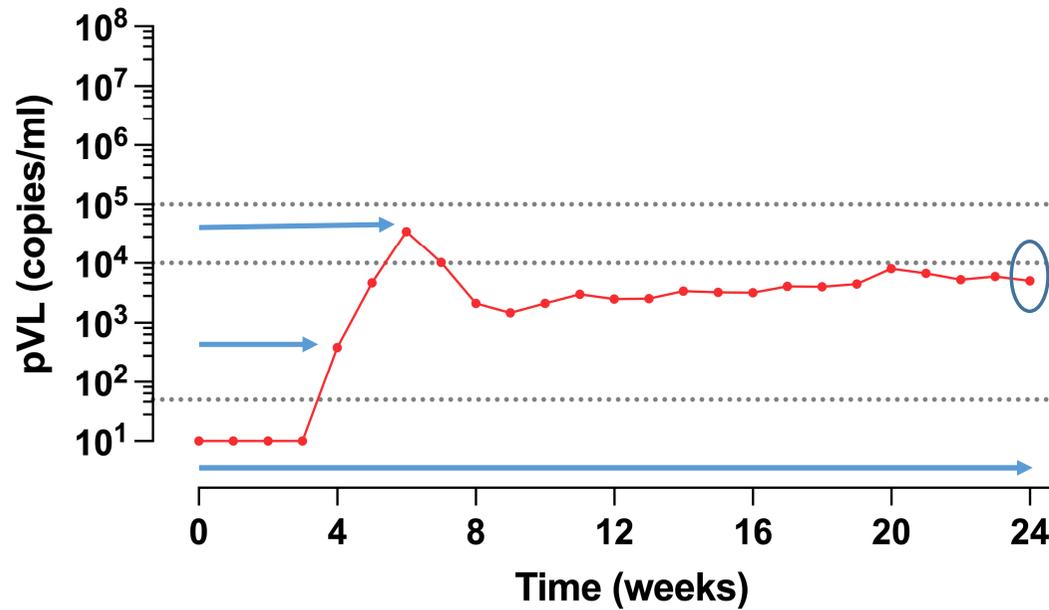
All participants rebounded  
Similar initial pVL kinetics



How to improve this effect?

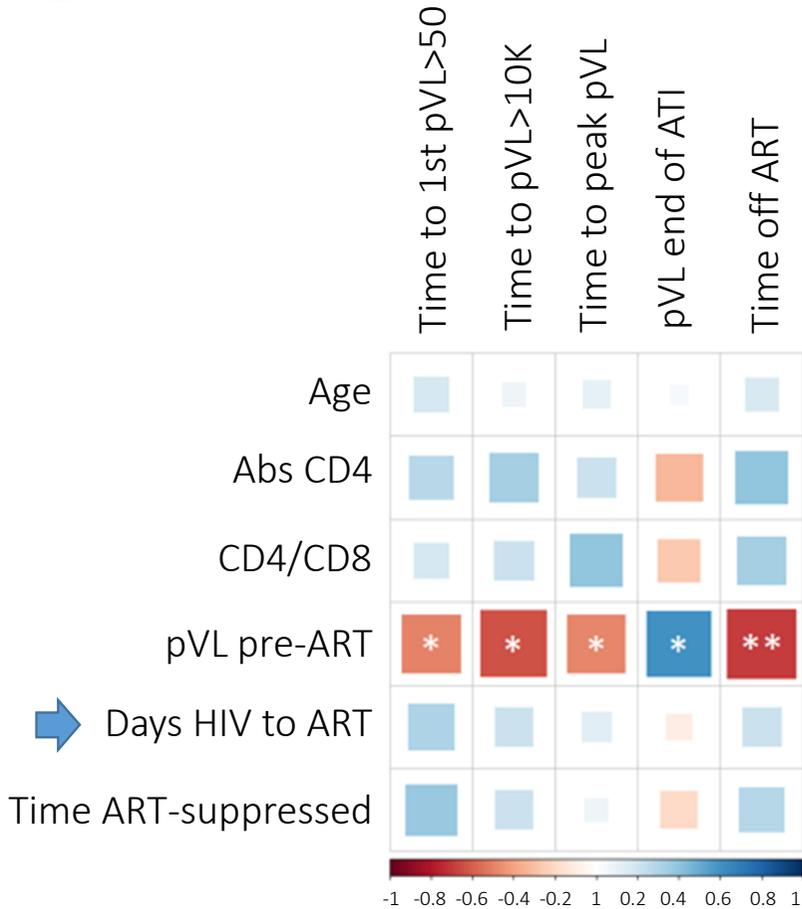
- HOST / Baseline conditions
- VIRUS
- VACCINE-INDUCED RESPONSES

# ATI endpoints

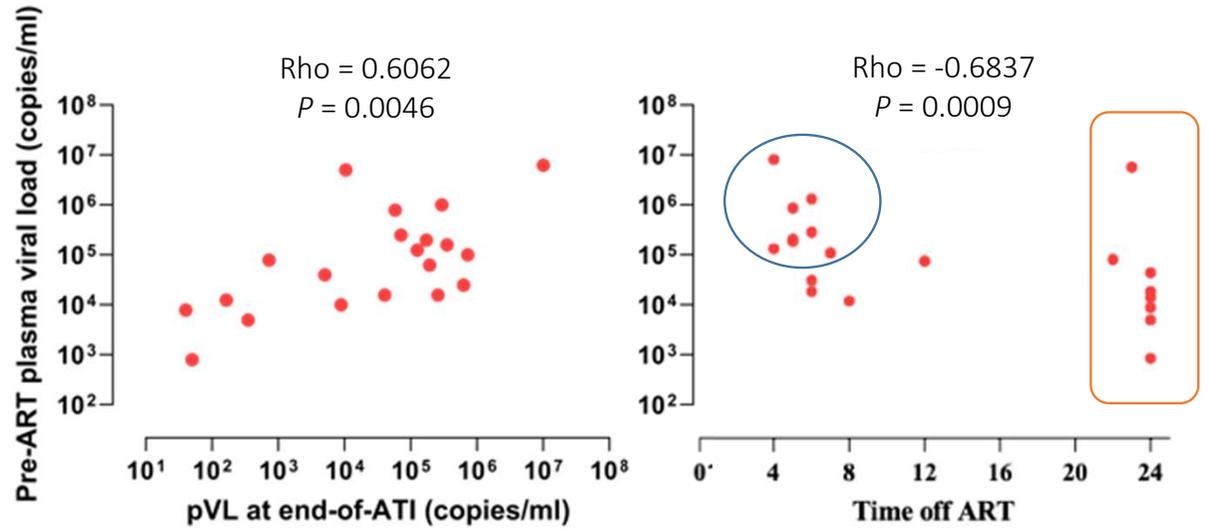


- Time to 1st pVL > 50
- Time to pVL > 10K
- Time to peak pVL
- pVL end of ATI
- Time off ART

# Host / Baseline conditions : pVL pre-ART



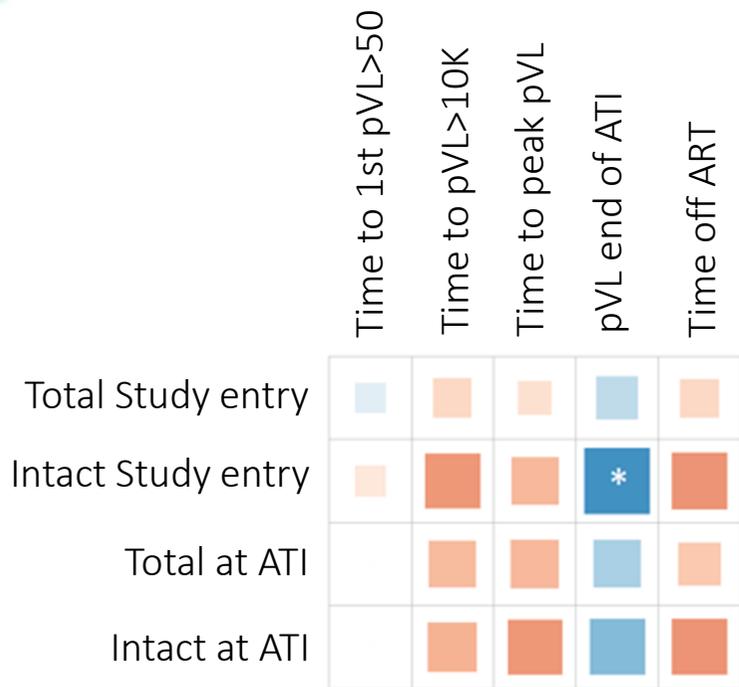
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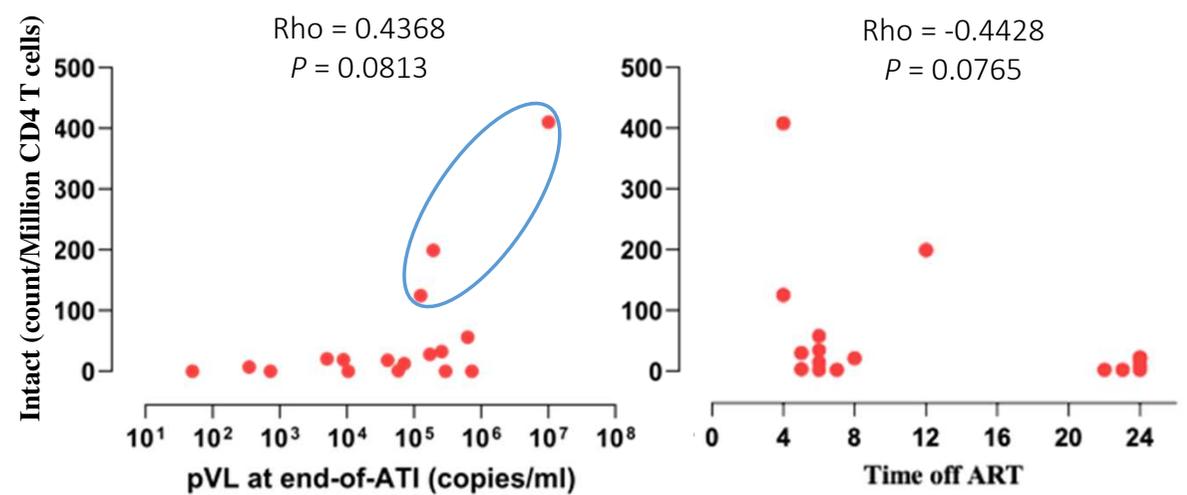
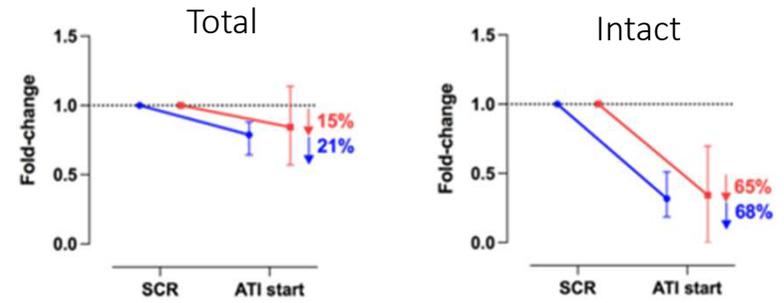
CHAMP; Namazi JID 2018



# Virus : ~reservoir

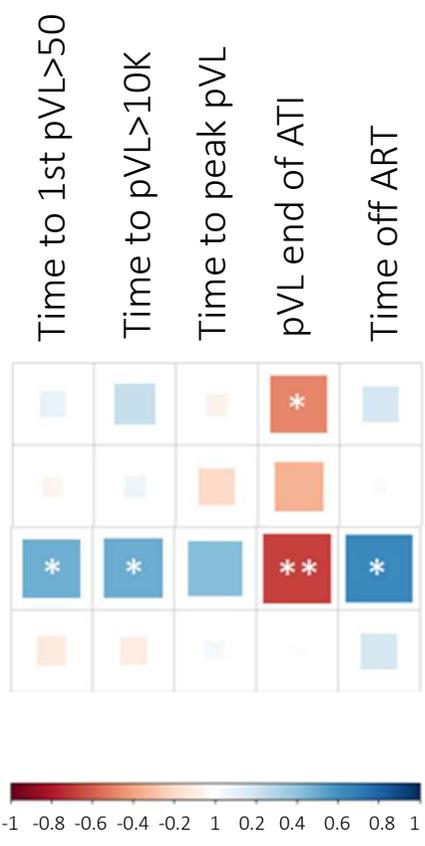


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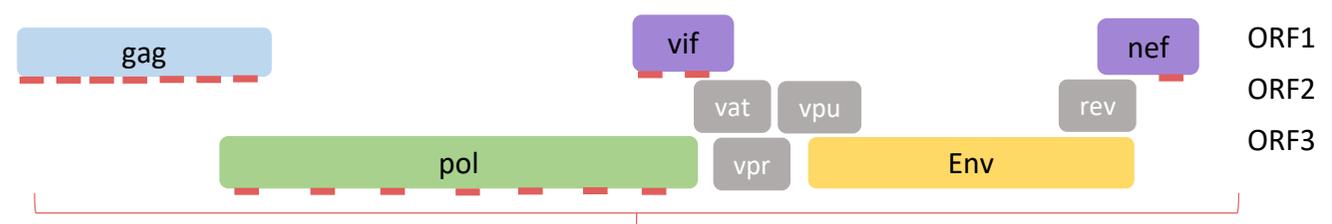
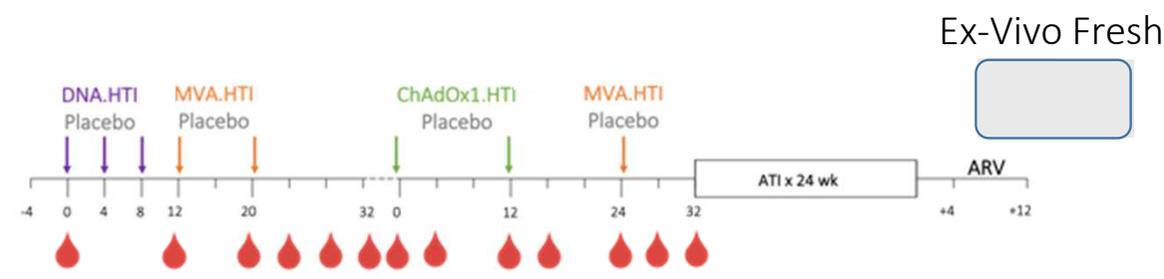


Accelevir  
 Anuska Llano  
 Marc Noguera

# HTI Magnitude



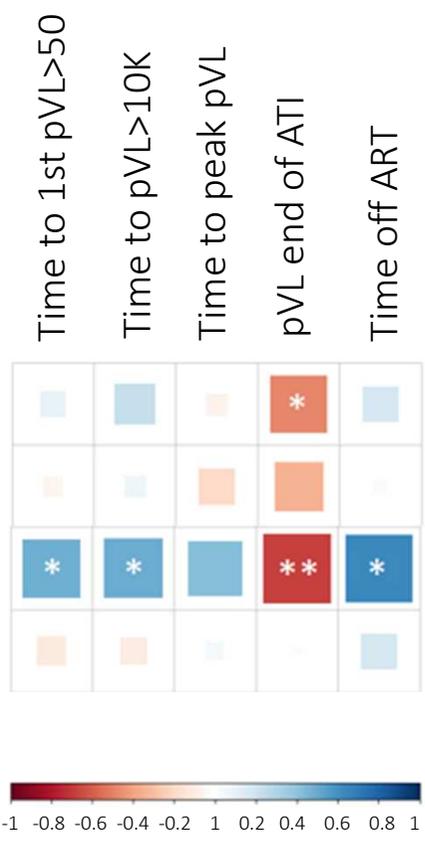
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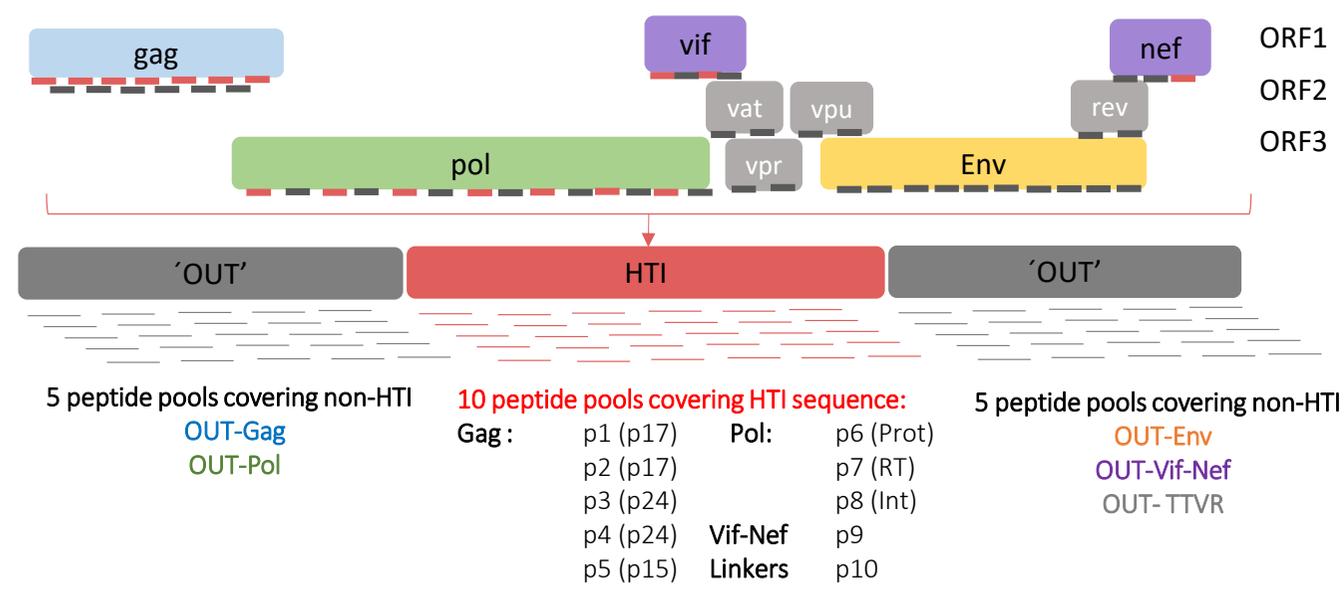
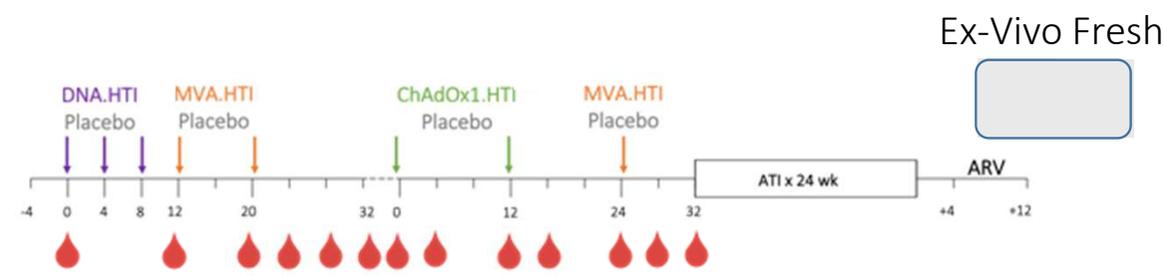
- 10 peptide pools covering HTI sequence:**
- Gag: p1 (p17), p2 (p17), p3 (p24), p4 (p24), p5 (p15)
  - Pol: p6 (Prot), p7 (RT), p8 (Int), p9
  - Vif-Nef Linkers: p9, p10

Samandhy Cedeño  
 Tuixent Escribà

# HTI Magnitude

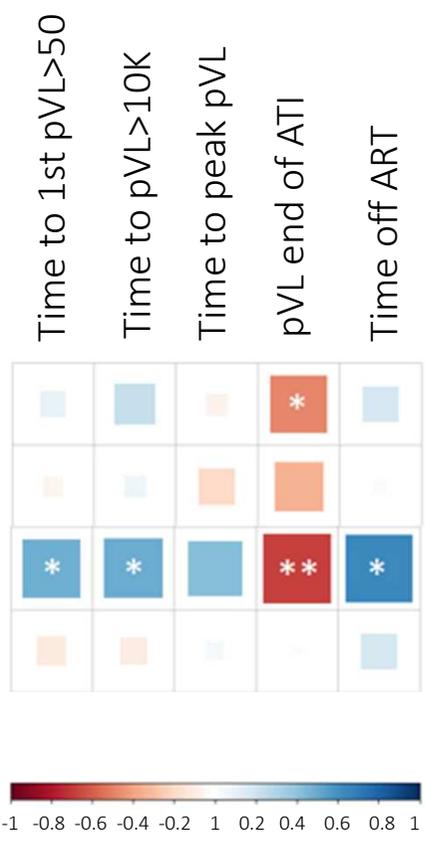


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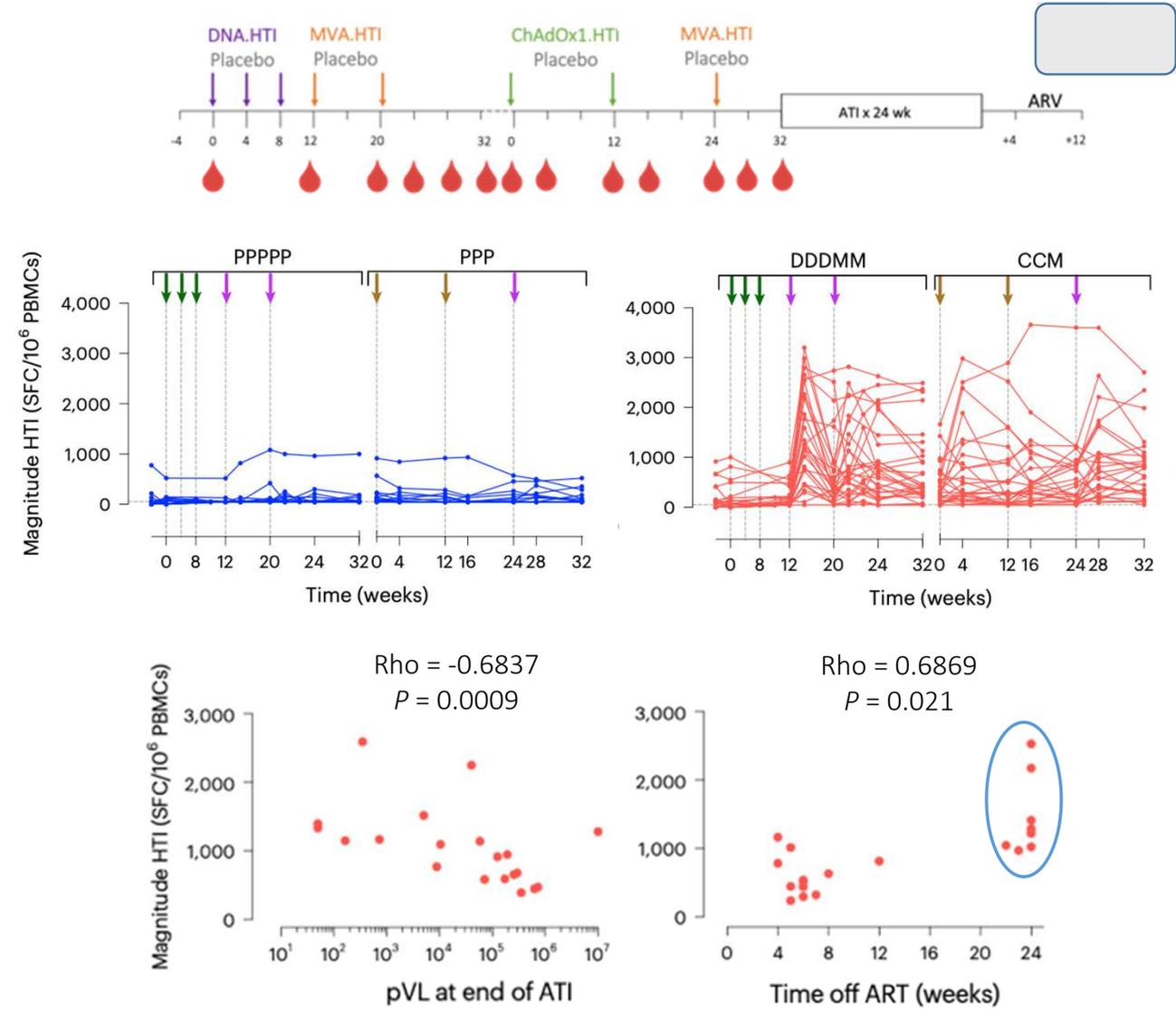


# HTI Magnitude

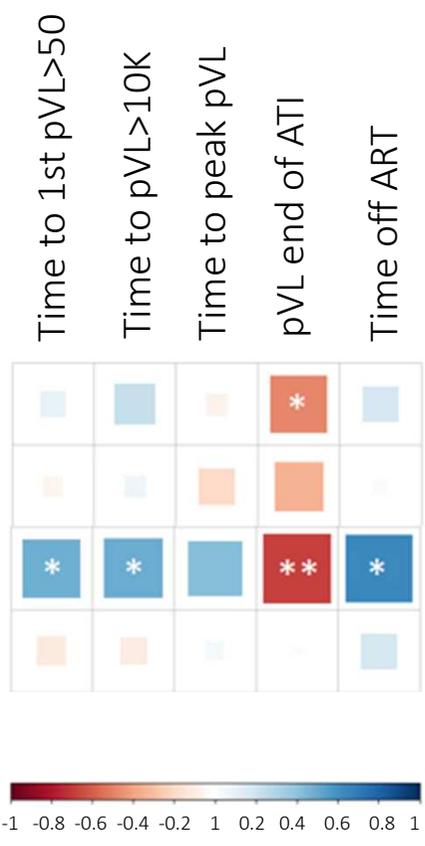
Ex-Vivo Fresh



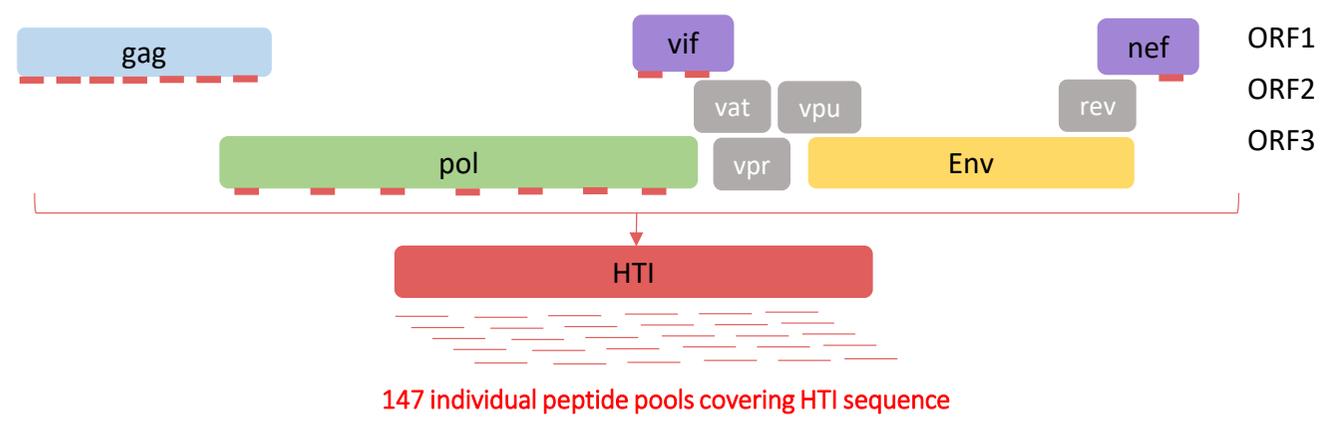
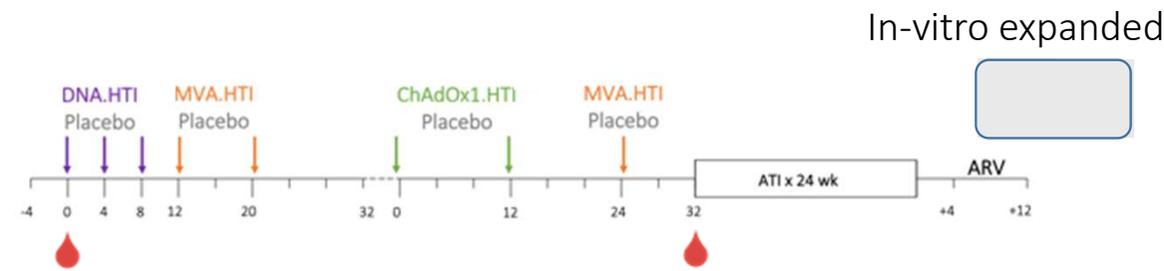
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# HTI Breadth

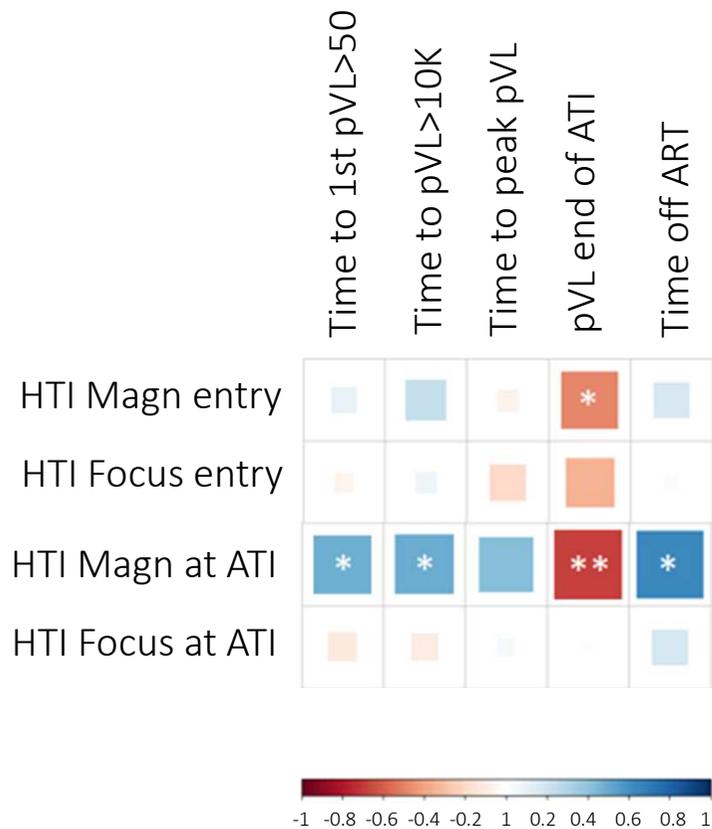


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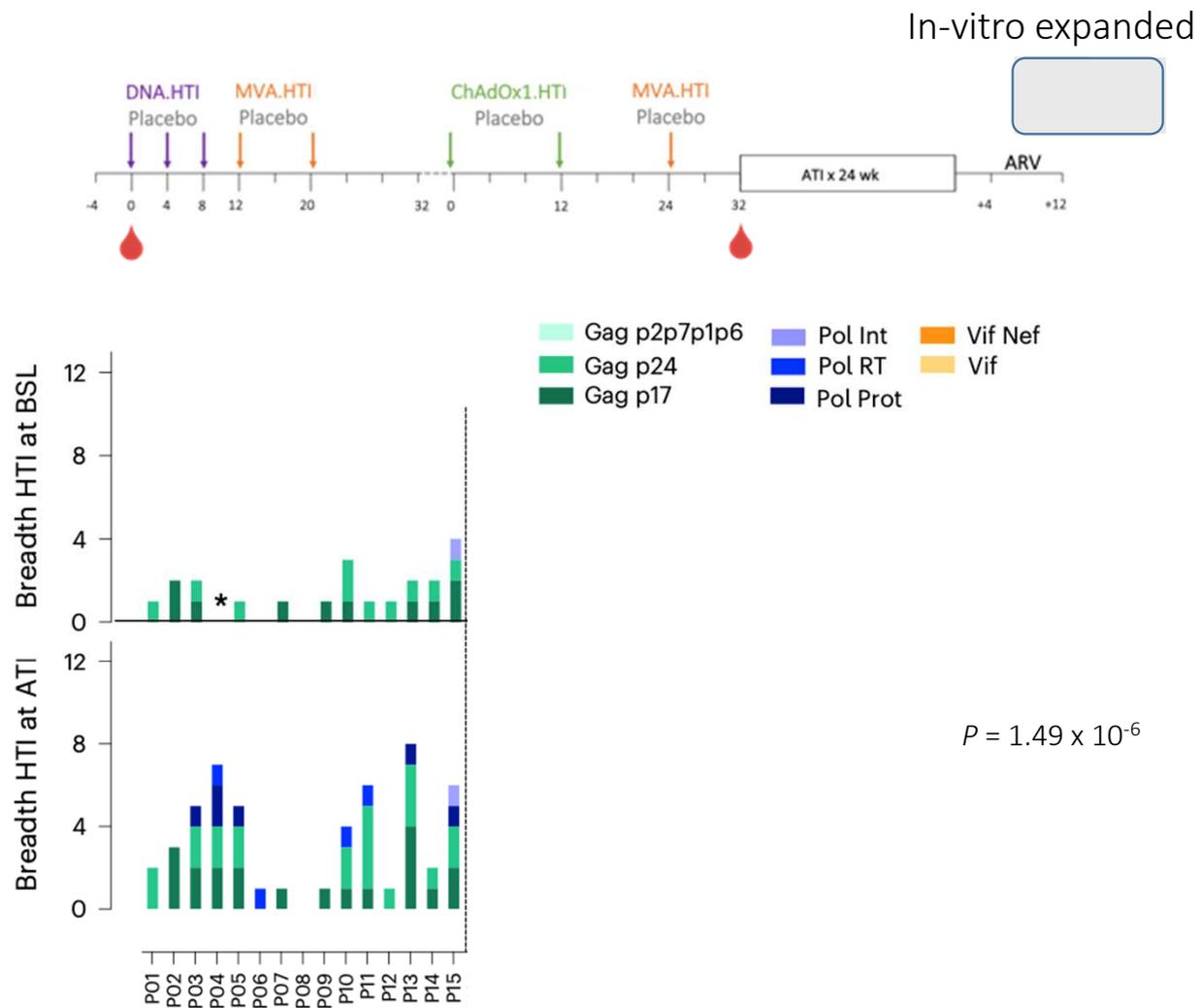


Anuska Llano  
 Tuixent Escribà

# Immune responses

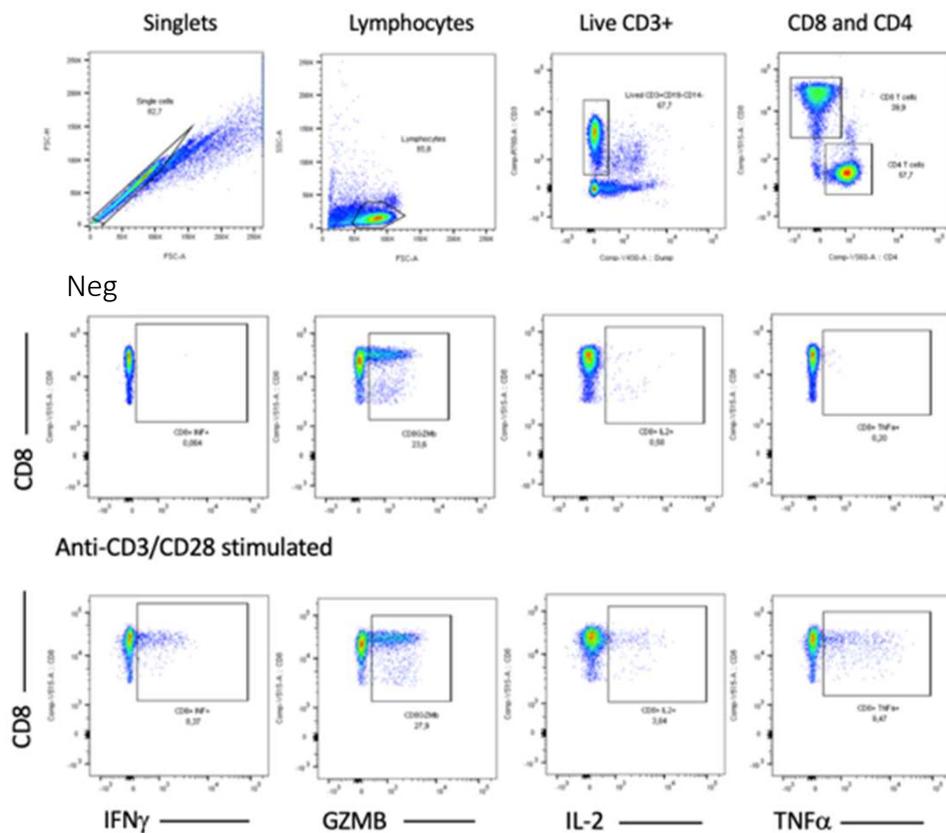
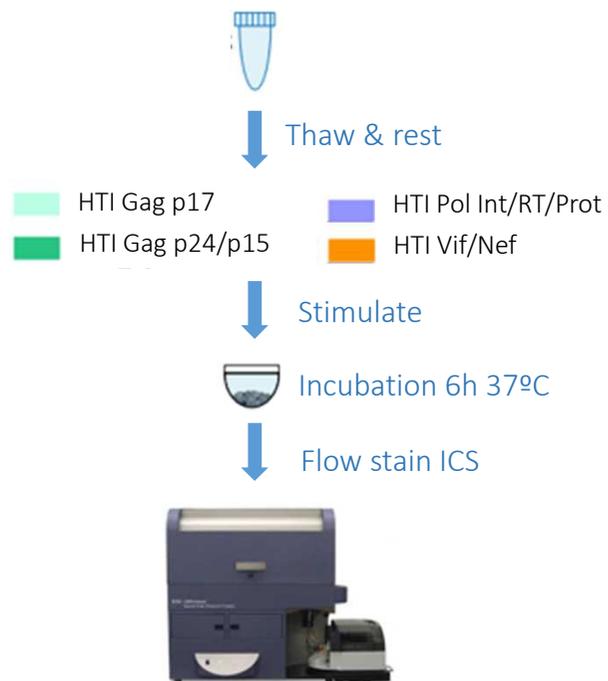
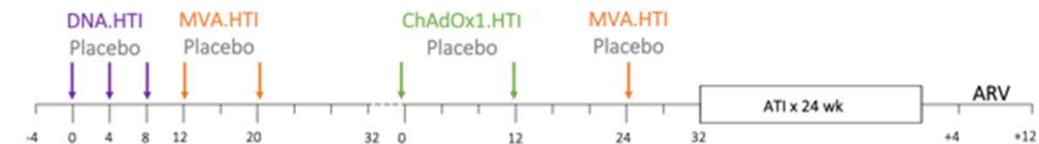


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De-novo responses being confirmed by TCR sequencing

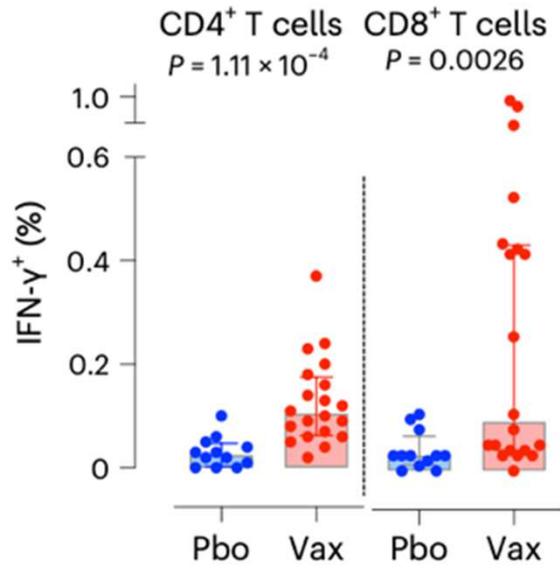
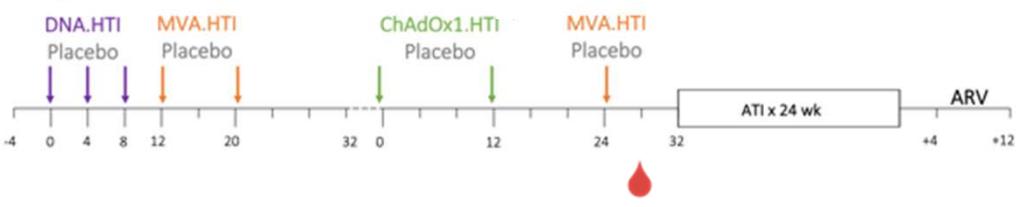
# Characterization of HTI-specific responses



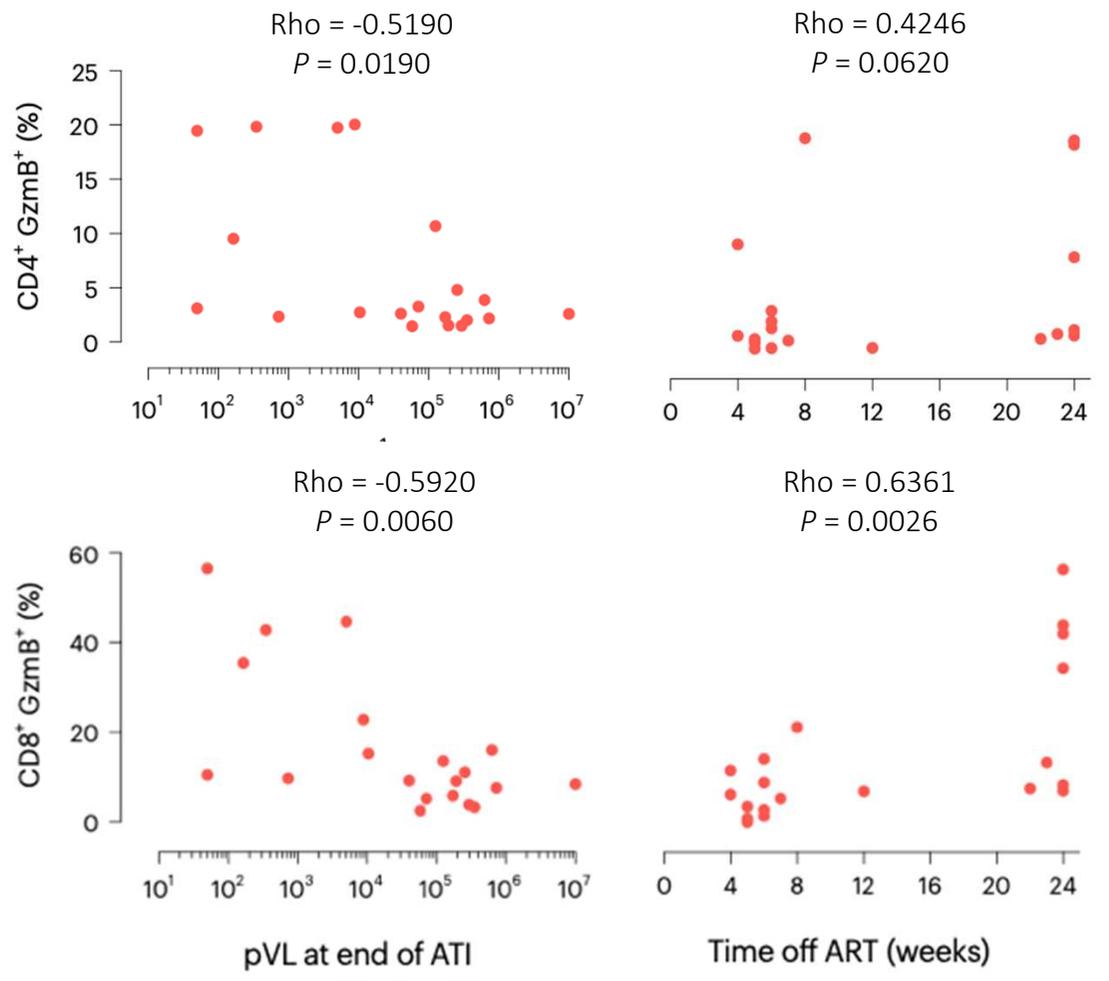
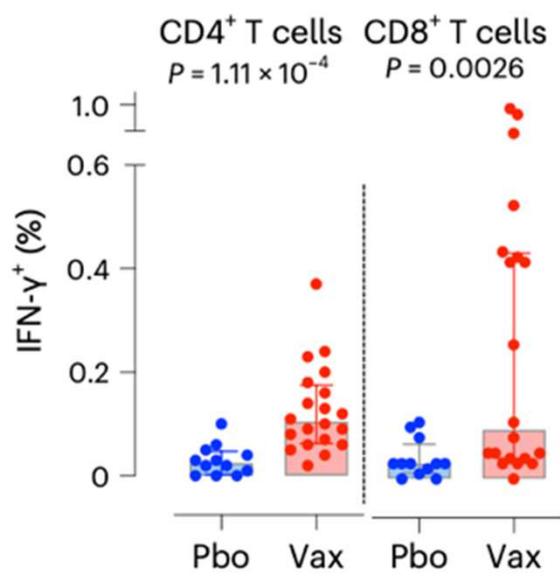
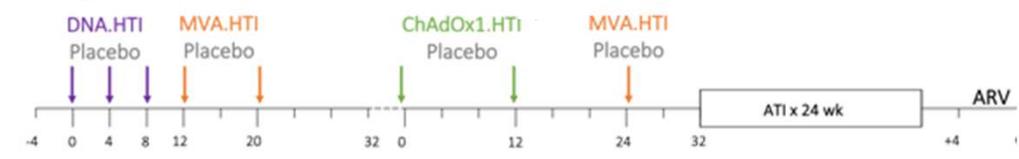
Anuska Llano  
Samandhy Cedeño



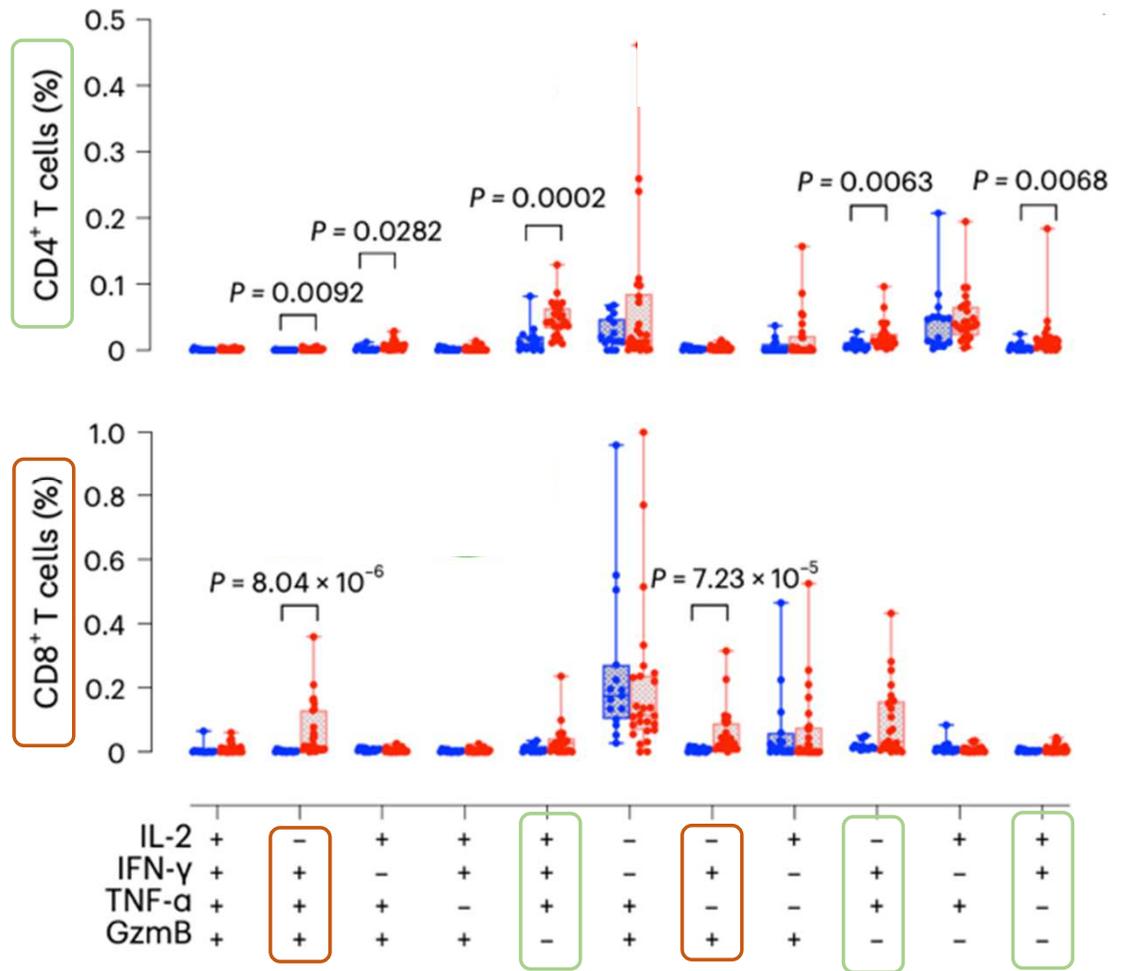
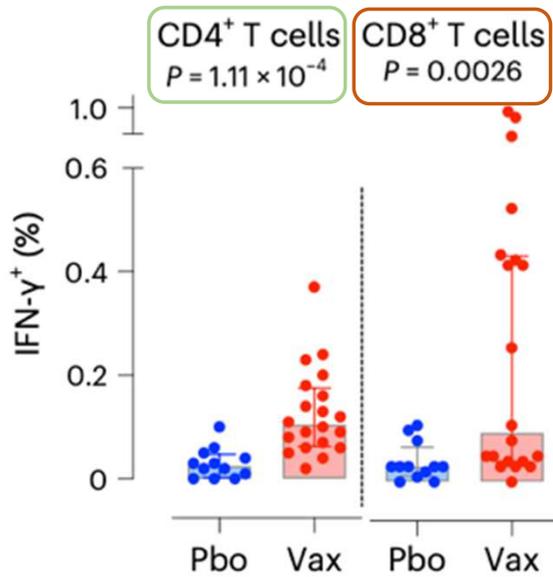
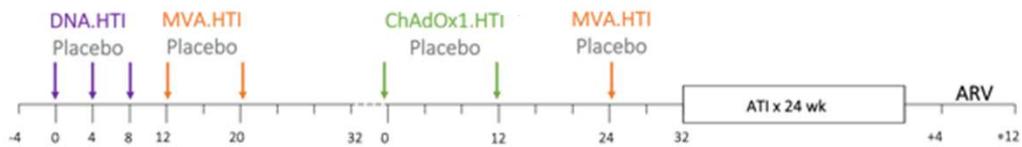
# Both CD4 & CD8 T cells induced



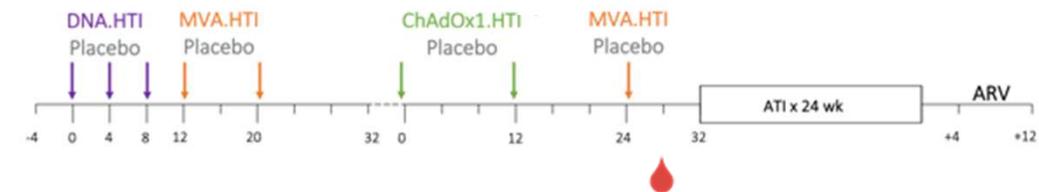
# CD8<sup>+</sup> GzmB<sup>+</sup> (&CD4) correlates w/ ATI outcomes



# Polifunctionality



# Polifunctionality



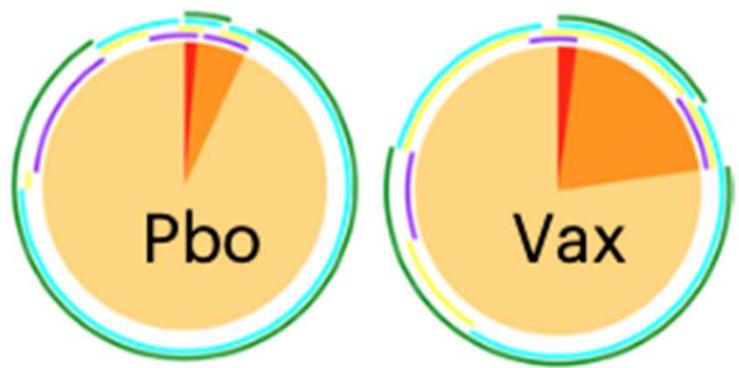
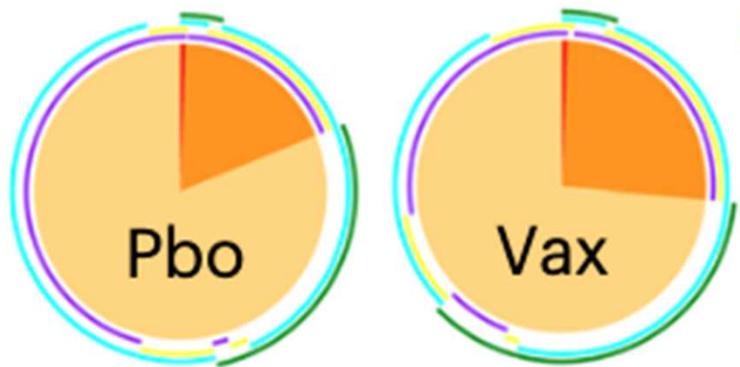
++
  +++
  +++++

CD4 T-cells

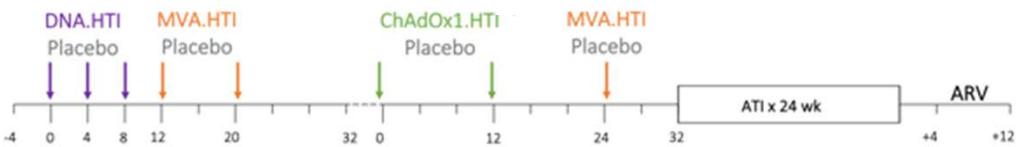
CD8 T-cells

TNF- $\alpha$ <sup>+</sup>  
 IL2<sup>+</sup>  
 IFN- $\gamma$ <sup>+</sup>

GzmB<sup>+</sup>  
 TNF- $\alpha$ <sup>+</sup>  
 IFN- $\gamma$ <sup>+</sup>



# Exhaustion markers



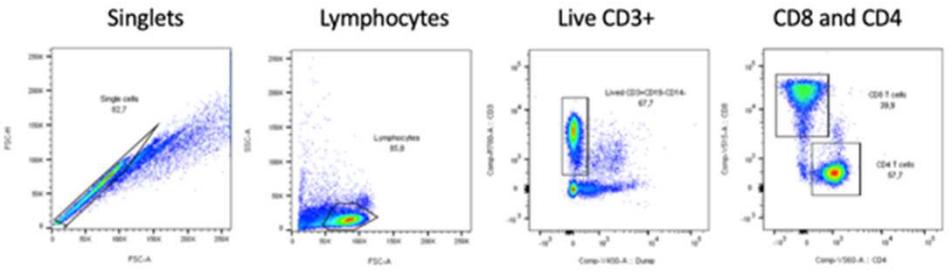
Thaw & rest

- a-CD28/a-CD49d
- DMSO

Stimulate

Incubation 6h 37°C

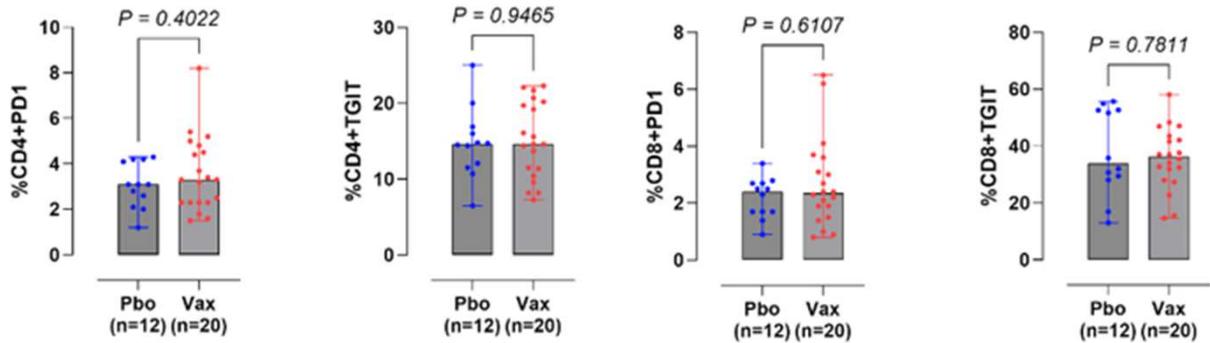
Surface markers  
Flow stain



Phenotype  
CD45RA/CCR7

Exhaustion  
PD1/TIGIT

Activation  
HLADR/CD69





# Conclusions

- HTI vaccines induced high frequency of broad and polyfunctional CD4 & CD8 T cell responses
- HTI magnitude, breadth and frequency of GzmB<sup>+</sup> T cells at ATI correlated with time off ART and pVL at ATI end
- In the univariate and multivariate logistic regression models, reservoir levels were not associated with higher chances of remaining off ART
- In the multivariate, when accounting for pVL pre-ART and CD4/CD8 ratio, vaccination increased probability for being off ART.

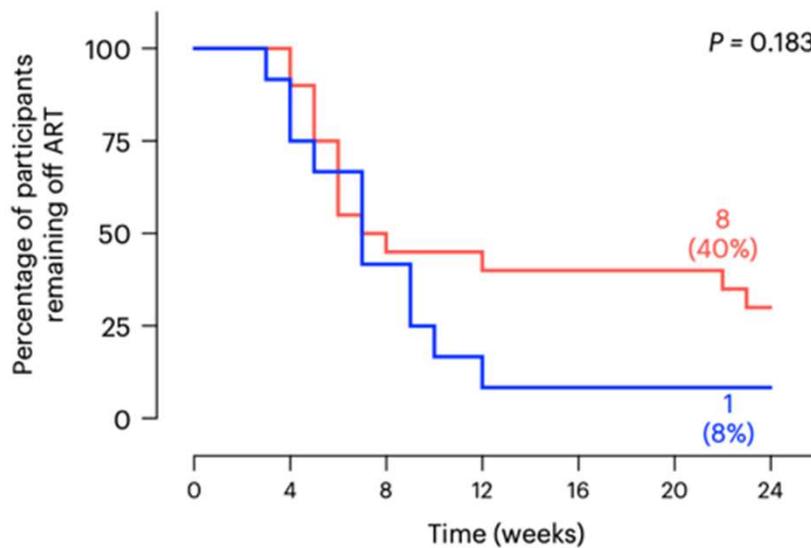
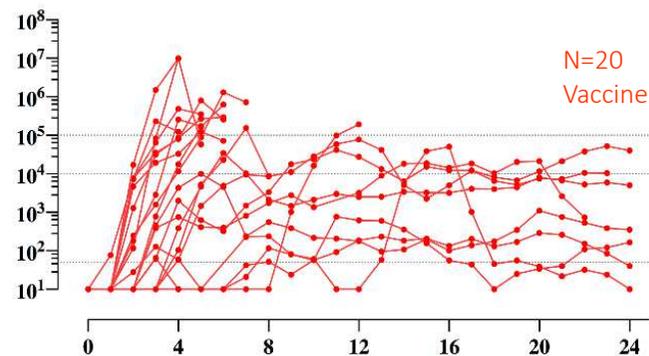
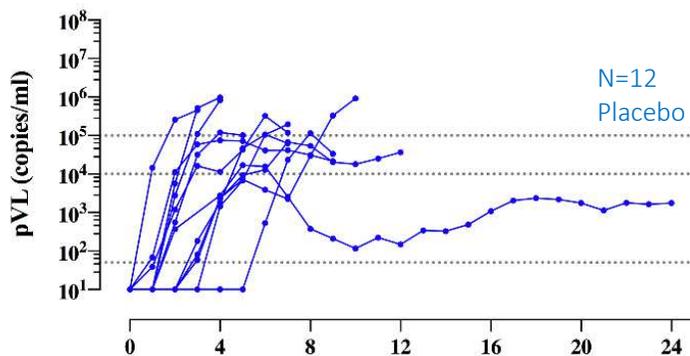
	$\hat{\beta}$	<i>s. e.</i> ( $\hat{\beta}$ )	$\widehat{OR}$	95% CI ( $\widehat{OR}$ )
(Intercept)	2.9567	3.2682		
Treatment (Vax)	2.1105	1.1929	8.25	1.05 ; 140.36
pVL at ART initiation (1 log <sub>10</sub> copies/mL)	-1.5881	0.7807	0.20	0.03 ; 0.73
Ratio CD4/CD8 at AELIX-002 entry (0.2 units)	0.4070	0.8943	1.50	1.10 ; 65.77

*Vax, vaccine; pVL, plasma viral load; ART, antiretroviral treatment.*



# Next steps

## Participants Without Beneficial HLA class I alleles



How to improve this effect?  
More individuals & better viral control!

HOST / Baseline conditions  
VIRUS

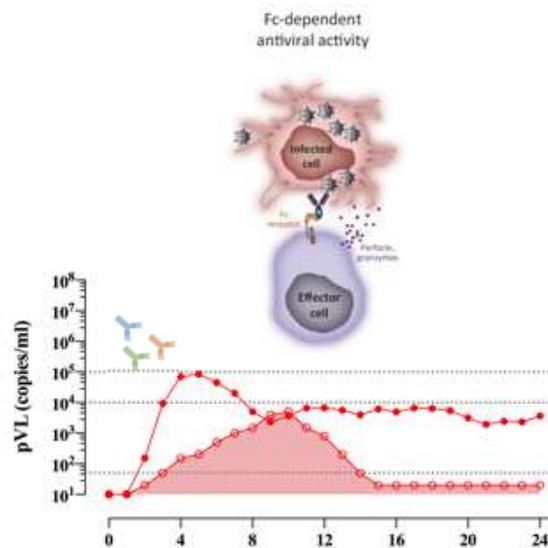
VACCINE-INDUCED RESPONSES

# Next steps

## VIRUS

Reduce or Silence viral reservoir

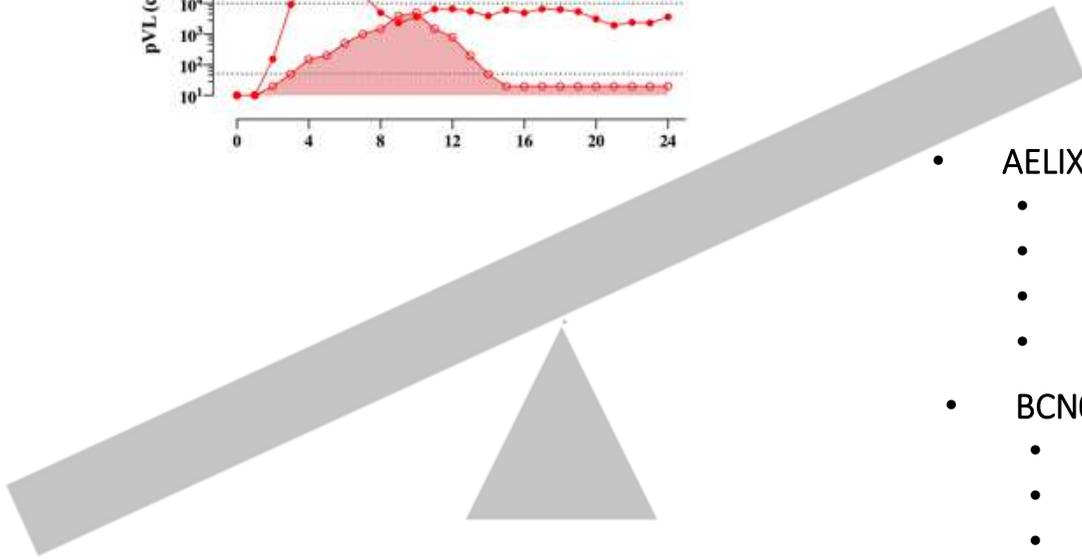
- Reverse Latency
- Target escaped variants
- Lock the reservoir



## IMMUNE

Improve vaccine immunogenicity

- New vectors (mRNA)
- Able to sensor latent infected cells
- Reversion of T-cell exhaustion / CTL resistance



- AELIX-003 (NCT04364035)
  - ChAdOx1.HTI + MVA.HTI + Vesatolimod
  - 57 early-treated
  - ATI
  - Unblinding (Q1 2023)
- BCN03 (NCT05208125)
  - ChAdOx1.HTI + MVA.HTI + SOSIP
  - 30 chronics
  - ATI
  - Ongoing (Q4 2023)

# Acknowledgements



Jose Moltó  
Lucía Bailón  
Cora Loste  
Miriam Lopez  
Paco Perez  
Aroa Nieto  
Patricia Cobarsí  
Jordi Puig  
Cristina Martinez  
Jose Muñoz

Jessica Toro  
Roser Escrig  
Helena Pera  
Lara Teruel  
Myriam Solà

Yovaninna Alarcón-Soto

BONAVENTURA CLOTET



Eulàlia Grau  
Rafi Ayen  
Lucía Gómez  
Cristina Ramirez

Samandhy Cedeño  
Tuixent Escribà  
Anuska Llano  
Miriam Rosàs-Umbert  
Bruna Oriol  
Luis Romero  
Marta Ruiz-Riol  
Cristina Peligero

Roger Paredes  
Marc Noguera  
Maria Casadellà  
Mariona Parera

CHRISTIAN BRANDER



Pep Coll  
Angel Rivero  
Félix Pérez  
Jorge Saz  
Javier Fernández

MICHAEL MEULBROEK  
FERRAN PUJOL



Devi SenGupta  
Romas Geleziunas



Anne Leselbaum  
Marga Garcia  
Ian McGowan  
Lance Berman  
Jordi Naval  
Marc Mansour

M. Pierre Malice (ext)

JOSE LUIS CABERO



45 participants and their families

# Funding



European Union's Horizon 2020  
research and innovation program  
GA 681137



P01-AI131568



Spanish Research Agency and the  
European Regional Development Fund  
RTC-2017-6473-1



*Una manera de hacer Europa*

ISCIII PI 20/01039



**COMMUNITY SUMMARY**

- HTI vaccines were designed based on human immune data to induce better viral control
- FIH RCT in early-treated PWH show safety and immunogenicity, inducing responses with similar characteristics to those described in HIV controllers, regardless of favourable HLAs
- All participants experienced viral rebound upon ART interruption. However, vaccine responses were associated with better HIV control, despite not reaching undetectable levels.
- **Next Steps:**
  - Data support the use of HTI as a potential 'T-cell backbone' vaccine in combination trials.
  - Two RCT already ongoing (in early-treated and PWH that did not start ART in acute/recent HIV infection) with results expected in 2023-24 respectively