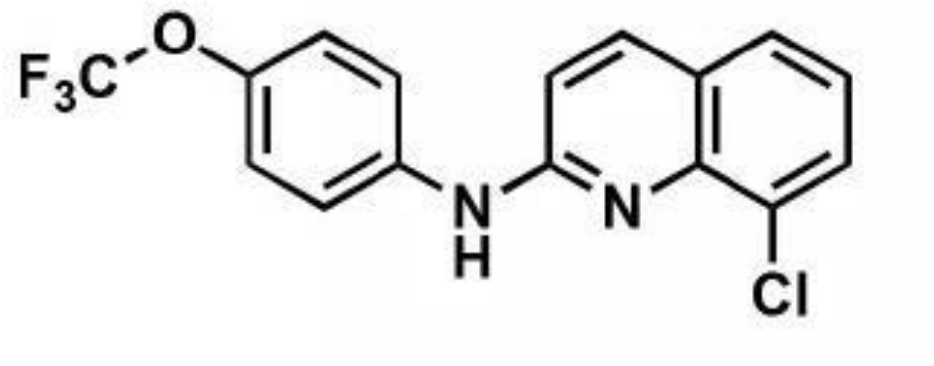
Oral ABX464 has a Dose Dependent Reduction in the HIV-1 DNA Reservoir in CD4+ Peripheral Blood T Cells (Study ABX-005)



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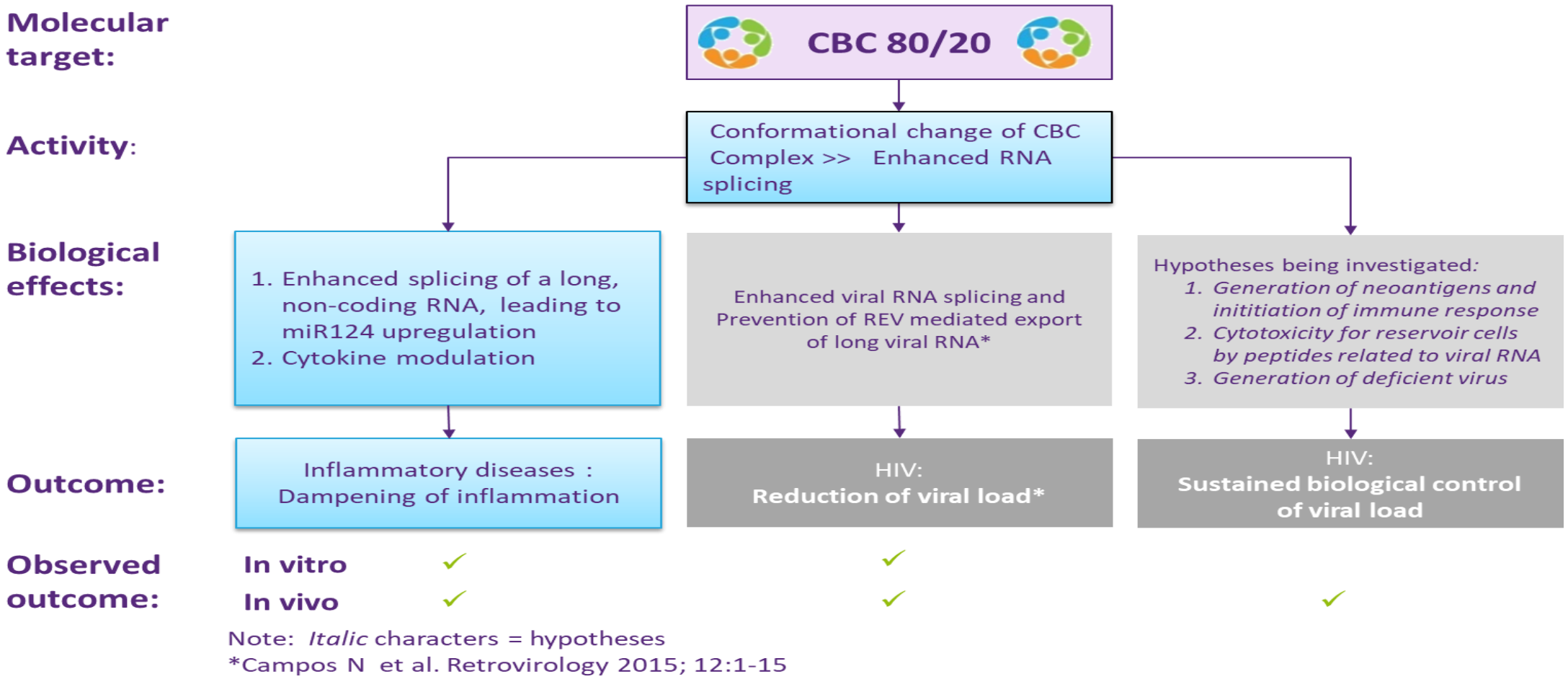
Disclosures

- GSK
- ABIVAX

ABX464 targets the Cap Binding Complex (CBC)



Note: *Italic* characters = hypotheses

*Campos N et al. Retrovirology 2015; 12:1-15

ABX464-005 Study

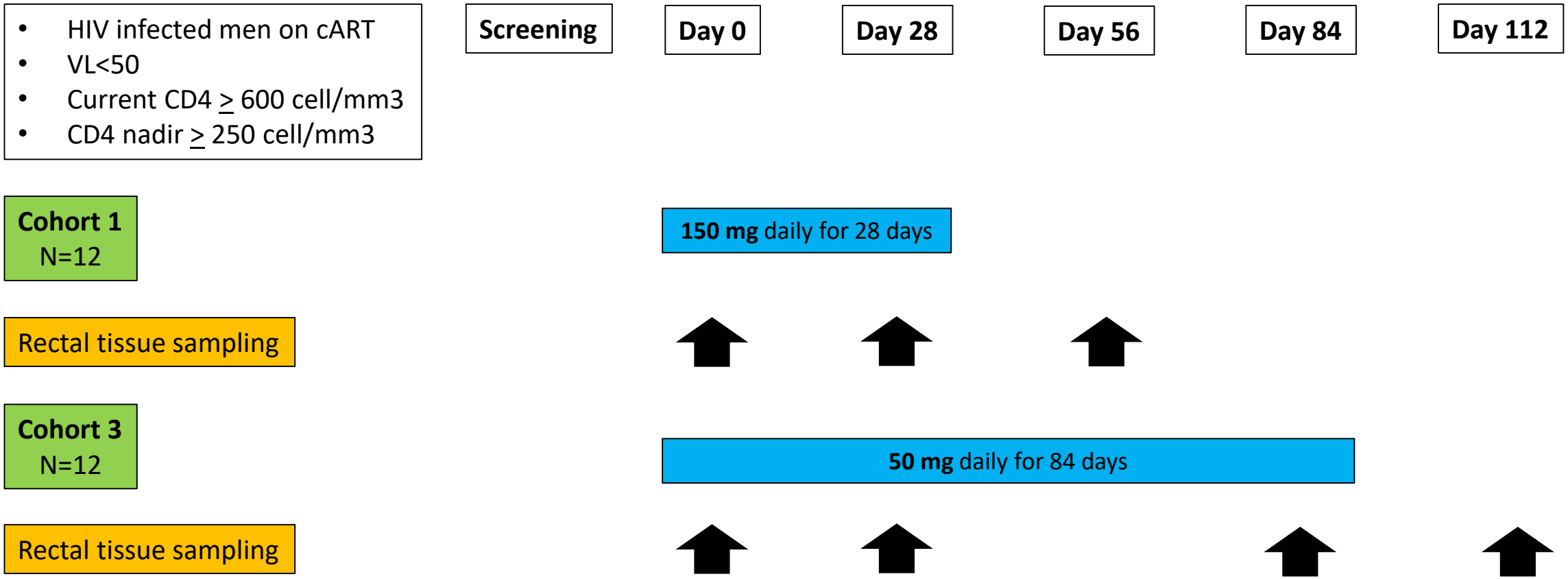
Title: An Open-Label Study of the Safety, Pharmacokinetics, and Pharmacodynamics of ABX464 in HIV-1 Seronegative and Seropositive Adults

Primary objective:
To evaluate the distribution of ABX464 and its main metabolite (N-Glu) in various compartments in HIV-1 Seronegative and Seropositive adult subjects

Secondary objectives:
To evaluate the safety of ABX464 administered once daily at one dose, alone in HIV-uninfected subjects and in combination with ARTs in HIV-1 infected adult subjects;
To evaluate the effect of ABX464 on the HIV reservoir cells in HIV-infected adult subjects;
To evaluate the effect of ABX464 on the control of the viral load and the CD4+/CD8+ in HIV-infected adult subjects

ABX464-005 Study Schema

- HIV infected men on cART
- VL<50
- Current CD4 ≥ 600 cell/mm3
- CD4 nadir ≥ 250 cell/mm3



ABX-005: Sampling

Peripheral blood

- Systemic safety
  - haematology
  - renal
  - hepatic
- PK (up to 8h post dose)
- Peripheral CD4+ T cell purification
  - HIV DNA
  - HIV RNA
- Plasma viremia

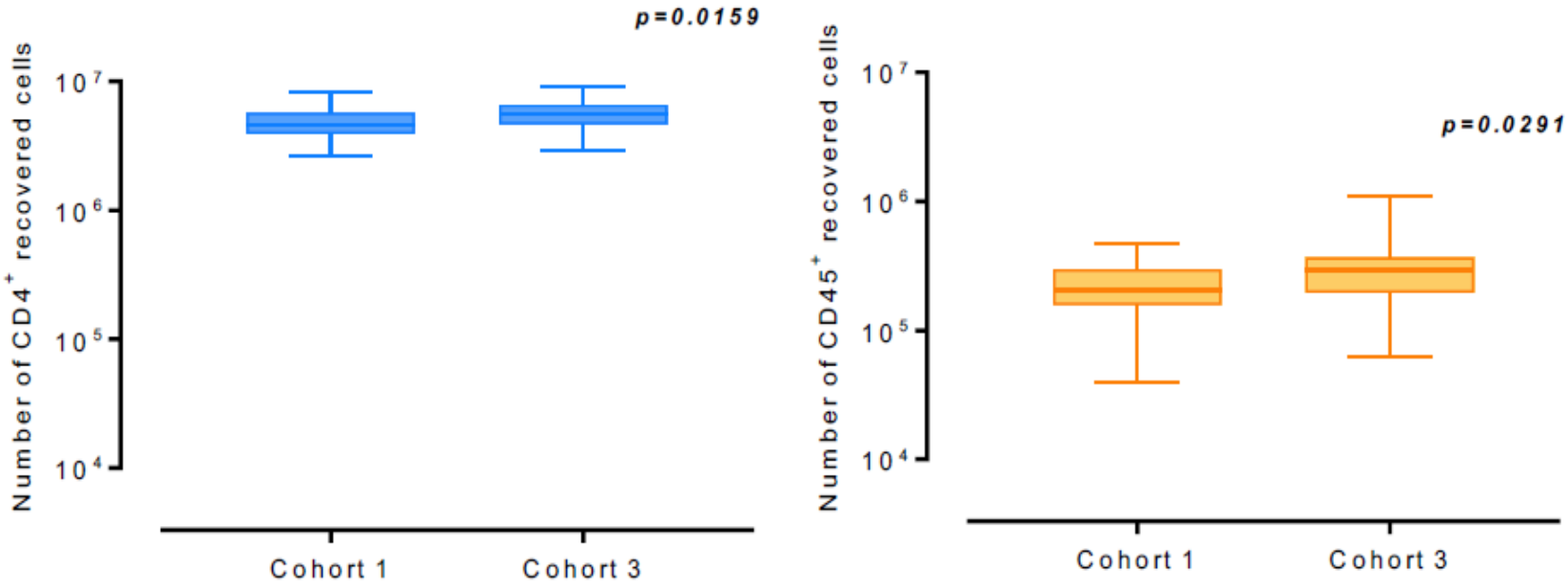
Rectal tissue

- PK
- MMC
  - HIV DNA
  - HIV RNA
- Flow cytometry
- Proteome
- Transcriptome

Rectal secretions

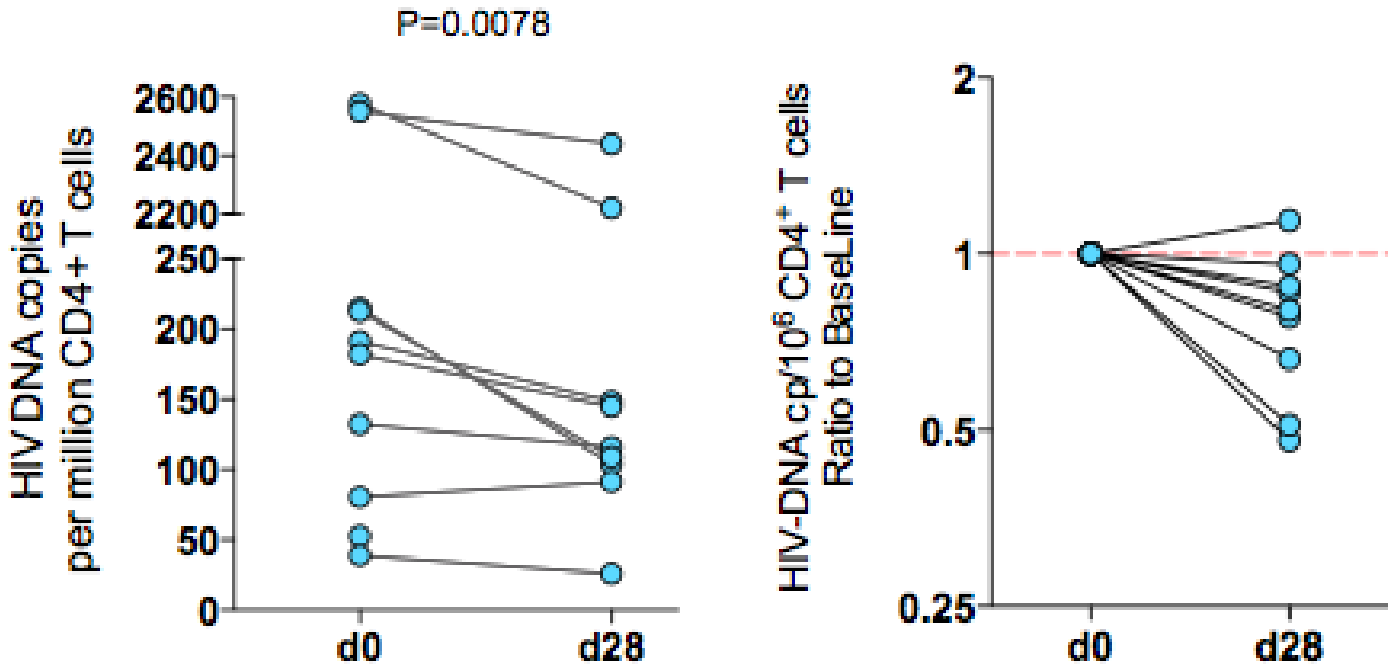
- Microbiome

Cohort 1 vs. 3: Recovered Cells



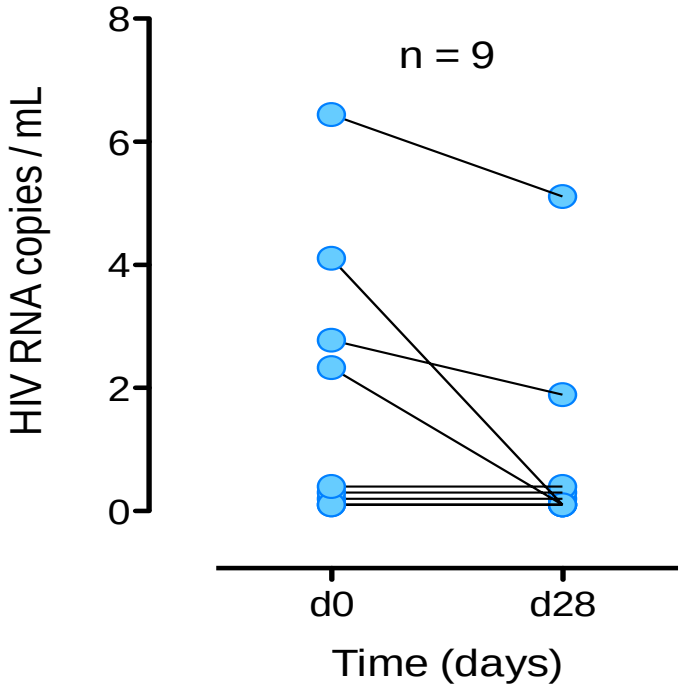
- Number of recovered cells significantly increases between cohort 1 and cohort 3 from peripheral $CD4^+$ T cells and CD45+ T cells from rectal tissue

ABX464-005: Cohort 1 HIV DNA in Peripheral CD4+ T-cells at Baseline and Day 28



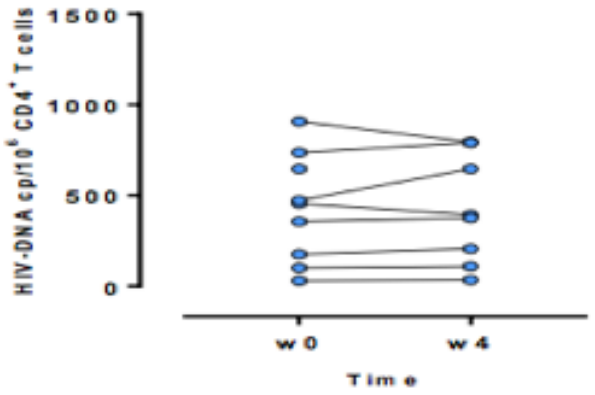
ABX464-005: Cohort 1 Residual Plasma HIV Viremia (SCA)

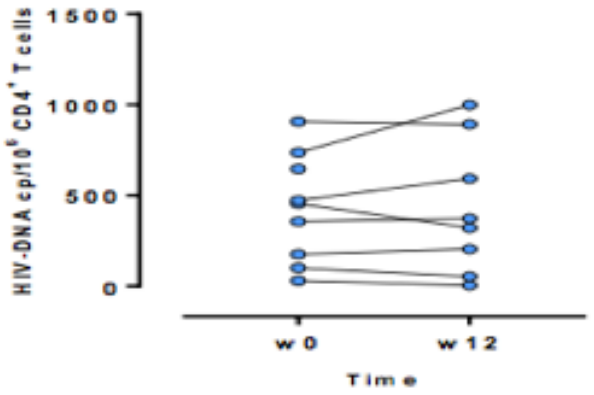
- All participants had <50 copies of HIV RNA at study enrollment
- LOQ = 0.5 HIV RNA copies/mL
- Residual viremia was detected in 5 participants
- In 4 participants there was a decrease between d0 and d28; one participant did not attend for d28 sampling
- 9/9 patients either decreased (n=4) or maintained their residual pVL suppressed from d0 to d28

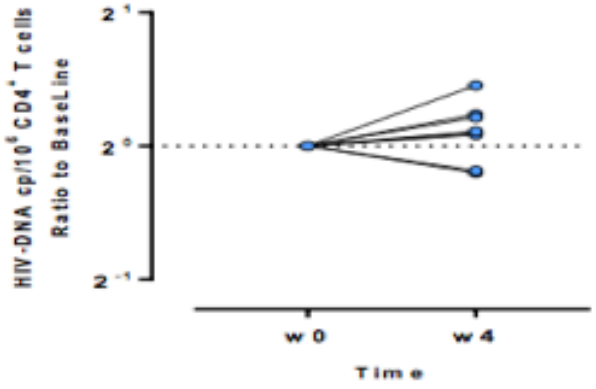


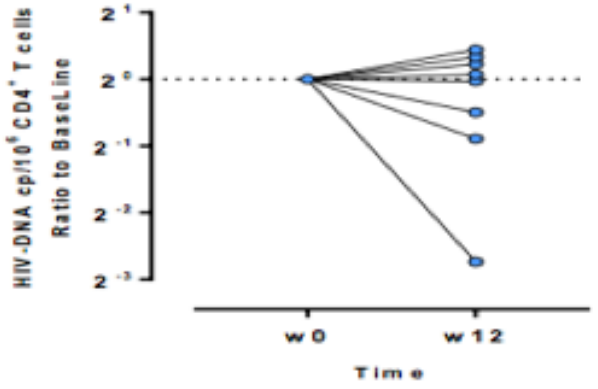
Increase: 0/9
Decrease: 4/9
Stable: 5/9

ABX464-005: Cohort 3 HIV DNA in Peripheral CD4+ T-cells









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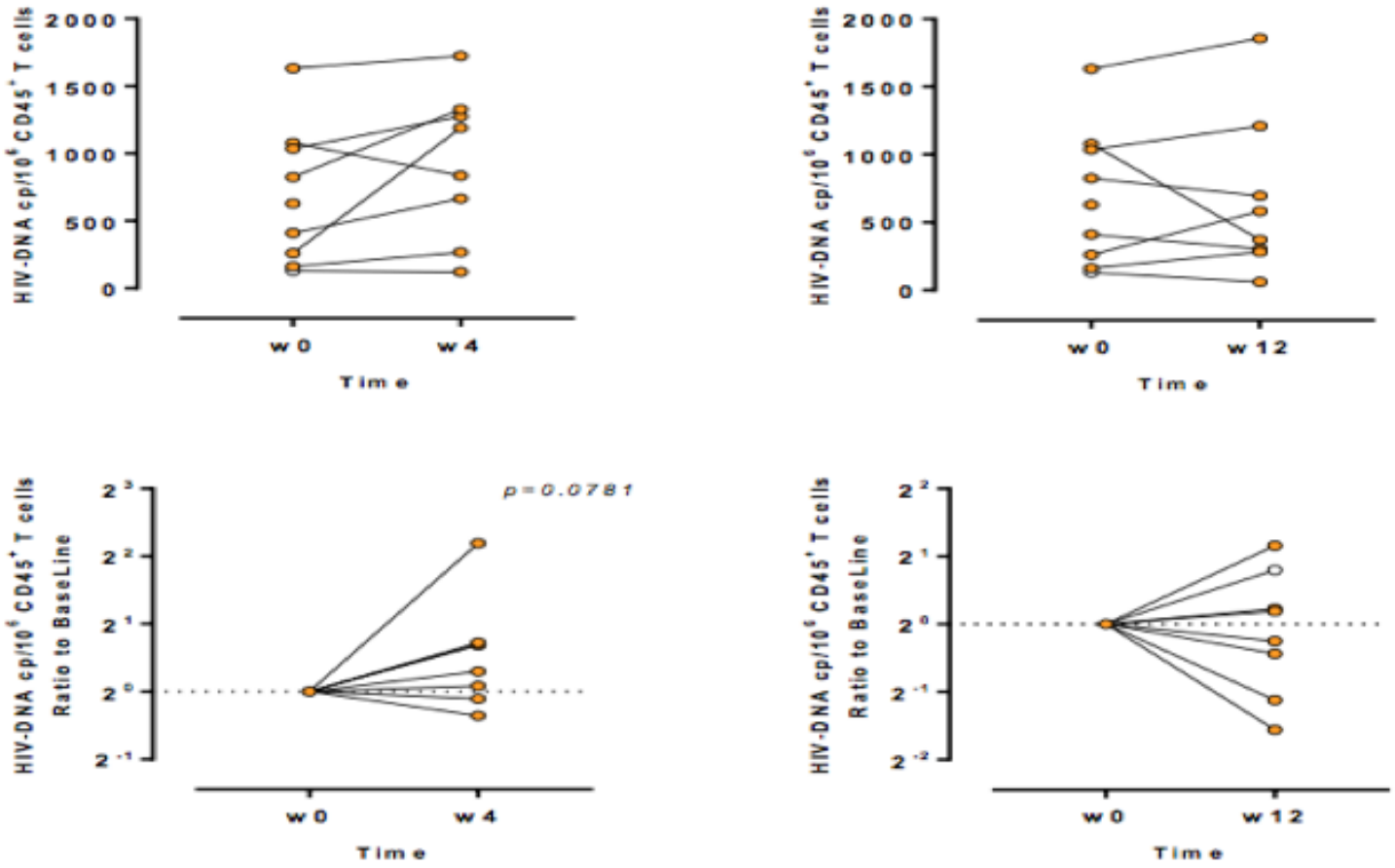
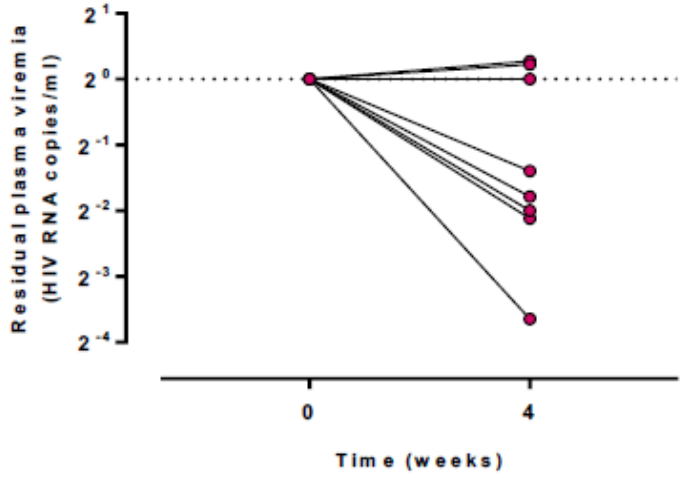
ABX464-005: Cohort 1 HIV DNA in Tissue CD45+ T-cells



ABX464-005: Cohort 3 Residual Plasma HIV Viremia (SCA)

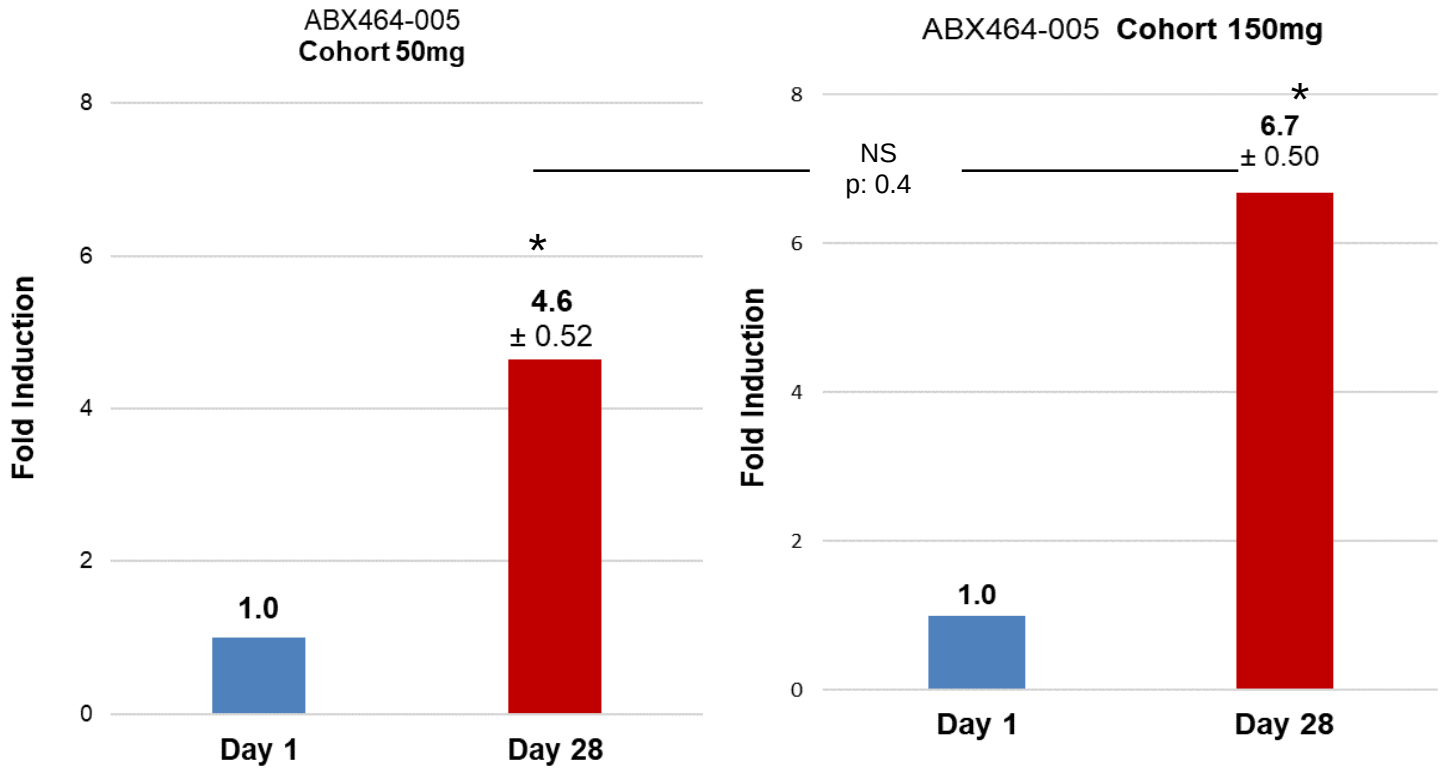
- 23/34 samples were detectable (range: 0.67 – 7.33)
- No statistically significant differences between w0-w4-w12-w16
- 6/8 patients either decreased (n=5) or maintained suppressed (n=1) their residual pVL from w0 to w4
- 5/8 patients decreased their residual pVL from w0 to w12
- 5/8 patients either increased (n=4) or maintained suppressed (n=1) their residual pVL from w12 to w16
- No association between changes in ca-HIV DNA and residual plasma viremia between w0 and w4.



Decrease 5/8 (>2-fold)
Increase 2/8 (<2-fold)
Stable 1/8

ABX464-005: miR124

- 150 mg q.d for 28 days
- 50 mg q.d for 84 days (with a time point at Day 28)



** pvalue < 0.05*

Statistically significant increase in miRNA 124 expression shows anti-inflammatory activity

ABX464-005Safety: Cohort 1 and 3

	Grade 1		Grade 2	
Treatment Emergent Adverse Event (TEAE)	**150 mg n=11**	**50 mg n=13**	**150 mg n=11**	**50 mg n=13**
Any TEAE (Related*): Participants experiencing at least one TEAE, n (%)	7 (63.6)	5 (38.5)	2 (18.2)	1 (7.7)
Abdominal pain	2 (18.2)	1 (7.7)	-	1 (7.7)
Epigastric pain	1 (9.1)	2 (15.4)	-	-
Flatulence	-	1 (7.7)	-	-
Nausea	4 (36.4)	-	-	-
Diarrhea	1 (9.1)	2 (15.4)	-	-
Headache/migraine	7 (63.6)	4 (30.7)	1 (9.1)	
Myalgia/lumbar pain	6 (54.6)	1 (7.7)	-	-
Cramps	1 (9.1)	1 (7.7)	-	-
Chest pain	1 (9.1)	-	-	-
Hyperamylasemia	-	-	1 (9.1)	-
Hyperlipasemia	-	-	1 (9.1)	-
Folliculitis	1 (9.1)	-	-	-
Rash erythematous	1 (9.1)	-	-	-

*In the opinion of the investigator of record

ABX464-005: Conclusions

- In Cohort 1 ABX464 150 mg po daily for 28 days was associated with:
  - a significant decrease in HIV-1 DNA in CD4+ T cells
  - reduction or maintenance of residual plasma HIV-1 RNA by SCA
  - an increase in tissue anti-inflammatory marker miRNA124
- In Cohort 3 ABX464 50 mg po daily for 84 days was associated with:
  - individual increases and decreases but no overall effect on HIV-1 DNA in CD4+ T cells
  - individual increases and decreases but no overall effect on HIV-1 DNA in CD45+ MMC
  - a lower increase in tissue anti-inflammatory marker miRNA124 than in Cohort 1
- In participants treated with cART, ABX464-005 supports the continued development of ABX464 as a component of cure eradication strategies

Acknowledgements ABX464-005

- Study participants
- Fundació Lluita contra la Sida
  - Ross Cranston
  - Roser Escrig
  - Aroa Nieto
- IrsiCaixa
  - Javier Martinez-Picado
  - Sílvia Bernal
  - Mª Carmen Puertas
  - María Salgado
  - Roger Paredes
  - Eulalia Grau
  - Mariona Parera
  - Bonaventura Clotet
- ABIVAX
  - Hartmut Ehrlich
  - Paul Gineste
  - Josianne Nitcheu
  - Sandrine Crabe
  - Didier Scherrer
- University of Pittsburgh
  - Ian McGowan