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On behalf of the HVTN 804/HPTN 095/A5390 study team

OA06 Monoclonals for prevention

Analytical Treatment Interruption (ATI) in Peru: Stakeholder Engagement & Early Clinical Data

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HPTN HIV Prevention Trials Network

ACTG AIDS CLINICAL TRIALS GROUP

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Summary

What is your main question?

Can durable virologic control (low or undetectable viral load) off ART be achieved among individuals with early ART initiation +/- **VRC01**, close to HIV acquisition?

- Is it possible to implement an ATI in LMICs, e.g. Peru?

What did you find?

Yes, with strong local stakeholder engagement, we successfully implemented an ATI in Peru. However, we did not observe evidence of durable off-ART virologic control in our participants

Why is it important?

ATIs could serve as safe & effective tools for evaluating new HIV prevention & cure/remission strategies, including vaccines and monoclonal antibodies

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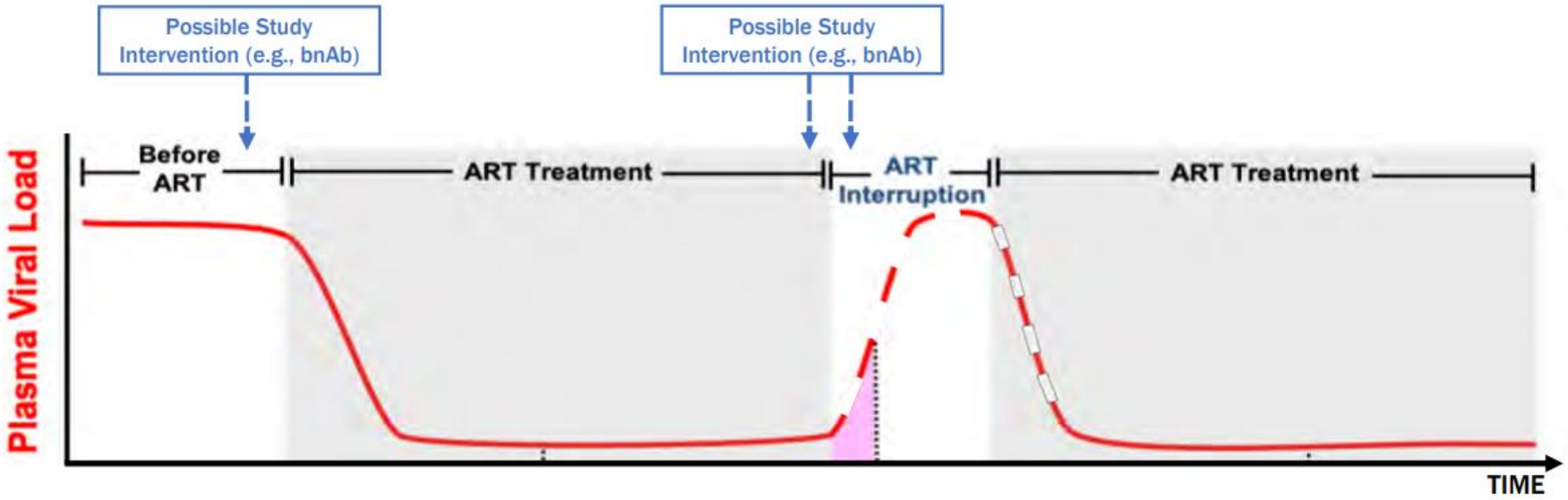
Analytical treatment interruption (ATI)



- A carefully monitored ART pause for an individual living with HIV
- Historically used as part of therapy, in hopes of minimizing ARV toxicities, addressing multiresistant virus, & treatment failure
- Now used in research to evaluate options for HIV viral suppression, including for sustained, ART free virologic remission (SVR); safe & well-tolerated "design of choice" in HIV cure research

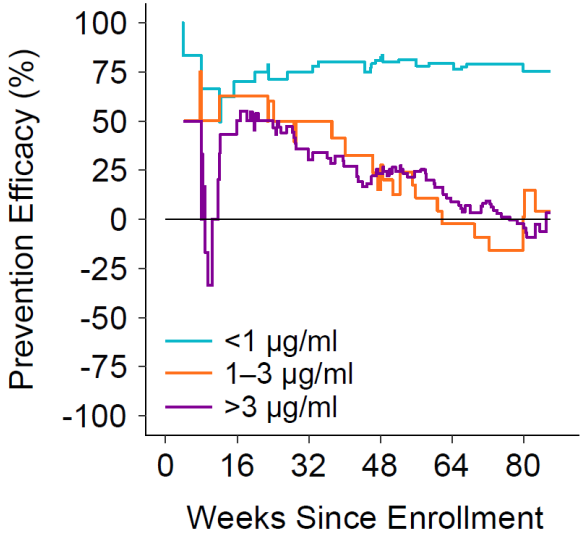
Antibody Mediated Prevention: The AMP studies

Sub-Saharan Africa

Americas/Europe AMP
- Peru: 48.9% (1131/2701) ppts

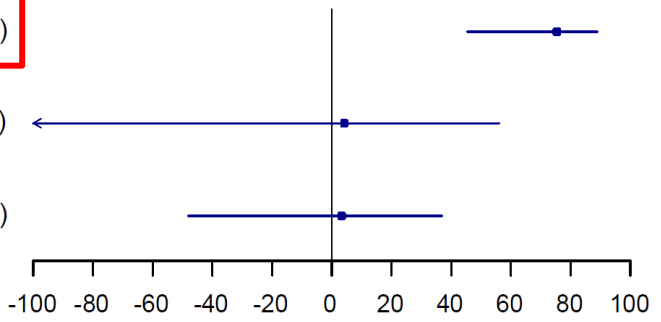
Proof of concept: The mAb VRC01 showed prevention efficacy against neutralization-sensitive HIV viruses

A

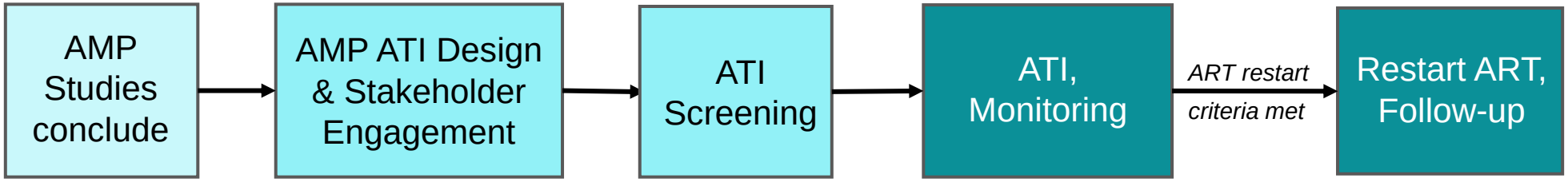


B

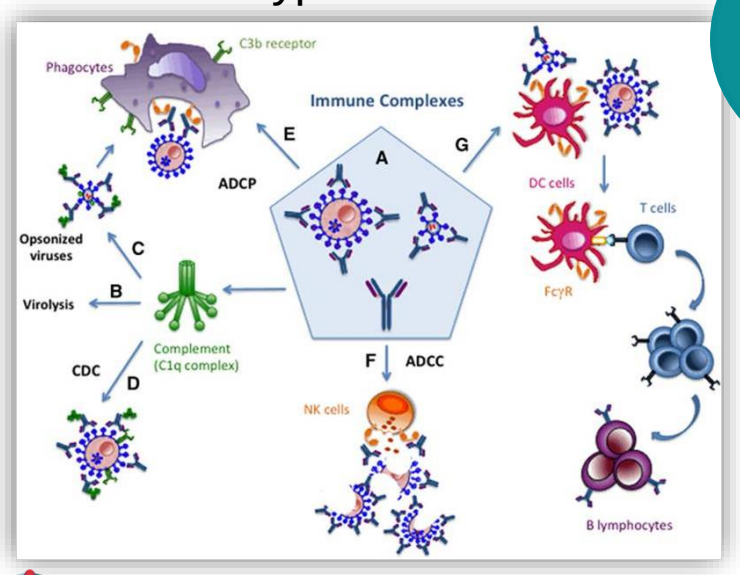
Pre-Specified IC_{80} Category	Treatment Arm	No. of HIV-1 Inf.	No. of Person-Years	Rate per 100 Person-Years	PE (95% CI)
<1 µg/ml	Control	19	2203	0.86	
	VRC01 Pooled	9	4427	0.20	75.4 (45.5, 88.9)
1-3 µg/ml	Control	10	2203	0.45	
	VRC01 Pooled	19	4427	0.43	4.2 (–108.7, 56.0)
>3 µg/ml	Control	35	2203	1.59	
	VRC01 Pooled	70	4427	1.58	3.3 (–48.0, 36.8)



AMP ATI Design & Select Endpoints



Hypothesis



Vaccinal Effect?

Objectives/endpoints

To evaluate the effect of **early ART initiation**, **with or without VRC01** receipt in the immediate pre-HIV acquisition period and/or during early infection on:

- **Duration of ART-free viral control**
- **Development of HIV-specific immune responses**

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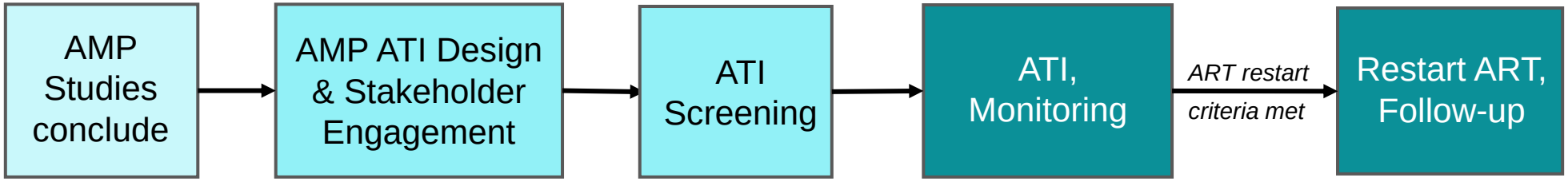
Lambour J, et al. Emerg Microbes Infect. 2016 Aug.

AMP ATI Design & Select Endpoints



Key inclusion criteria

- Acquired HIV within 8 weeks of an AMP infusion
- Initiated ART early & remained virally suppressed for at least a year
- Meet other eligibility criteria

ART re-initiation criteria

- Viral load > 1,000 copies/mL for ≥ 4 consecutive weeks & not declining by 0.5 log from prior week.
- CD4+ T cell count < 350 cells/mm3, confirmed on a second sample.
- Any HIV-related syndrome (eg, acute retroviral syndrome, an opportunistic infection).
- Participant or provider wish to re-initiate ART.

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Peru Stakeholder engagement (2019)

Multi-Stakeholder meetings with:

- Community members
- Investigators
- ART providers
- MoH officials
- Regulatory bodies (INS)

Helped to build trust, addressed misconceptions, and facilitated regulatory review

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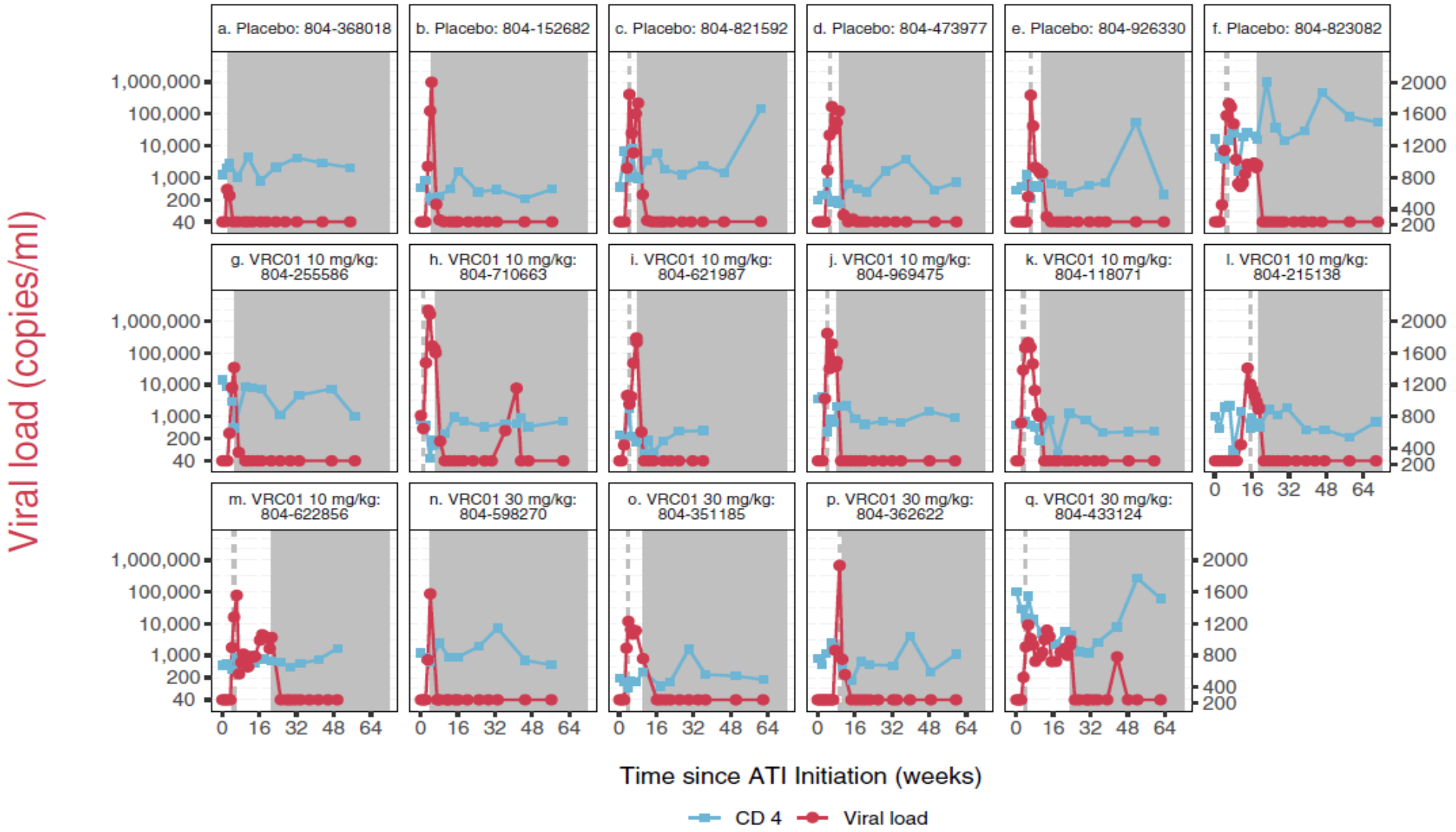
Viral load & CD4 over 64 weeks since ATI, n=17

No evidence of durable viral control
(VL < 200 copies/mL for >24 wks off ART)



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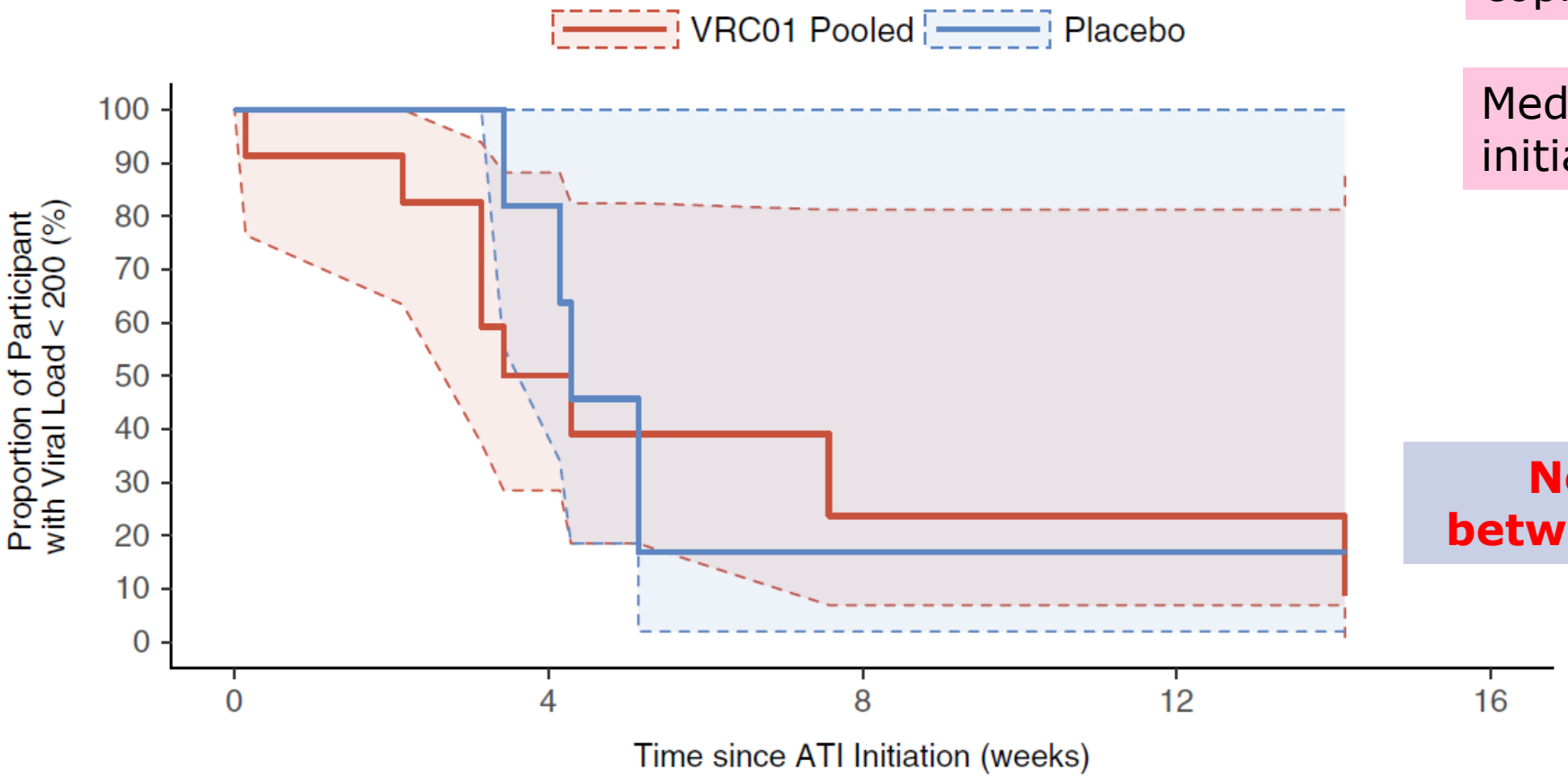
Time to VL>200 copies/mL



Median time to VL>200 copies/mL: 4.1wks (0.1-14.1)

Median time to ART re-initiation: 7.9wks (2.7-23)

No significant difference between VRC01 & placebo ppts

Peru AMP ATI: Clinical data

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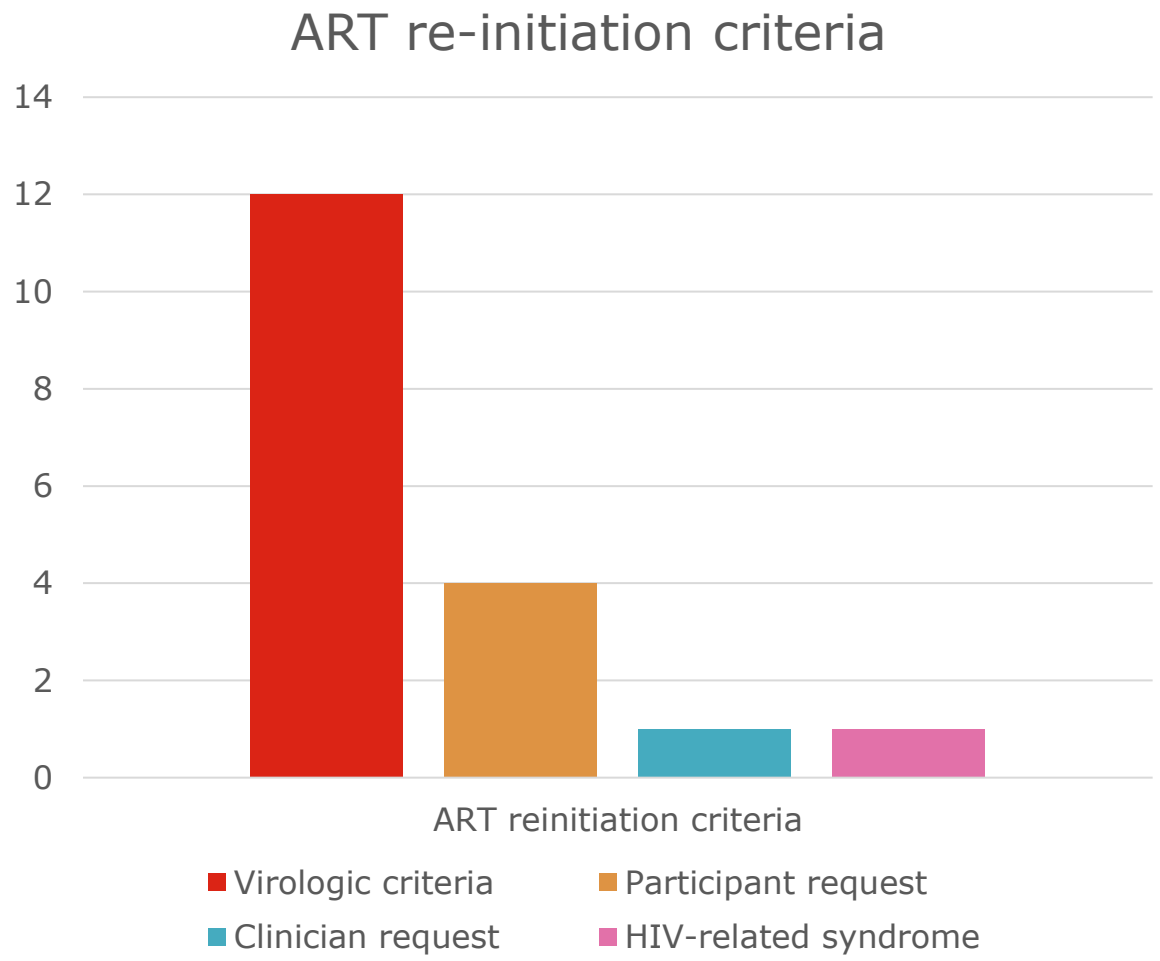
Total participants in Peru ATI: 18

- 14 MSM, 3 trans individuals, 1 gender non-binary
- No HIV transmissions
- No SAEs or AEs Grade ≥ 3
  - One ppt reported ARS
- 9 STIs in 8 ppts
- One participant with tenofovir levels compatible with ongoing ART use (excluded from analysis for virologic control; included in safety analyses)



Next steps

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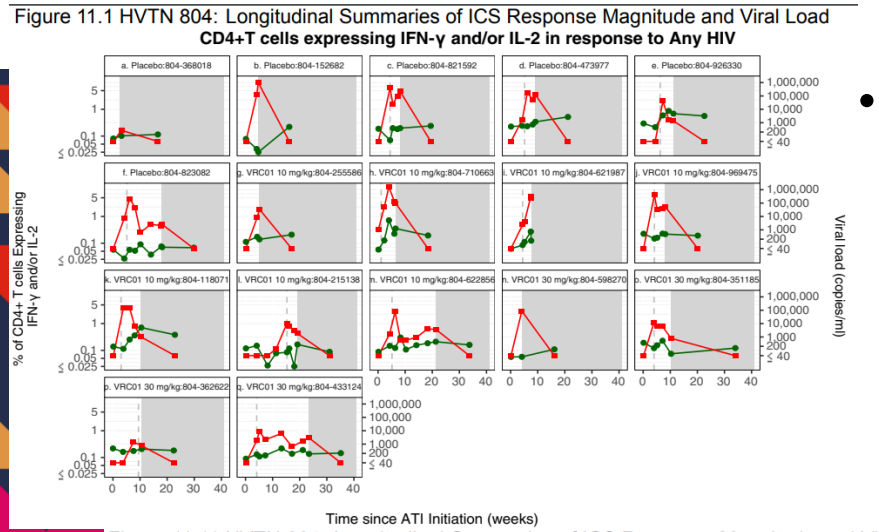

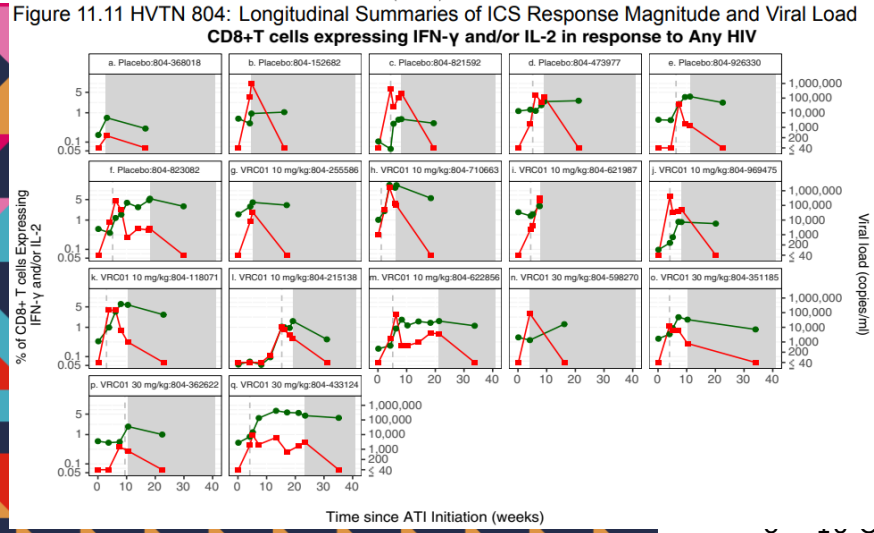

- To evaluate the effect of early ART initiation +/- VRC01 on the development of anti-HIV immune responses and the potential association of those immune responses with time to ART re-initiation criteria:
  - HIV-specific CD4+ and CD8+ T-cell responses
  - Autologous & heterologous neutralizing antibody responses
  - Non-neutralizing, FcγR-mediated antibody effector functions
  - Dendritic cell activation and maturation markers
  - T- and B-cell activation and exhaustion markers

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Conclusions

- The AMP ATI in Peru was successfully implemented with strong local stakeholder engagement
- We did not observe evidence of durable virologic control in our participants, nor differences on time to VL > 200 copies/mL between VRC01 & placebo recipients
- There is ongoing work to better understand the immune landscape of these participants and inform HIV vaccine development

AMP ATI Site Acknowledgements

Thank you to all the site investigators, clinic coordinators, community engagement teams, and pharmacists.

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HVTN 804/HPTN 095/A5390 Sites

- Iquitos
- Lima – Barranco
- Lima – San Marcos
- Lima – San Miguel
- Lima – Via Libre

Thank you, AMP ATI participants!

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AMP STUDY

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