Clinical and virologic outcomes of an ART interruption in treated controllers and non-controllers

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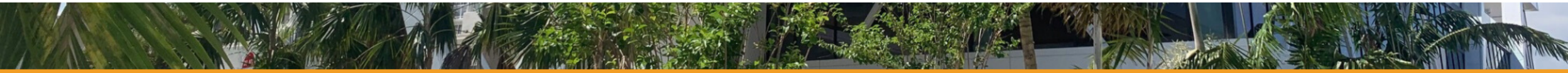


CONFLICTS OF INTEREST

Dr. Peluso has served on a Data Safety Monitoring Board for American Gene Technologies.

Community Summary

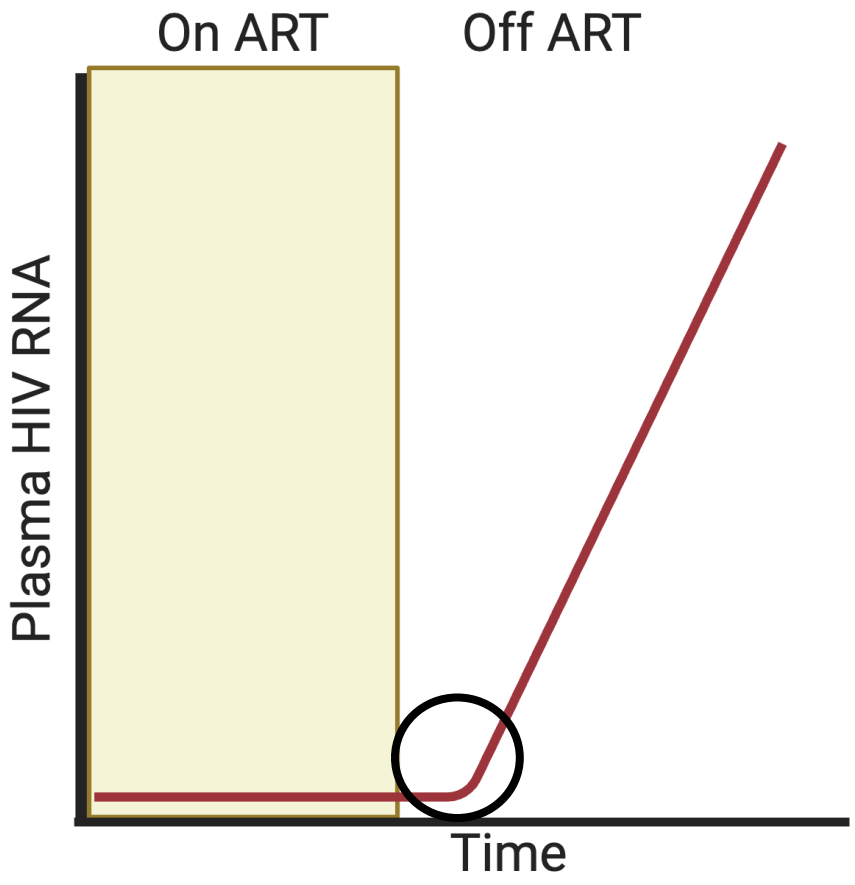
- In an non-interventional study, we evaluated HIV rebound dynamics in PWH pausing ART who were prior non-controllers vs. controllers
- In comparison to non-controllers, controllers had different rebound dynamics including reduced slope of rebound
- The rebound dynamics in an immunotherapy trial among PWH who exhibited post-intervention control was indistinguishable from the spontaneous controllers in the non-interventional study
- Understanding the interactions between the virus and immune system in both contexts can guide future HIV cure trials

Background

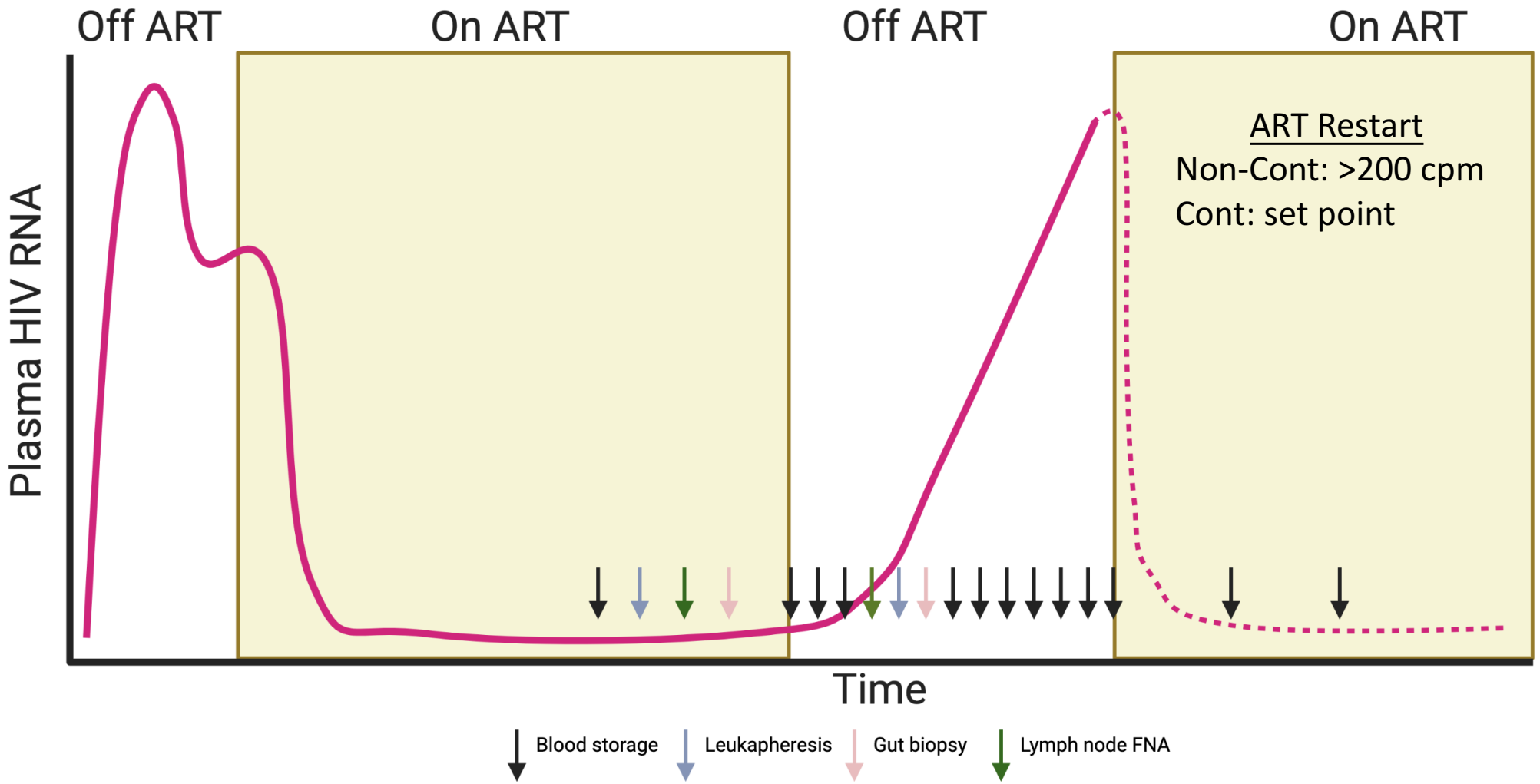
- The early host-virus interactions immediately post-ART ("the intercept") likely determine how well the immune system can control HIV

- Deep investigation of this early period may lead to novel cure strategies or biomarkers of delayed rebound or low set point

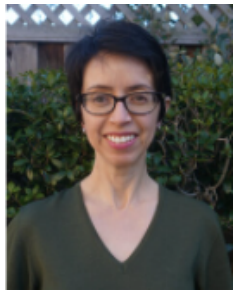
- We explored the early viral dynamics of spontaneous and post-intervention control



Methods: SCOPE-ATI Study



Lillie Cohn



Becky Hoh

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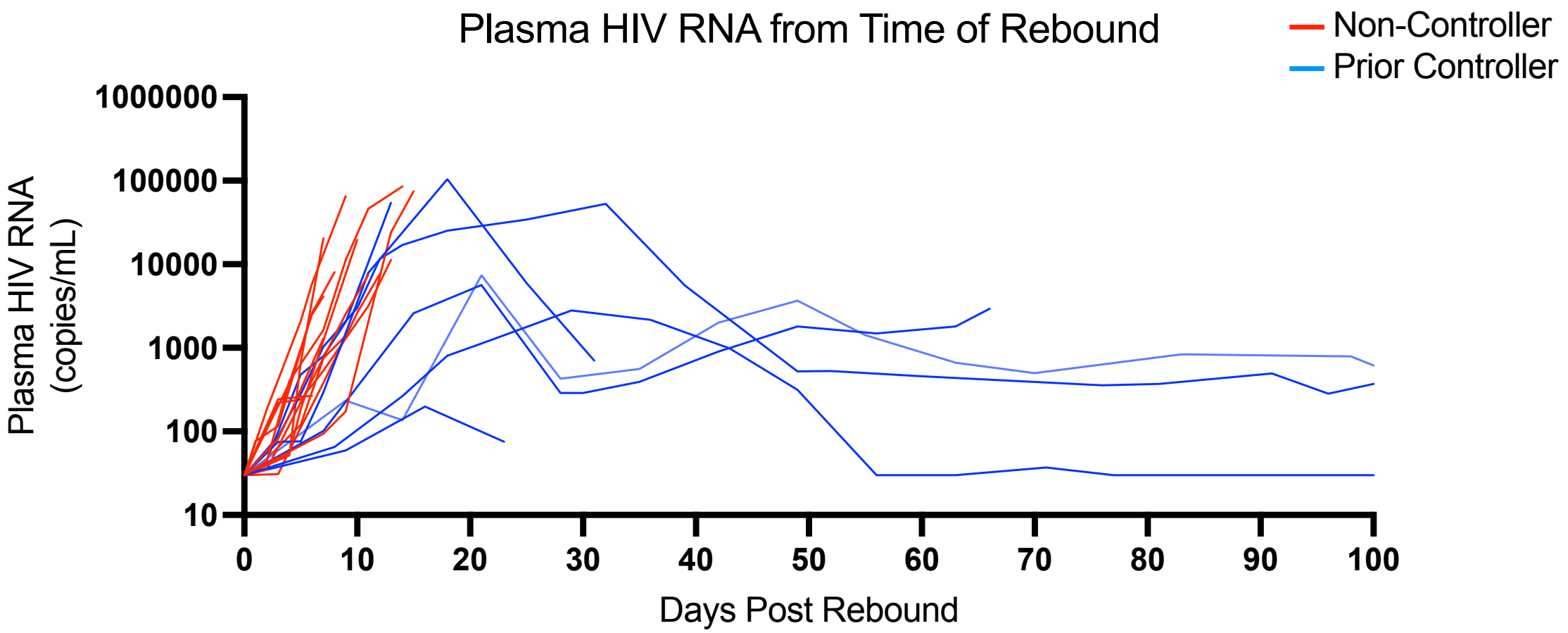
Results: SCOPE-ATI Study

- 20 PWH on ART: 13 prior non-controllers and 7 prior controllers on ART
  - Median age 59 years (range 32-75)
  - 25% women
  - 70% White, 20% Black, 10% Latino

- Compared to non-controllers, known prior controllers had:
  - Longer time to rebound: 15 vs 38 days, p=0.004
  - Longer duration of “detected, not quantifiable”: 8 vs 21 days, p=0.1
  - Longer duration off ART: 23 vs 102 days, p<0.001

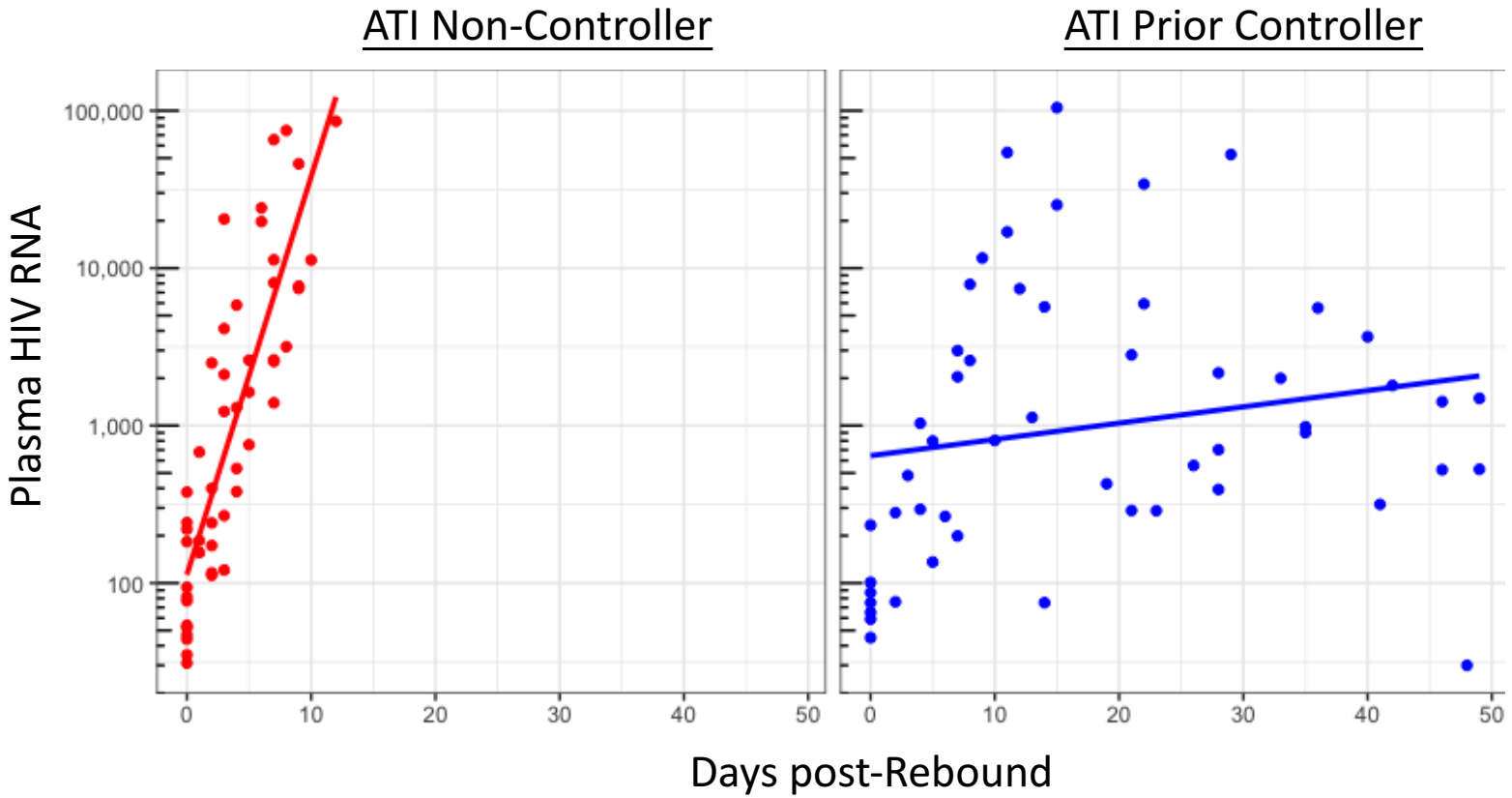
- Total duration of viremia (non-controller): median 7 days (3-13)
- CD4 counts stable, no acute retroviral syndrome, no transmissions

Results: SCOPE-ATI Study



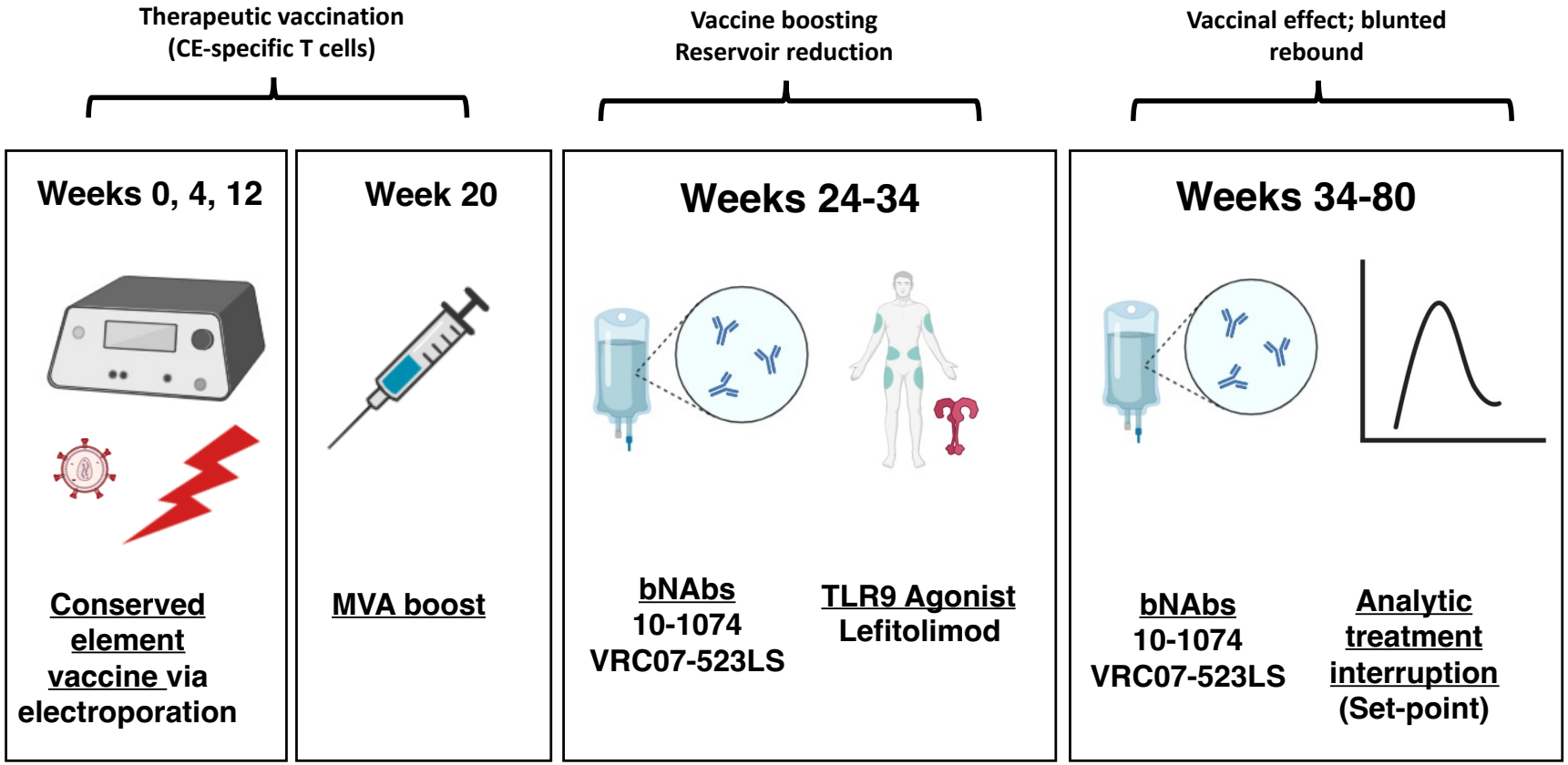
Results: SCOPE-ATI Study

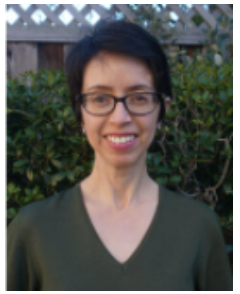
- Linear mixed effects model to regress for each individual over time
- Added each group to compare slopes of individual curves
- 0.24 log/day in non-controllers vs 0.03log/day in controllers, p<0.001



Amelia Deitchman

Methods: UCSF-amfAR Study





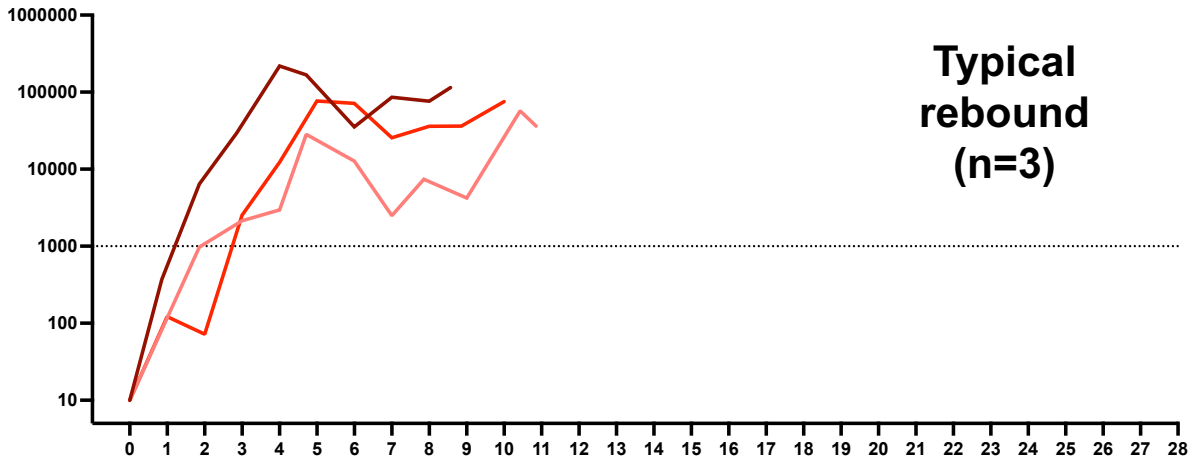
Becky Hoh

Meghann Williams

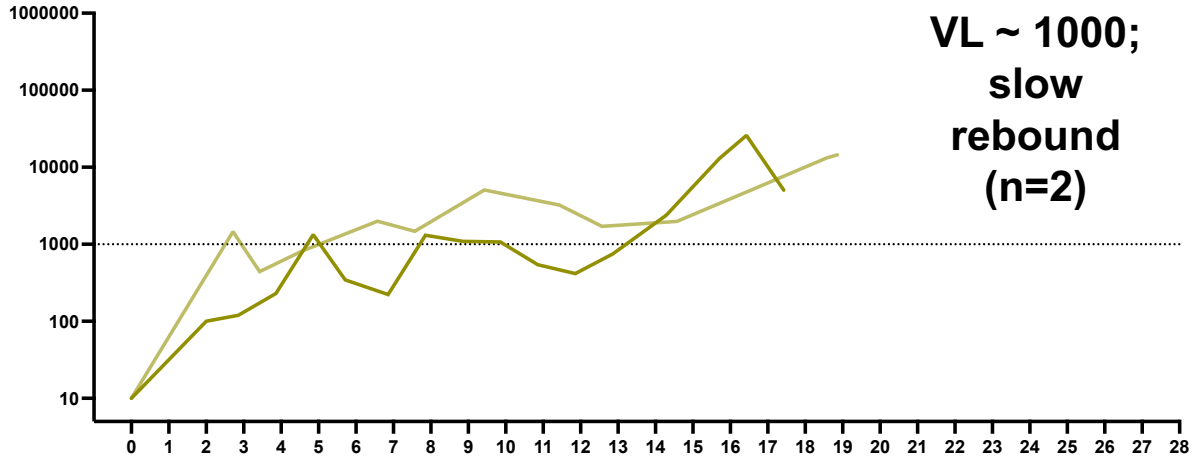
amfAR

- Phase 1, single-arm study of non-controllers on ART
- Conducted concurrently (2020-2023) with SCOPE-ATI study

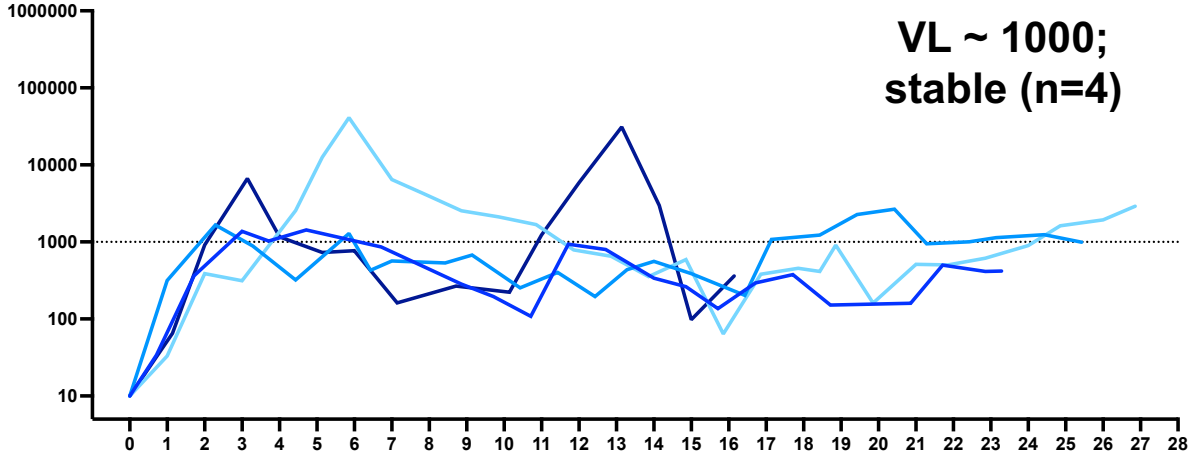
Results: UCSF-amfAR Study



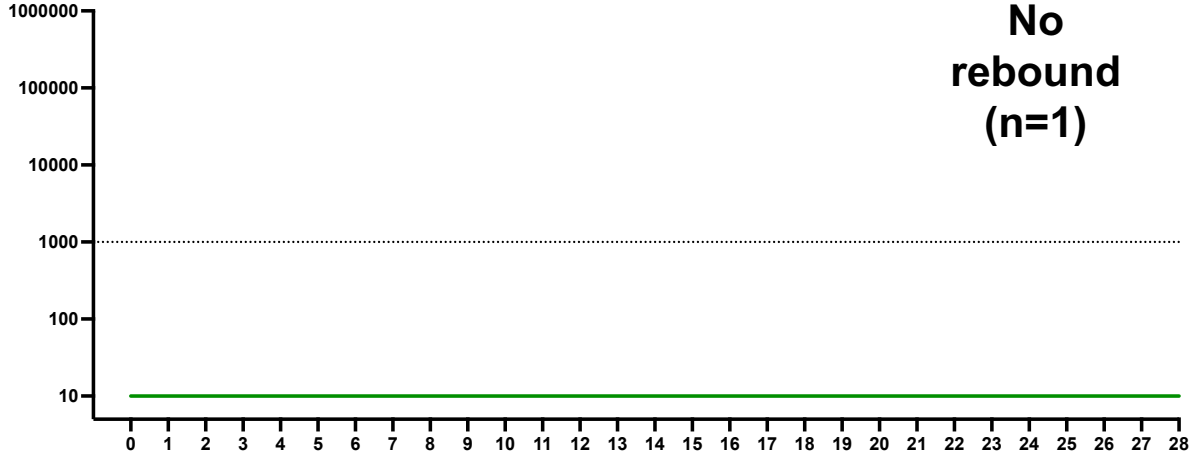
Typical rebound (n=3)



VL ~ 1000; slow rebound (n=2)



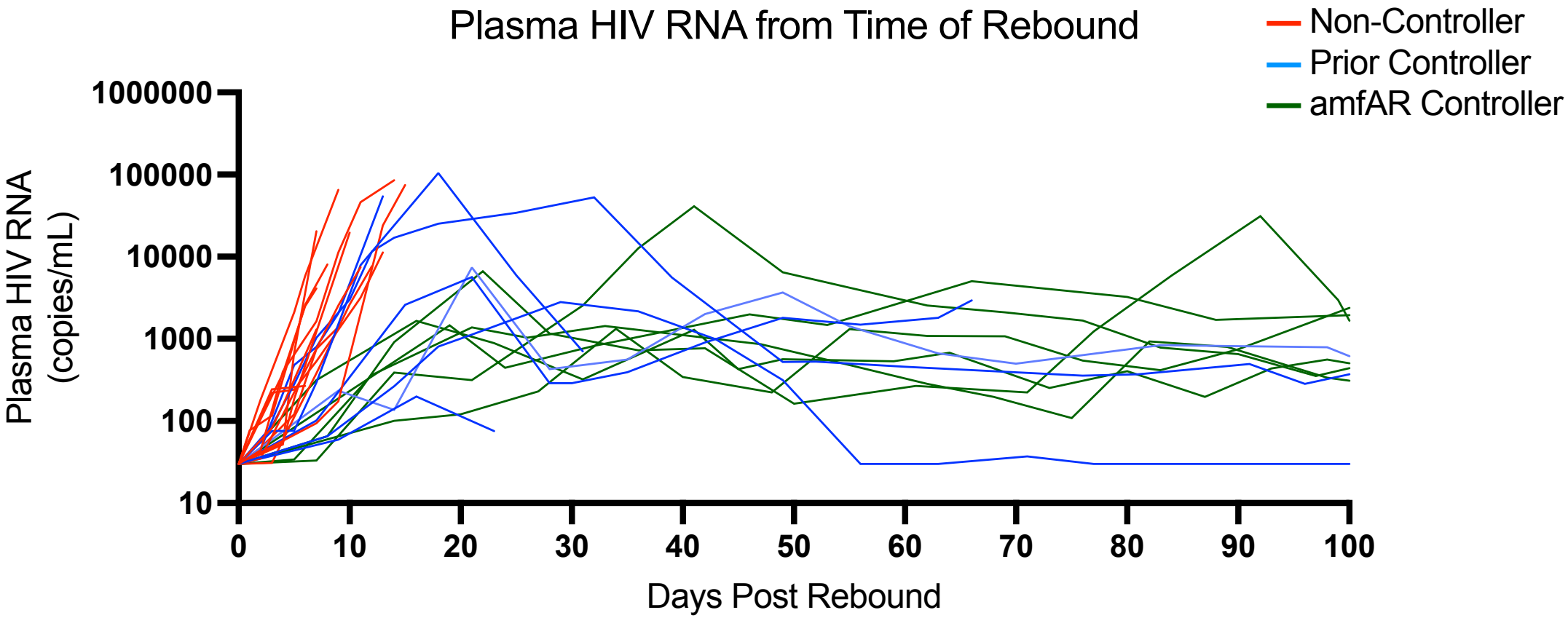
VL ~ 1000; stable (n=4)



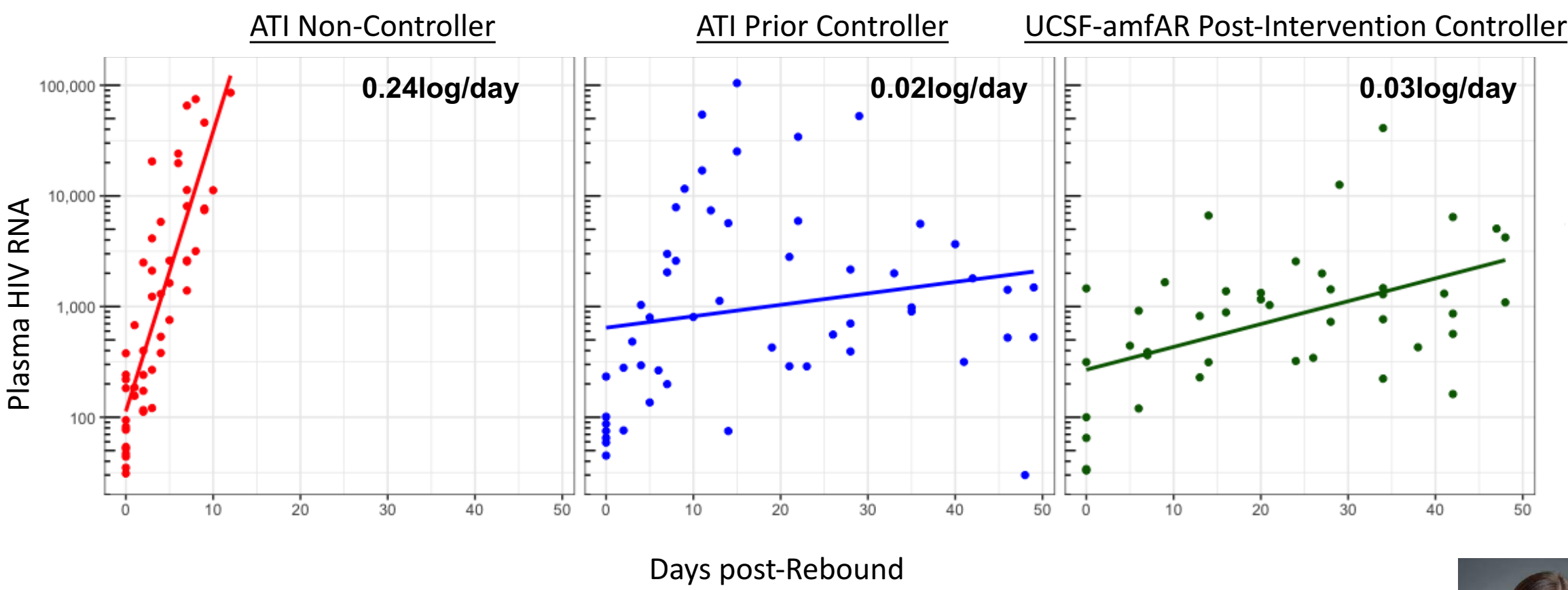
No rebound (n=1)

7/10 with viral load set points ~1000 copies/mL

Results: Modeling Rebound in Both Studies

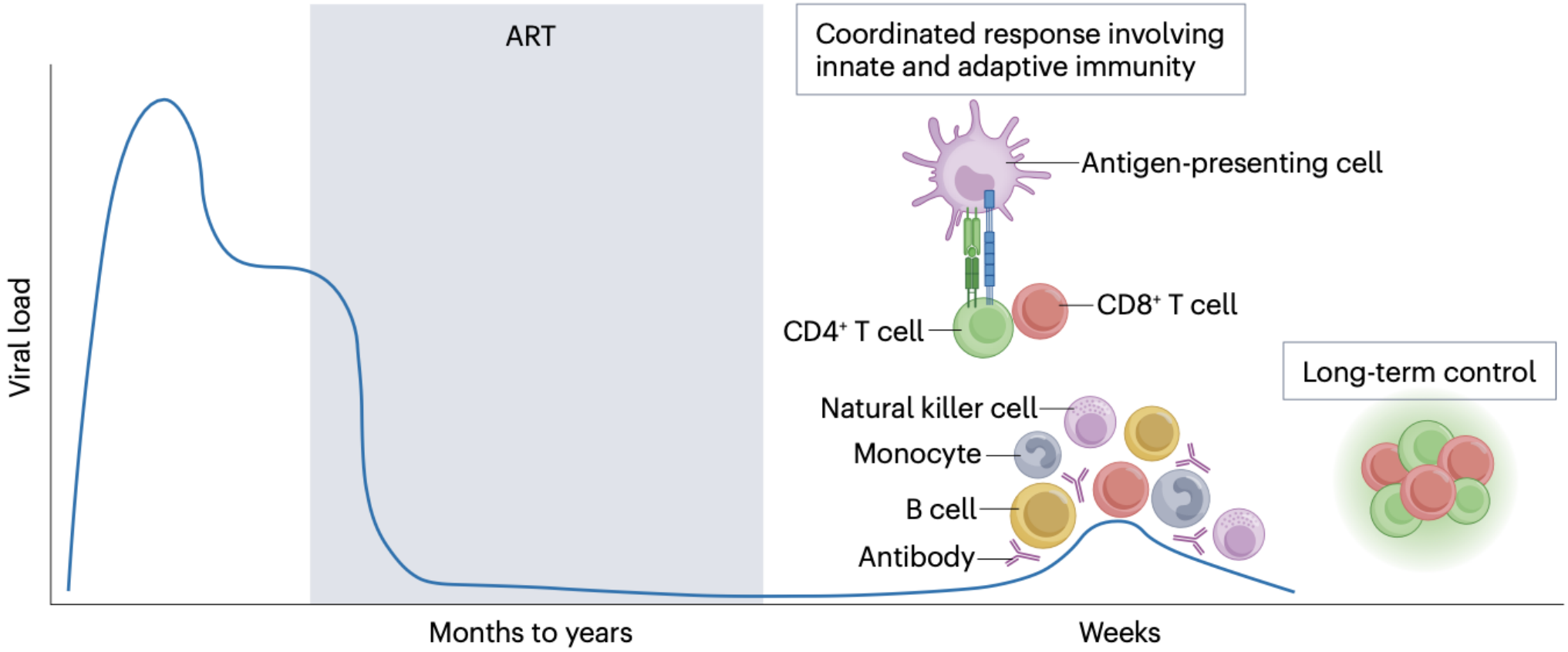


Results: Modeling Rebound in Both Studies



Amelia Deitchman

Conclusions



Landovitz, Scott, Deeks Nat Rev Microbiol 2023

Conclusions

- The HIV rebound dynamics of post-interventional control in the UCSF-amfAR study were similar to those observed in spontaneous controllers in the SCOPE-ATI study

- The delay in rebound and slow rate of increase suggest that for immune control to be achieved, the responses need to be present and functional just as the virus begins to spread

- Intense studies on the biology of the intercept period could lead to novel cure strategies and the identification of biomarkers that might predict how well virus may be controlled after rebound

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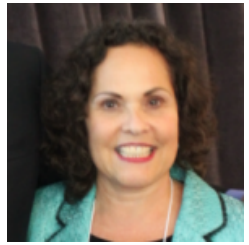
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NIH NATIONAL CANCER INSTITUTE

BILL & MELINDA GATES foundation

amfAR Institute FOR HIV CURE RESEARCH