



IMPAACT HIV Cure Scientific Committee Update

DEBORAH PERSAUD, MD

MAY 31, 2017

IMPAACT HIV CURE Scientific Committee

(Established in 2011)



Deborah Persaud (Chair)
Ellen G. Chadwick (Vice-Chair)

Members

Jintanat Ananworanich
William Borkowsky
Yvonne Bryson
Mark Cotton
Katherine Luzuriaga
Betsy McFarland
Steve Spector
Thor Wagner

Community Advisory Board Representatives: Sandra Boyd
Committee Specialists: Anne Coletti and Charlotte Perlowski

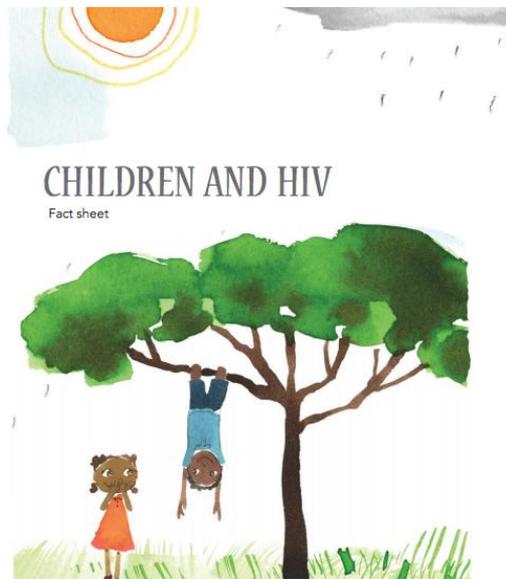
NICHD: Rohan Hazra, Eric Lorenzo

NIAID: Patrick-Jean Phillipe, Sarah Read

NIMH: Pim Brouwers

Biostatisticians: Camlin Tierney, Min Qin, Konstantia Angelidou

Mission: HIV Cure Committee



Identify safe, effective and feasible therapies to diminish HIV reservoirs in infants, children and adolescents to change the course of treatment from lifelong ART to time-limited ART, with the goal of sustained virologic suppression when ART is stopped (HIV Remission and Cure)

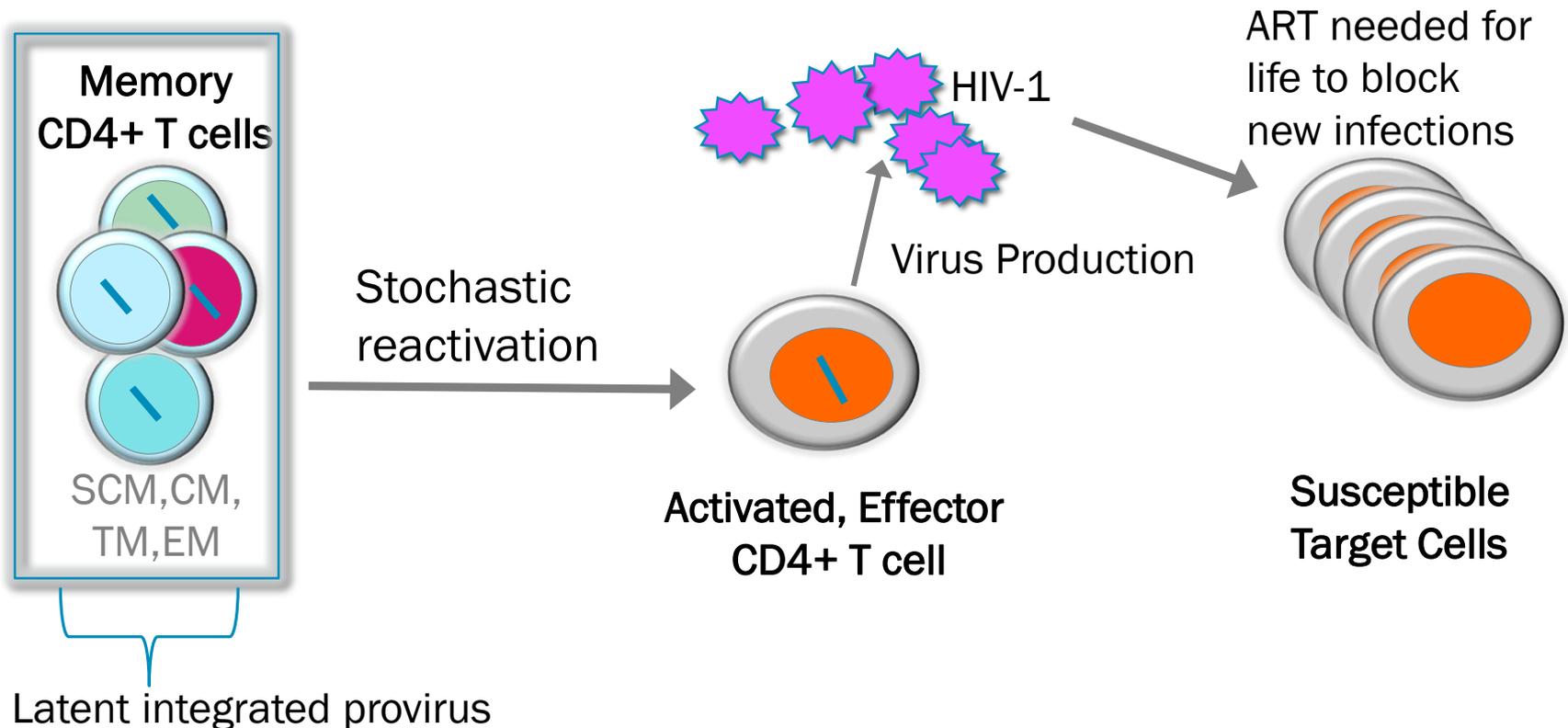
Complications of Chronic HIV Infection

Changing Trends in Complications and Mortality Rates Among US Youth and Young Adults With HIV Infection in the Era of Combination Antiretroviral Therapy

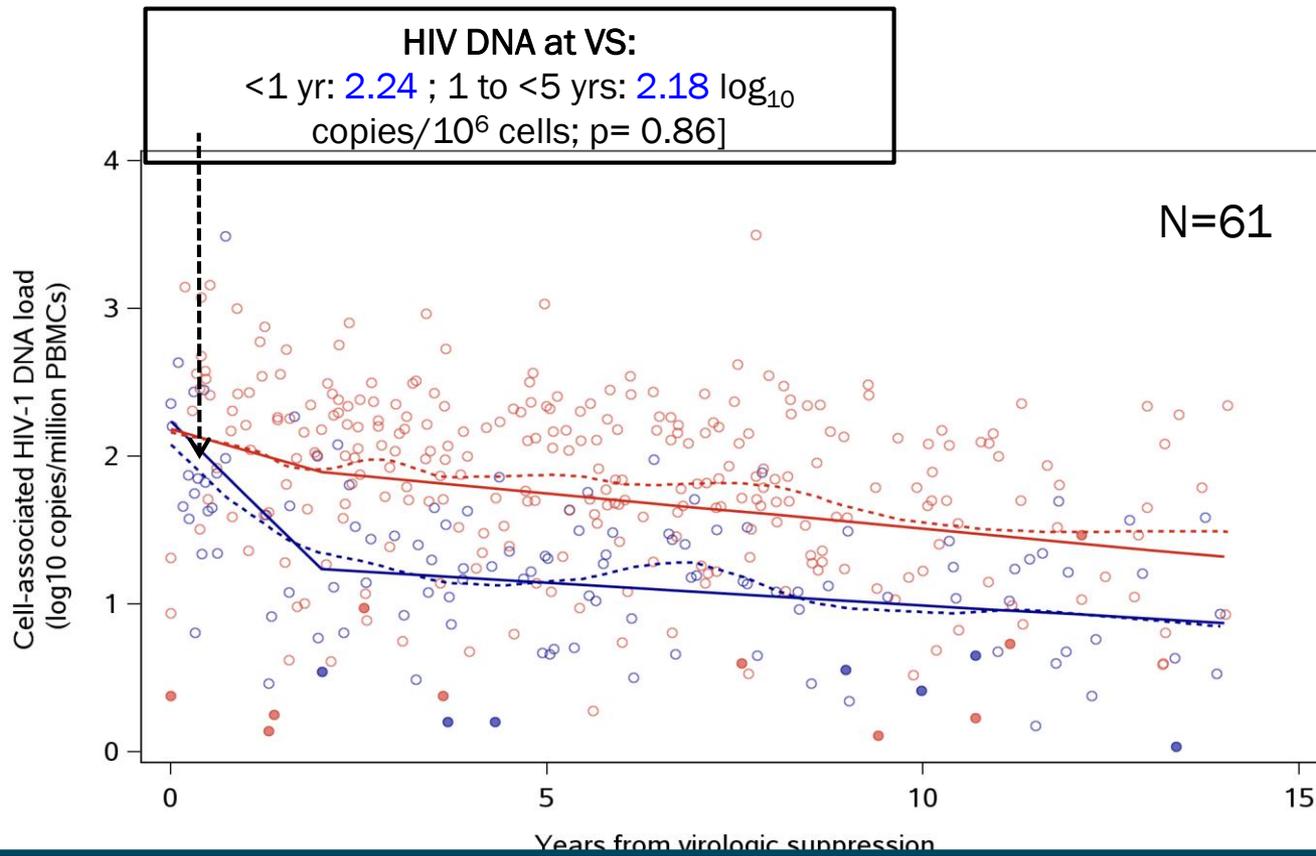
Gayatri Mirani,^{1,a} Paige L. Williams,^{2,3,4,a} Miriam Chernoff,² Mark J. Abzug,⁵ Myron J. Levin,⁵ George R. Seage III,⁴ James M. Oleske,⁶ Murli U. Purswani,⁷ Rohan Hazra,⁹ Shirley Traite,² Bonnie Zimmer,⁸ and Russell B. Van Dyke¹; for the IMPAACT P1074 Study Team

- IMPAACT P1074: Prospective multicenter cohort study from 4/2008-6/2014; 1201 HIV- infected youth- 87% perinatally-infected; median age 20.9 years
- High prevalence of co-morbid conditions-psychiatric and neurodevelopmental disorders, increased substance and alcohol use, anxiety disorders, metabolic conditions, fractures
- **Standardized mortality rate 31.5X the general U.S. population; most deaths from HIV-related medical conditions**

HIV-1 Incurable: Latent Reservoir in Resting Memory CD4+ T Cells



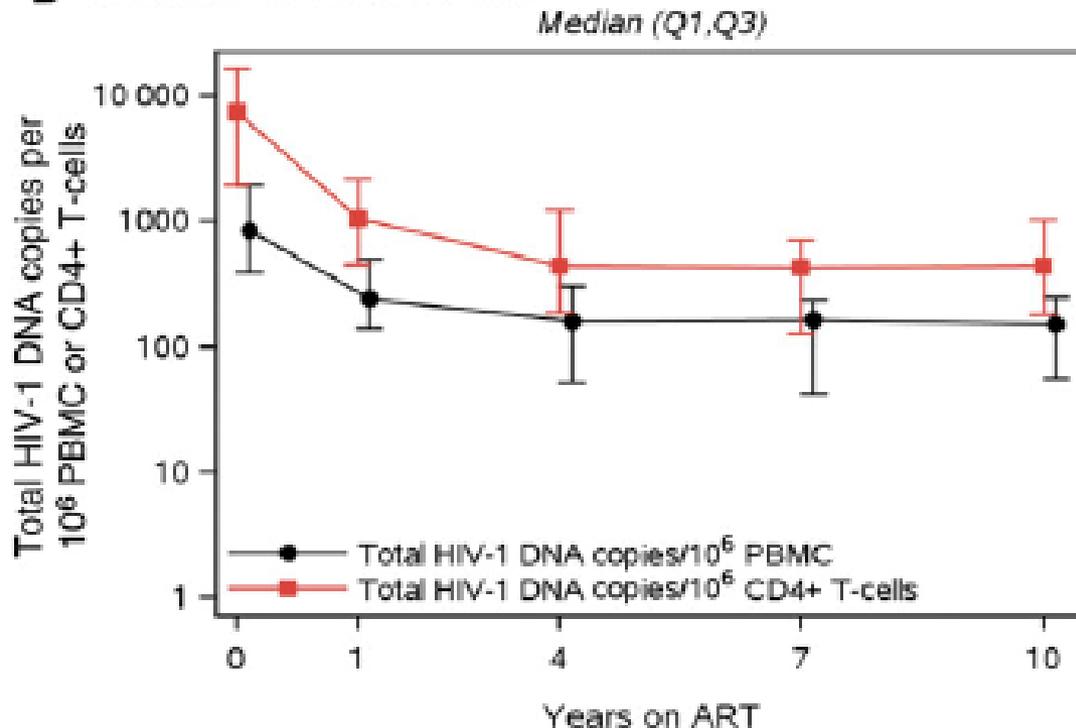
Proviral Reservoirs Decay with Long-term Virologic Control of Perinatal Infection and Differs by Age at Virologic Suppression



First two years-after VS-HIV-1 DNA levels decreased by (-0.50 and -0.15 \log_{10} copies/ million PBMCs per year, respectively); $p=0.005$
2-14 years after VS-HIV-1 DNA decay not statistically different
Estimated mean half-life of HIV-1 DNA from VS was 5.9 years and 18.8 years, respectively ($P = .09$)

HIV-1 DNA Dynamics During ART (Adults)

B Total HIV-1 DNA over time



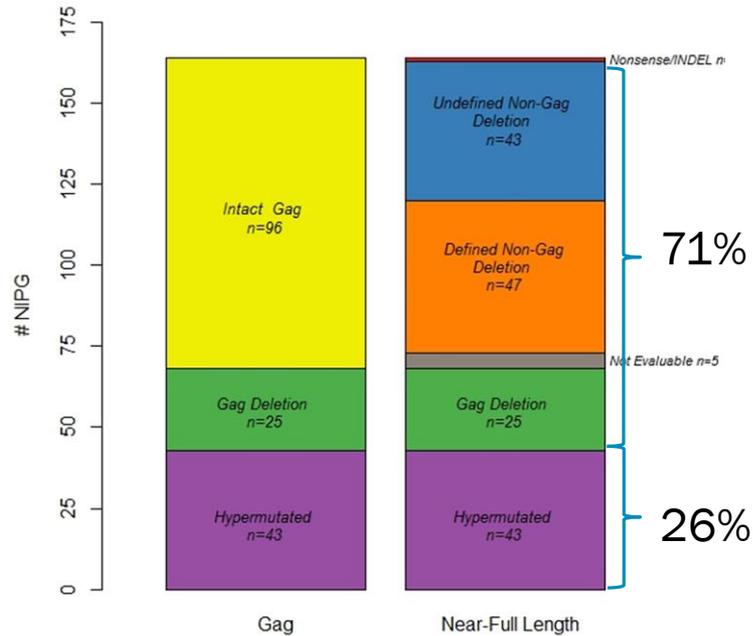
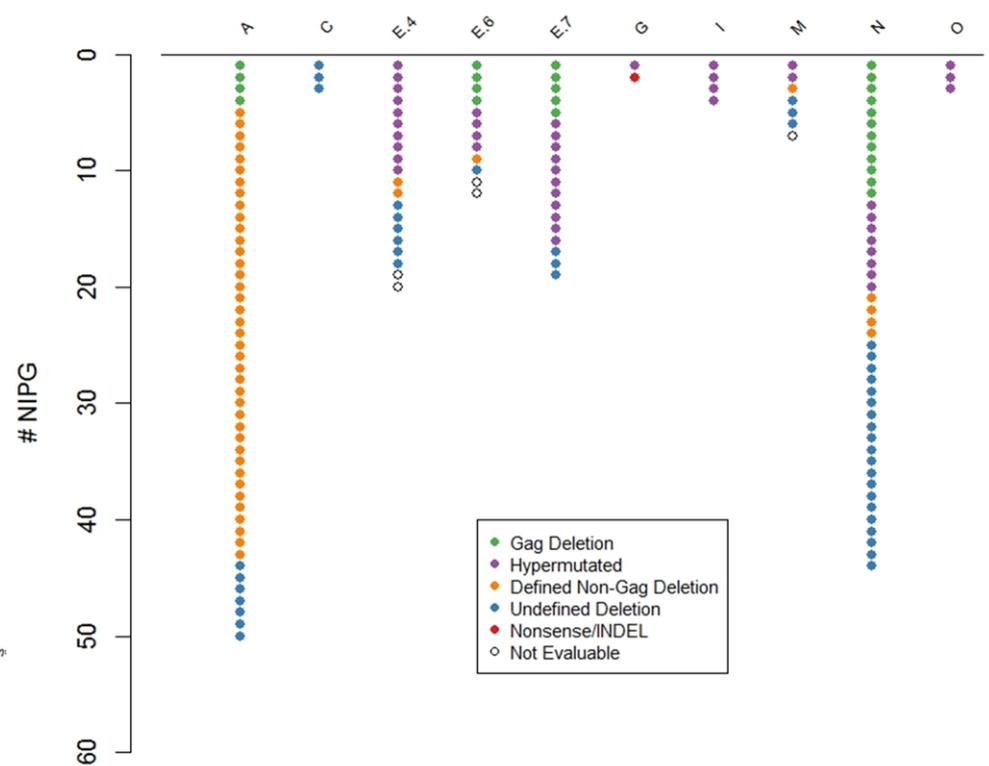
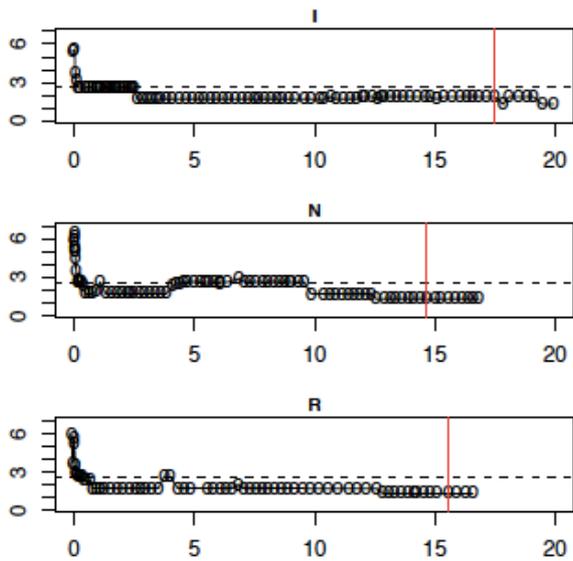
Year 0-1: median decay -0.86
 \log_{10} copies/million CD4+ T
cells

Year 1-4: median decay -0.11
 \log_{10} copies/million CD4+ T
cells

Years 4-7: -0.02 \log_{10}
copies/million CD4+ T cells

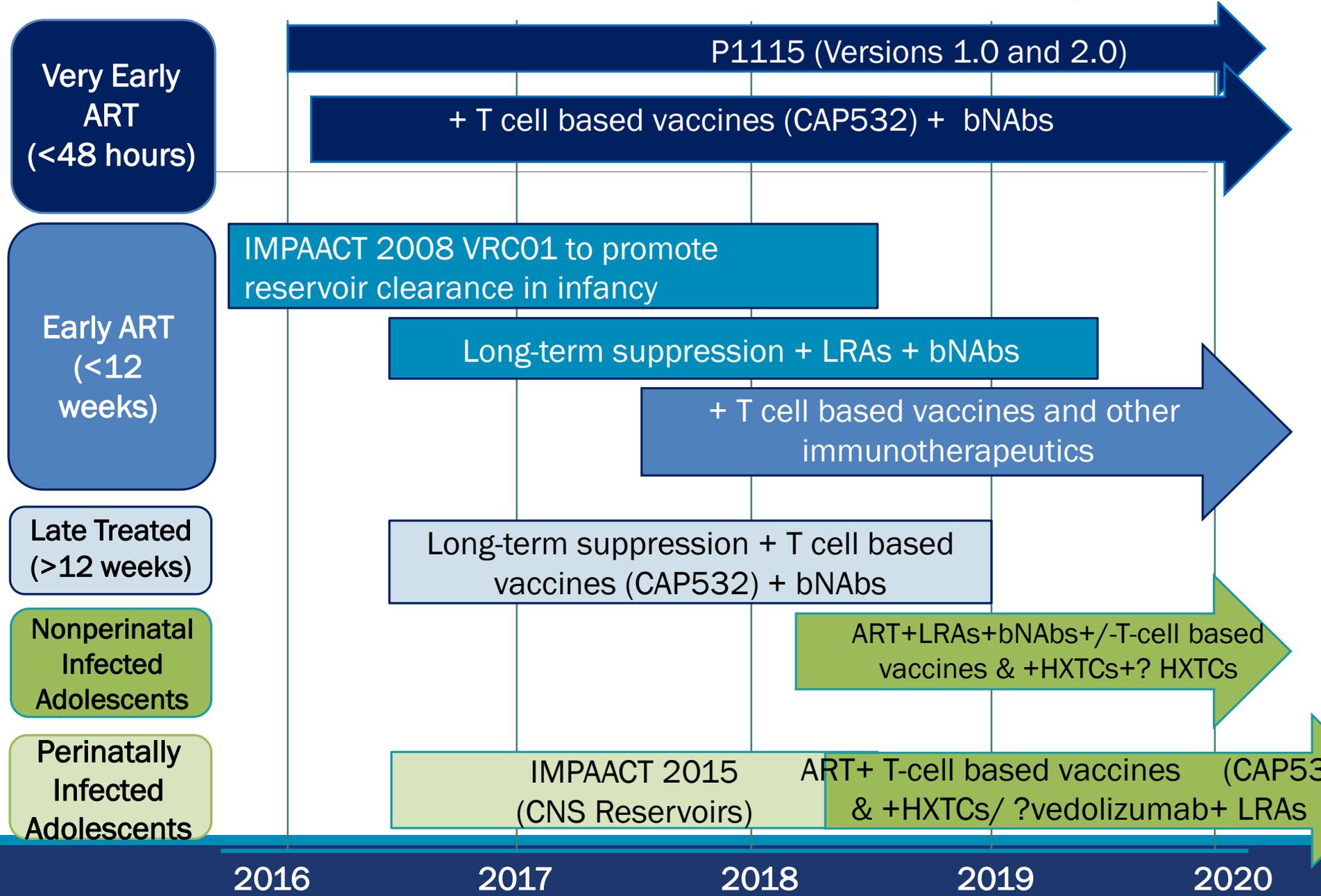
>7 years: -0.006 \log_{10}
copies/million CD4+ T cells

Median HIV-1 DNA after 10
years of ART 439
copies/million CD4 cells



**11 long-term early ART treated youth;
 No inducible reservoir detected (234 –
 one million replicates);
 No full-length, intact genomes identified
 in the 164 single near full-length
 genomes analyzed**

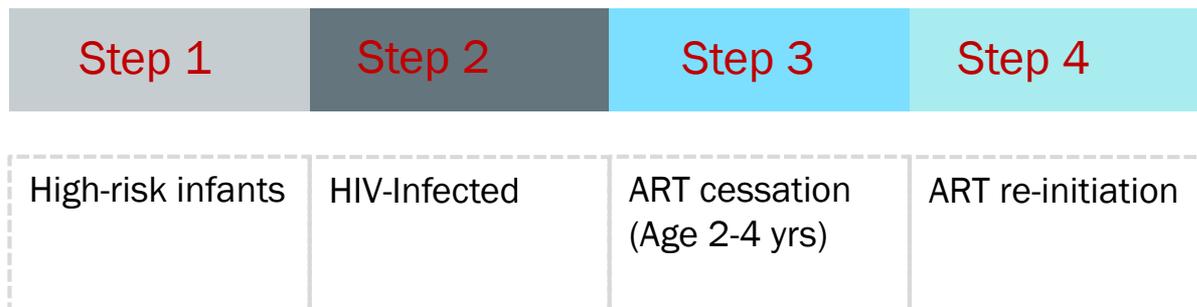
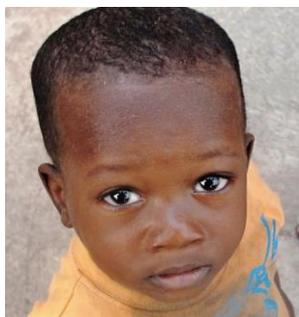
Roadmap to Pediatric HIV Remission and Cure



ART Cessation in Pediatric Cure Trials (P1115)



P1115 (Version 1.0)



IMPAACT HIV Cure Scientific Committee Meeting
IMPAACT Annual Meeting
31 May 2017
12:00 to 3:00 pm ET

12:00-12:20 pm	Committee Updates	Deborah Persaud and Ellen Chadwick
12:20-12:40 pm	Biomarkers of HIV persistence as Predictors of HIV Rebound off ART	Robert Siliciano
12:40 -1:00 pm	Is HIV-1 antibody a useful biomarker for cure studies?	Katherine Luzuriaga
1:00-1:20 pm	Effect of very early ART and therapeutic vaccines on reservoir size and viral rebound in non-human primates	Afam Okoye
1:20-1:40 pm	Break	
1:40-2:00 pm	Pediatric experience with ART interruption: What's to fear?	William Borkowsky
2:00-2:20 pm	Considerations for ART interruption in African infants participating in P1115	Mutsa Bwakura-Dangarembizi
2:20-3:00 pm	Moderated Discussion	Deborah Persaud and Ellen Chadwick

Discussion

- What is the optimal biomarker profile to safely stop ART in very early treated children (≥ 2 years of age) in P1115?
- How are NHP models relevant to pediatric HIV cure research?
- Is there a role for non-virologic biomarkers in HIV cure research?
- What are the most concerning risks about stopping ART in P1115?
- What are the benefits to stopping ART in P1115?
- Do the benefits of stopping ART in P1115 outweigh the risks?
- What is the most important information that should be provided to clinicians and study participants for informed consent to stop ART in P1115?