IMPAACT HIV Cure Scientific Committee Update

Deborah Persaud, MD
Chair, HIV Cure Scientific Committee
June 11th, 2019

IMPAACT Leadership: Sharon Nachman and James McIntyre

IMPAACT HIV Cure Scientific Committee Members
Deborah Persaud (Chair) and Ellen Chadwick (Vice-Chair)

Committee Members
Jintanat Ananworanich
William Borkowsky
Yvonne Bryson
Mark Cotton
Katherine Luzuriaga
Betsy McFarland
Steve Spector
Thor Wagner
Dan Barouch
Ann Chahroudi

Community Advisory Board Representatives
Steven Mphonda

Committee Specialists
Anne Coletti and Charlotte Perlowski

NICHD:Rohan Hazra, Eric Lorenzo
NIAID:Patrick-Jean Phillipe, Sarah Read, Judi Miller and Ellen DeCarlo
NIMH: Pim Brouwers

Biostatisticians: Camlin Tierney, Bryan Nelson, Jane Lindsey, Meredith Warshaw

IMPAACT SLG Liason:John Sleasman

IMPAACT International Maternal Pediatric Adolescent AIDS Clinical Trials Network

Clinical Trials Team

Parents, Children and Youth

NIH NIMH

NIH National Institute of Allergy and Infectious Diseases

NIH NICHD

Specific CAB Requests

- Update of HIV Cure Scientific Committee activities
  - ongoing studies (P1115, P2008, and P2015)
- Definitions of “Functional” cure
- Information on the ‘London” Patient
- Future Directions

Overarching Goal IMPAACT HIV Cure Scientific Committee (2012-Present)

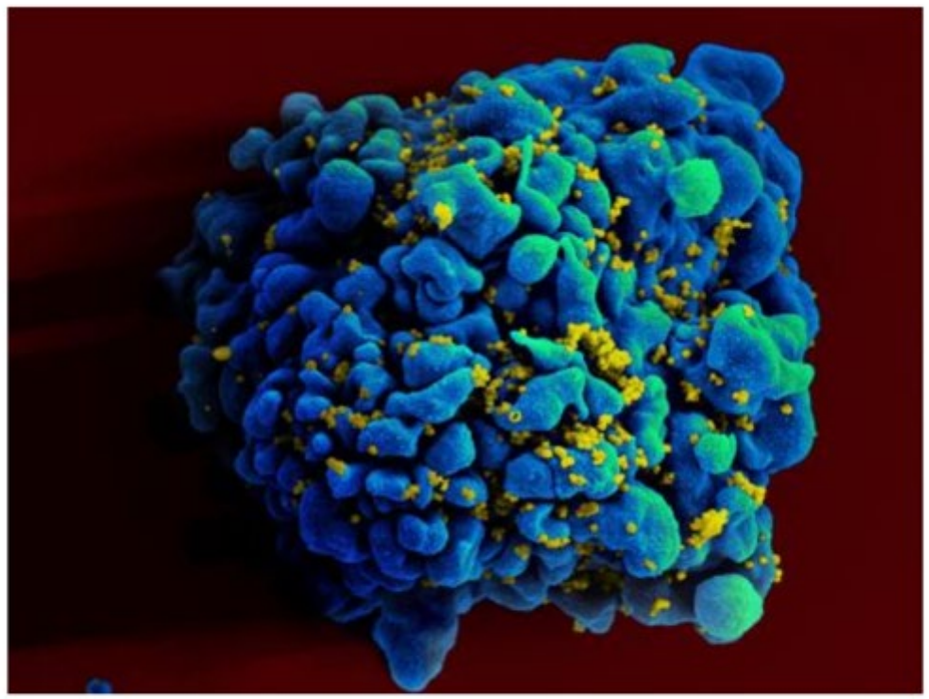
- Identify novel therapeutic strategies that will lead to ART-free remission and cure in pediatric populations (neonates to young adults)

IMPAACT
International Maternal Pediatric Adolescent AIDS Clinical Trials Network

June 2019

NIH HIV Experts Prioritize Research to Achieve Sustained ART-Free HIV Remission

June 6, 2019



Scanning electromicrograph of an HIV-infected T cell

Credit: NIAID

VIEWPOINT

Durable Control of HIV Infection in the Absence of Antiretroviral Therapy

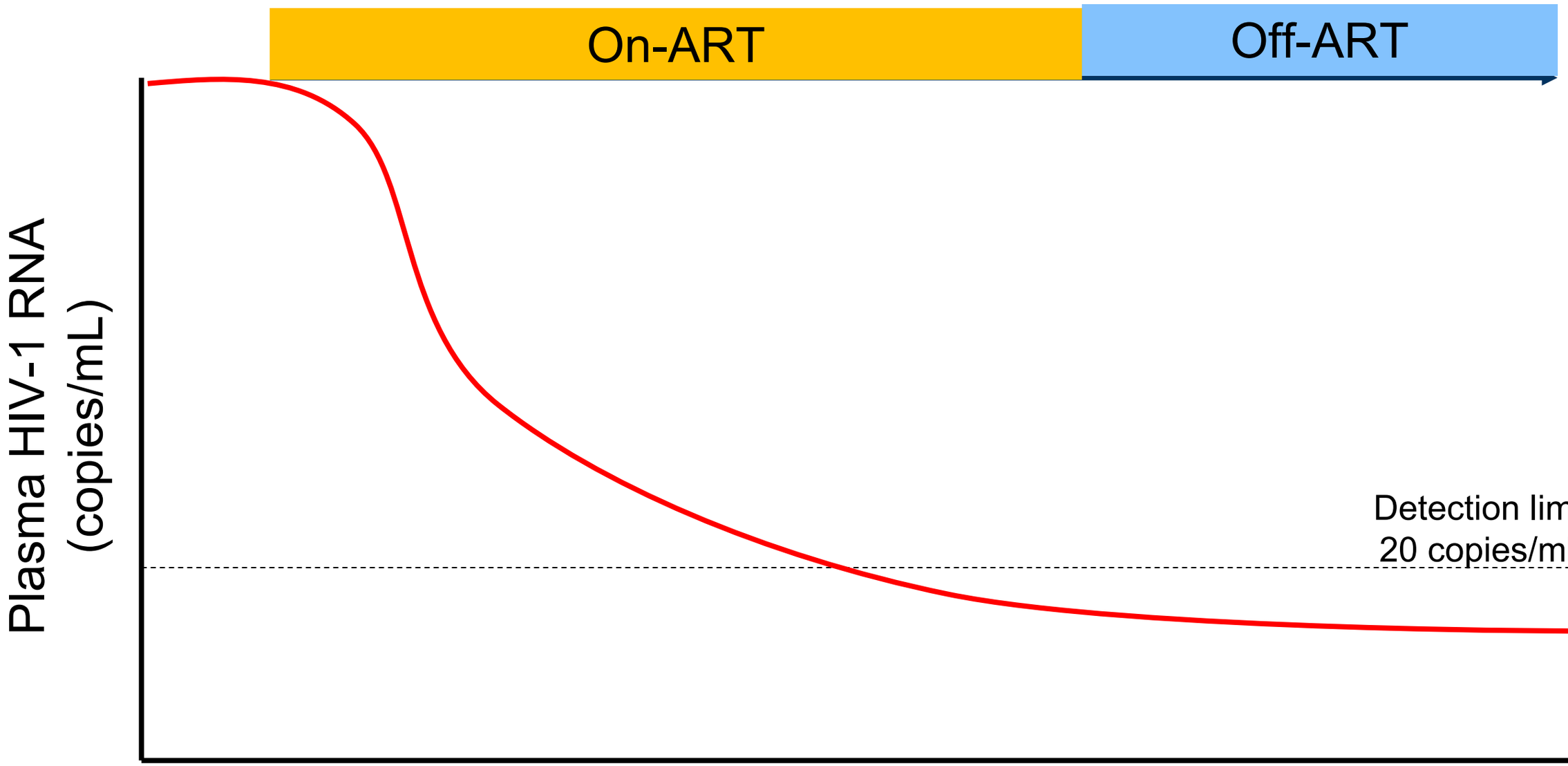
Opportunities and Obstacles

Chun TW, Eisinger RW, and Fauci AS. JAMA 2019

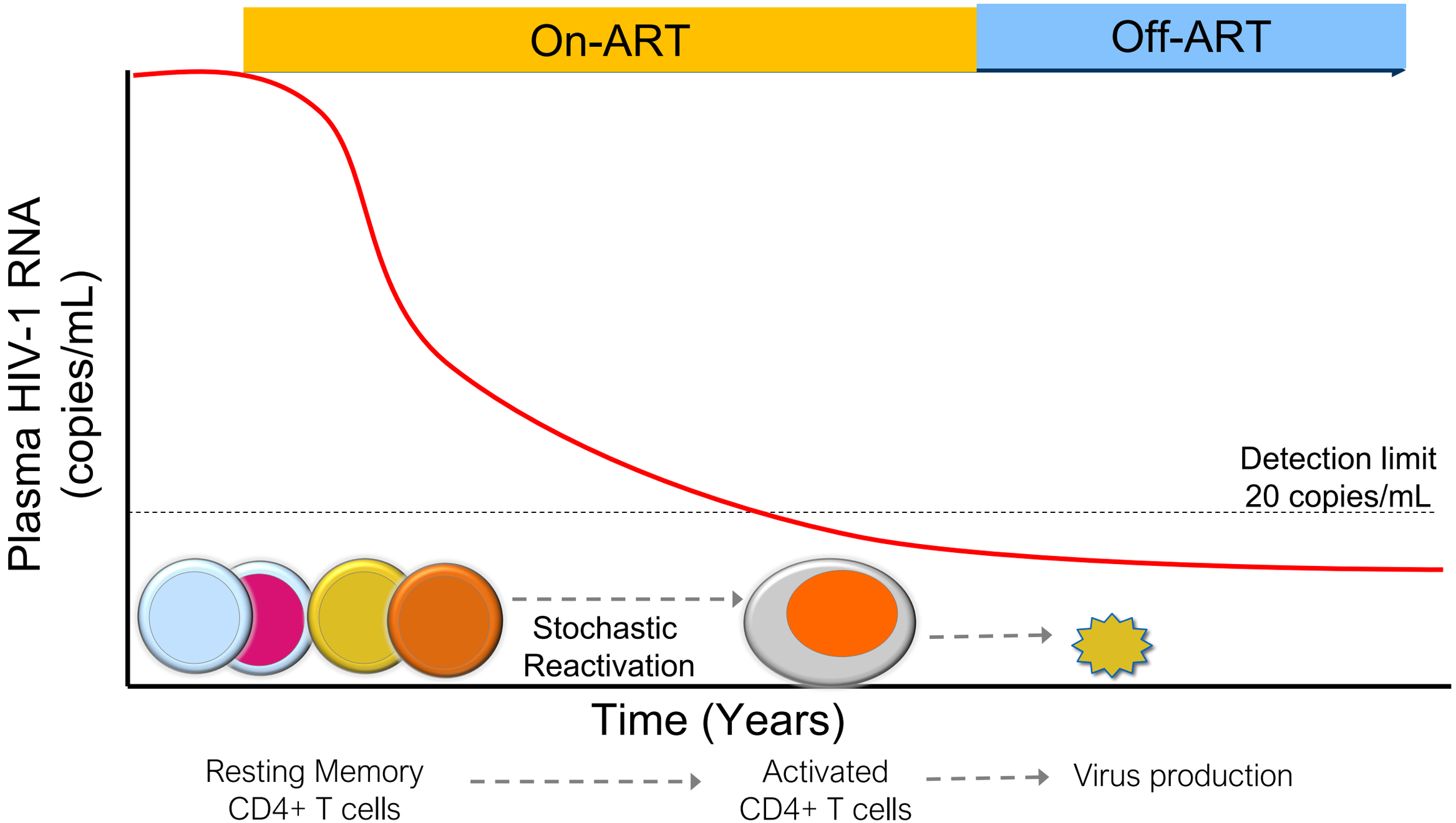
- "Recognized short-term and uncertain long-term toxicity of antiretroviral drugs"
- Commonly experienced feeling of "pill fatigue,"
- Stigma associated with taking daily ART
- Costs associated with lifelong ART
- Altogether, provide strong motivation to pursue such a goal"

Chun TW, Eisinger RW, and Fauci AS. JAMA 2019
(Published online June 6, 2019)

ART-Free HIV Remission



HIV Reservoirs preclude ART-Free HIV Remission and Cure



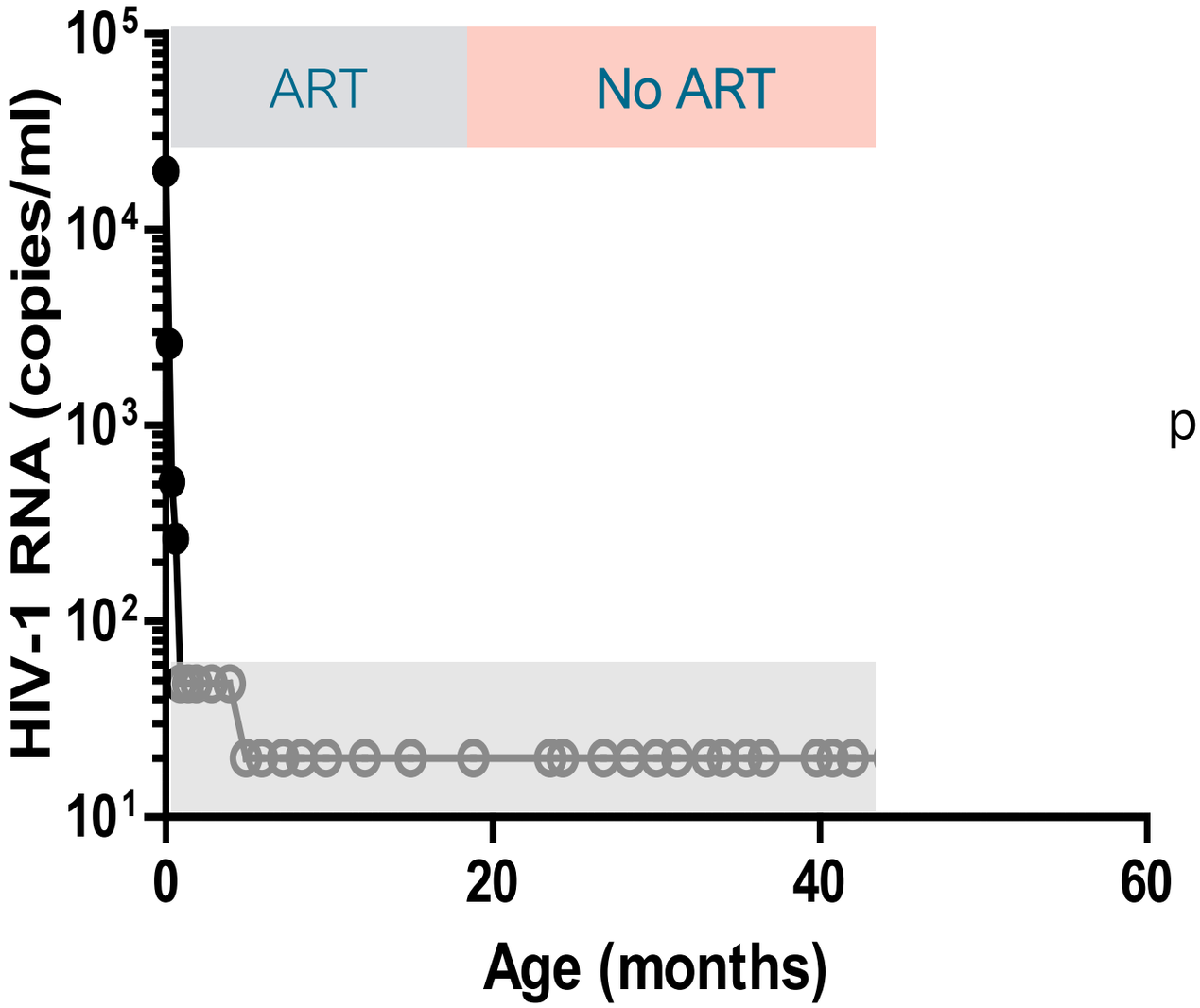
Pathways towards ART-Free Remission

- **“Cure”:** Eradication of the replication-competent HIV reservoir

- **“Sustained virologic remission”**: Control of plasma viral rebound in the absence of ART without eradication of the replication-competent HIV reservoir

Chun TW, Eisinger RW, and Fauci AS. JAMA 2019
(Published online June 6, 2019)

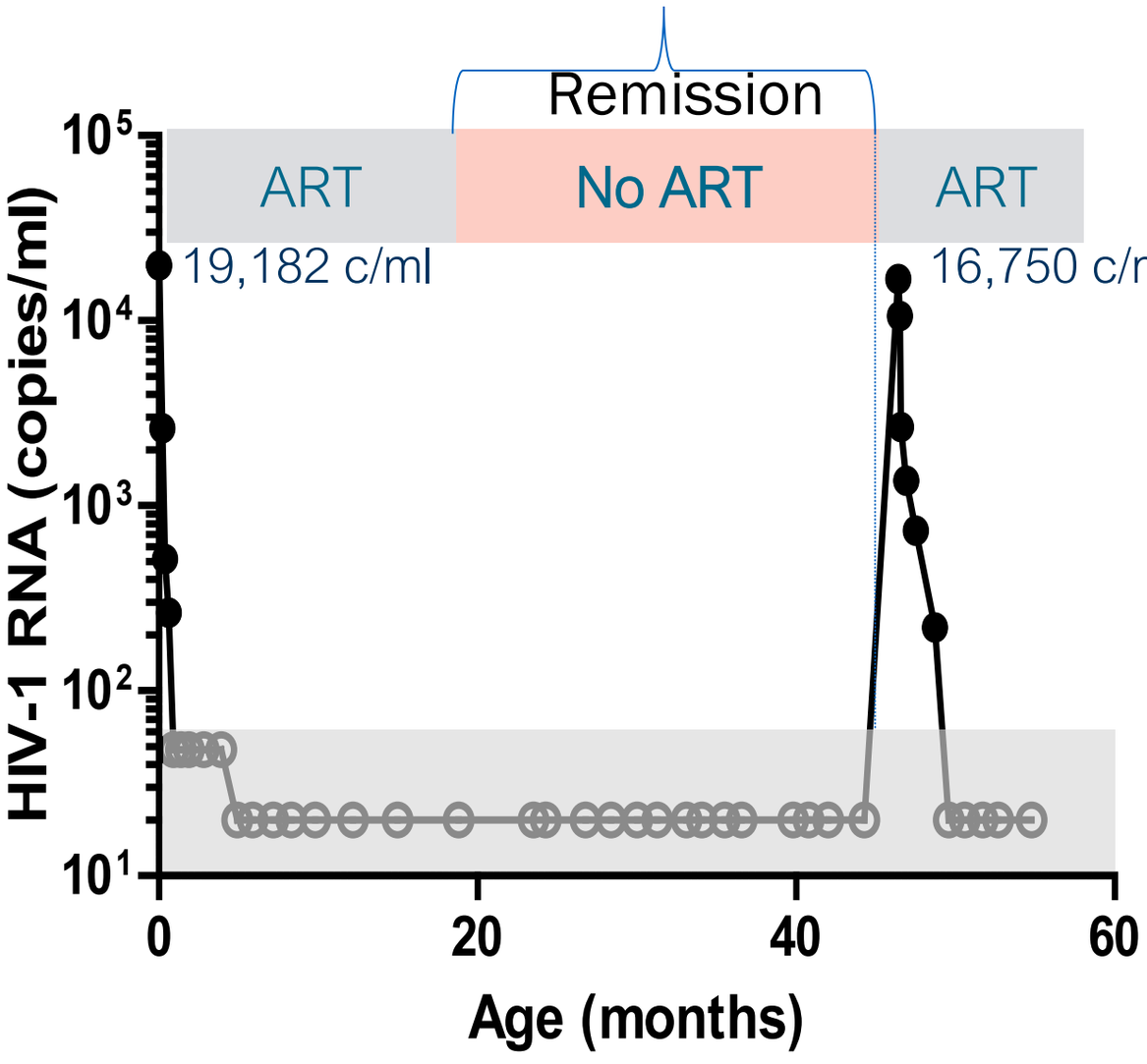
HIV Remission in Perinatal Infection: "Mississippi Baby" (2013)

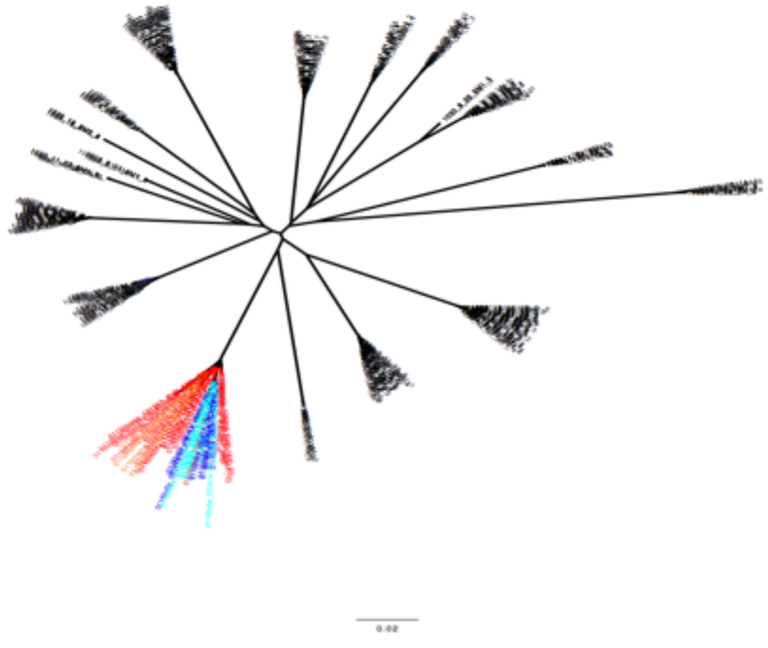


27 months of control of plasma viral rebound in the absence of ART

Persaud, Gay, Luzuriaga et al 2013 *NEJM*

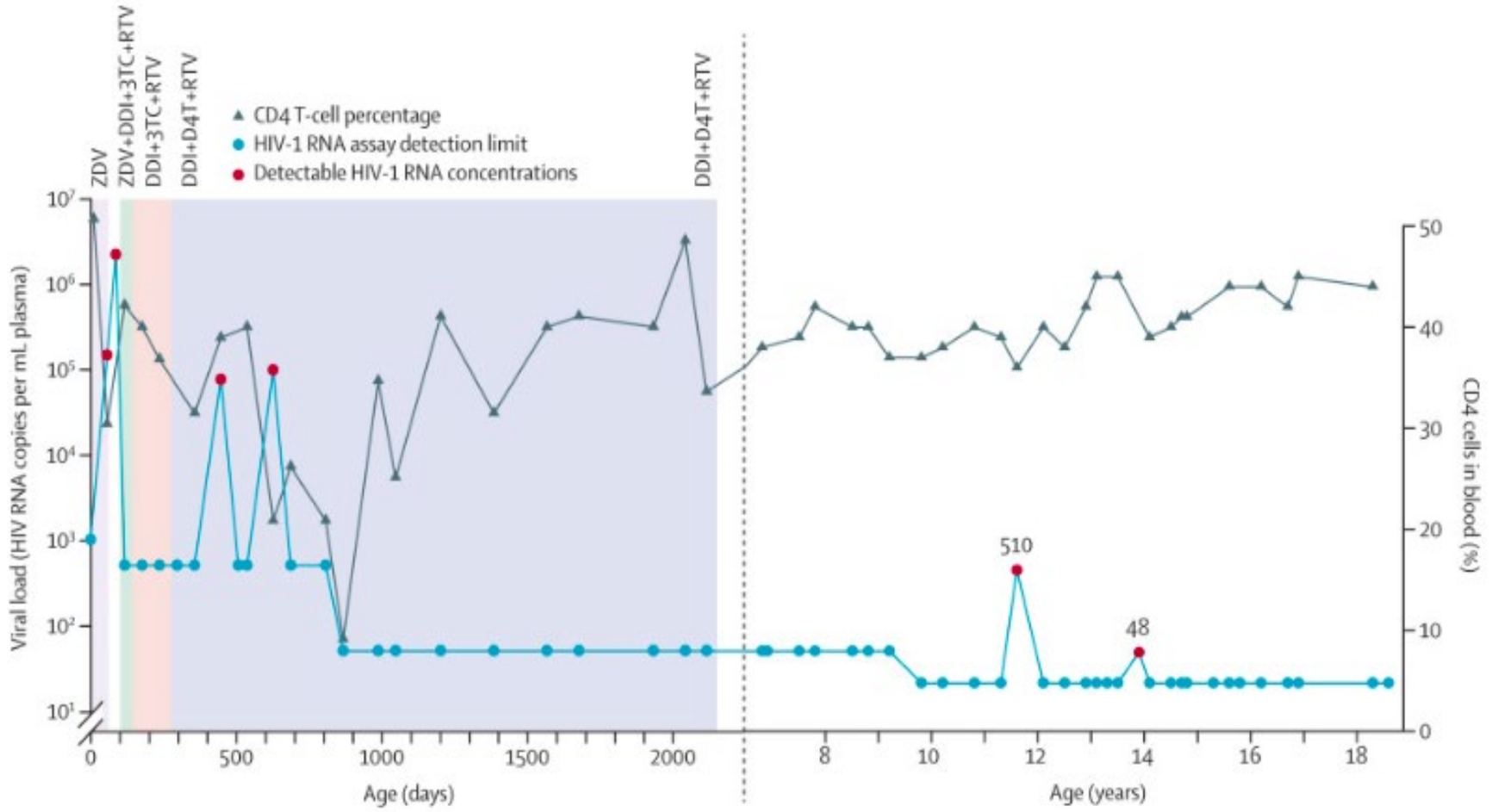
Viremic Relapse in the "Mississippi Baby" (2015)





Persaud, Gay, Luzuriaga et al 2013 *NEJM;* Luzuriaga, Gay, Persaud et al 2015 *NEJM*

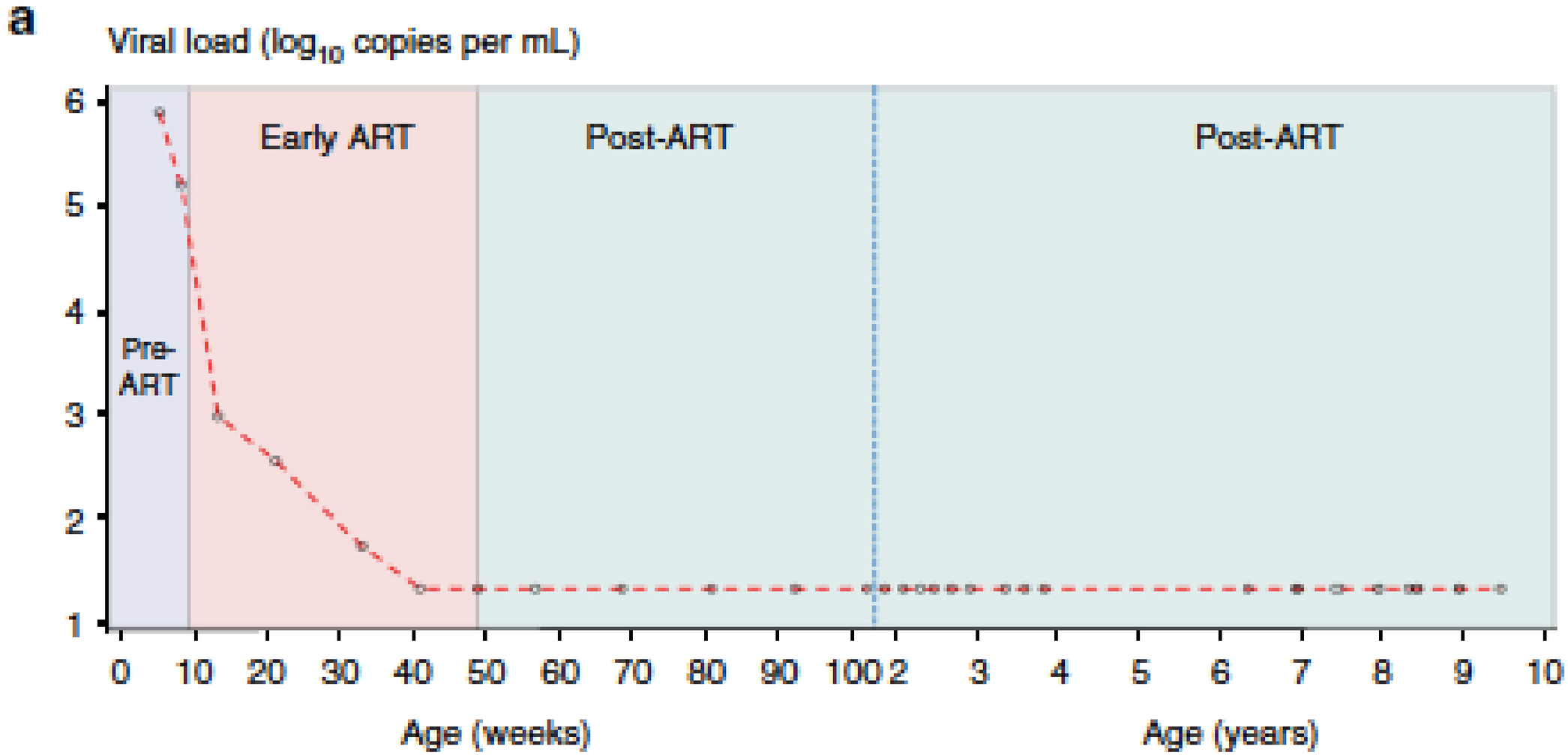
Case#2: HIV Remission in Perinatal Infection "French Teenager"-(2016)



Intervention: Early ART of perinatal infection
Identified at 18.8 years of age while off ART for 11.5 years
1/100 of the early-treated children in the ANRS EPH C010 Pediatric Cohort
ART at 3 months of age for intrapartum HIV infection
Family discontinued ART at 5.8-6.8 years of age
11.5 years off ART with undetectable HIV RNA but detectable HIV DNA (2.2 log 10 copies/million PBMCs
"Weak" HIV-specific CD8+ T cells; no protective HLA genotype identified

Frange P et al. Lancet HIV 2016

Case#3: ART-Free Remission in a Perinatally HIV-Infected Child: “South African Child” (2017)



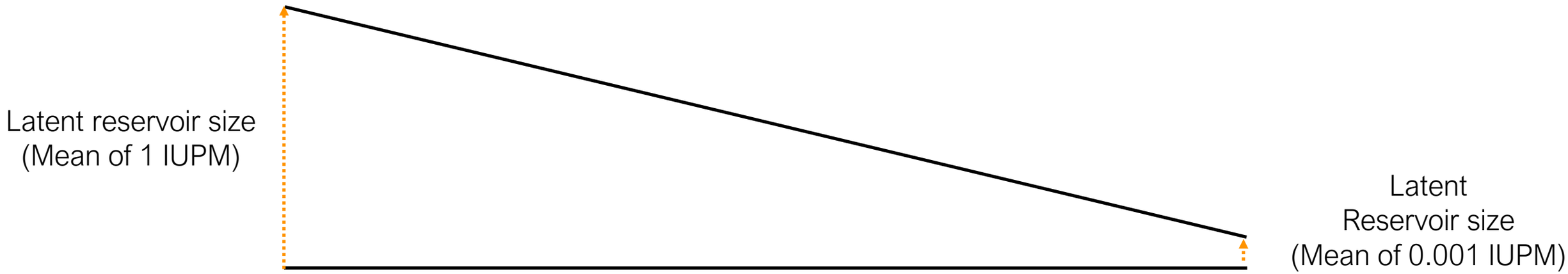
Intervention: Early ART of perinatal infection
ART at 8.7 weeks of age- Time-limited for 40 weeks
No rebound off ART for 8.5 years

Prevalence: 1/227(0.4%) in CHER Trial

Violari A et al Nature Communications 2019

Strategy #1: Very early and Early Treatment of Perinatal HIV Infection to Achieve ART-Free Remission (IMPAACT P1115 and P2008)

Overarching Goal of HIV Remission and Cure Therapeutics



Hill AM et al. PNAS 2014; Hill AM et al. PLoS PATH. 2016

P1115-Ongoing Prospective Phase I/II Proof-of-Concept Study of Very Early ART to Achieve ART-free HIV Remission in Infants

Step 1	**Initiation of ART within 48 hours of life for high-risk infants**
Step 2	Continued ART with confirmed HIV-1 infection with monitoring to determine eligibility for ART cessation between 2 -4 yrs of age
Step 3	ART cessation with close monitoring for viral rebound if antibody negative and no HIV infected cells detected
Step 4	ART re-initiation for infants who experience viral rebound

Primary Objective:

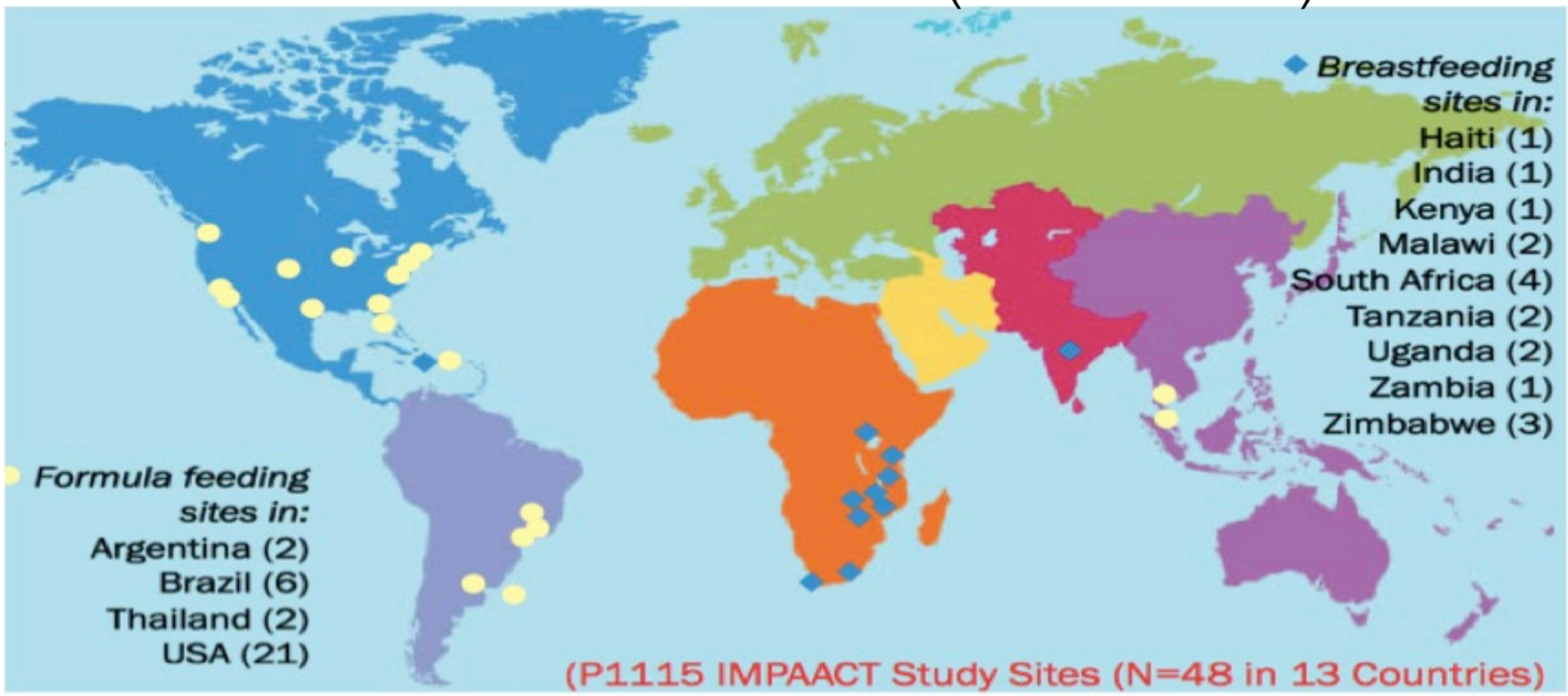
To assess HIV remission among *in utero* –infected neonates who initiate very early therapy within 48 hours of birth

HIV remission: Case Definition

No confirmed plasma HIV RNA ≥ limit of detection of the viral load assay through 48 weeks of stopping ART

clincialtrials.gov NCT02140255

P1115 (Version 1.0)-
440 Mother-Infant Pairs Enrolled in the Prospective Cohort from 11 Countries (2015-2017)



11 countries enrolled directly into Step 1 (Brazil, Haiti, Kenya, Malawi, South Africa, Tanzania, Thailand, USA, Uganda, Zambia and Zimbabwe);

5 countries enrolled directly into Step 2 (Brazil, South Africa, USA, Tanzania and Uganda)

Presented at CROI 2019: VIROLOGIC RESPONSE TO VERY EARLY ART IN NEONATES WITH IN UTERO HIV: IMPAACT P1115: (Poster #0799)
Protocol Co-Chairs: Ellen G. Chadwick, Yvonne Bryson
Clinical Trials Specialist: Anne Coletti
Statisticians: Camlin Tierney and Bryan Nelson
Clinical Site Team Investigators

	Cohort 1 High-Risk	Cohort 2 Infected, Early Treated≠	Overall
	N=34	N=20	N=54
Median Age (hours) at First ARV [Q1,Q3] [N]	7.3 [1.8,21.0] [34]	32.8 [0.4,40.1] [15]	8.0 [1.1,32.8] [49]
Median* Age (weeks) at LPV/r Initiation (95% CI)	4.1 (2.9,5.0)	3.2 (2.9,5.3)	4.0 (2.9,4.9)
Intended Feeding Method: Breastfed N (%)	31 (91.2%)	13 (65.0%)	44 (81.5%)
Sex: Female N (%)	23 (67.6%)	10 (50.0%)	33 (61.1%)
Median Gestational Age (weeks) [Q1,Q3]	38.5 [37.0,40.0]	39 [38.0,41.0]	39 [38.0,40.0]
Median Age (days) at Earliest Plasma HIV RNA level [Q1, Q3]	1 [0,1.0]	6.5 [2.0,8.0]	1 [0,3.0]
Median Earliest HIV RNA level (log_{10}(copies/ml) [Q1,Q3]	4.9 [4.0,5.3]	4.1 [3.2,5.2]	4.5 [3.5,5.3]
Median Age (days) at earliest %CD4 measurement [Q1,Q3]	15 [13.0,16.0]	8 [5.0,8.0]	12.5 [8.0,15.0]
Median Earliest-% CD4 [Q1,Q3]	50.4 [42.0,57.5]	53.5 [45.0,59.0]	52.1 [42.0,58.0]
Median Maternal Age (years) at Delivery [Q1,Q3] [N]	23.4 [20.5,29.0] [34]	26.5 [23.9,30.1] [19]	24.6 [21.7,29.1] [53]

Virologic Failure Definitions

- VL ≥200 copies/mL at Week 24
- Confirmed VL≥ limit of detection (LOD, target not detected) at later visits
- Only infants with confirmed viral load <200 copies/mL from study weeks 24 to 48 and with no confirmed detectable viremia from 48 weeks onward are maintained on study.

CROI 2019: IMPAACT P1115: Poster #0799

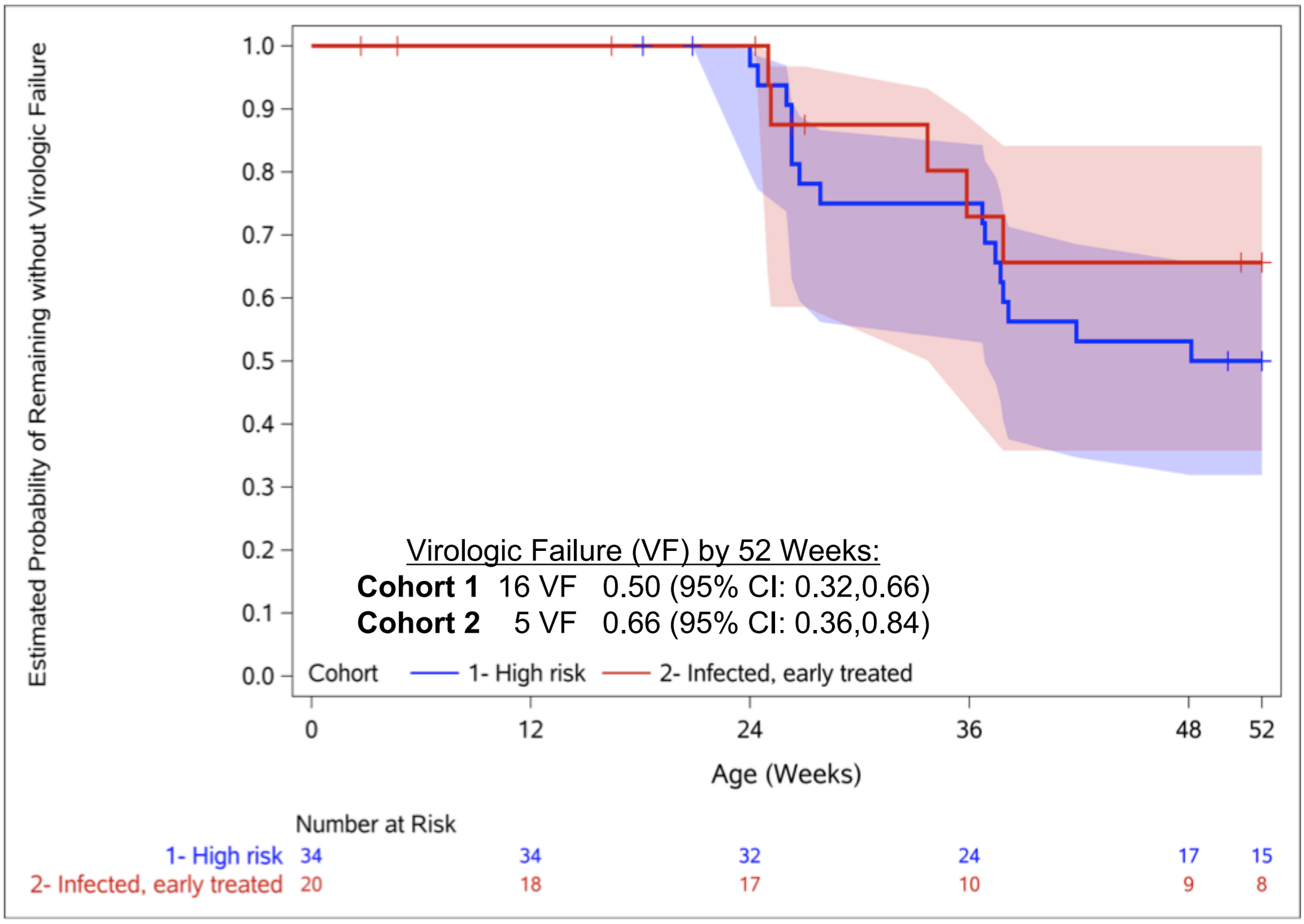
Rates of Virologic Suppression to <200 copies/mL by Week 24 of Study

HIV RNA at Week 24

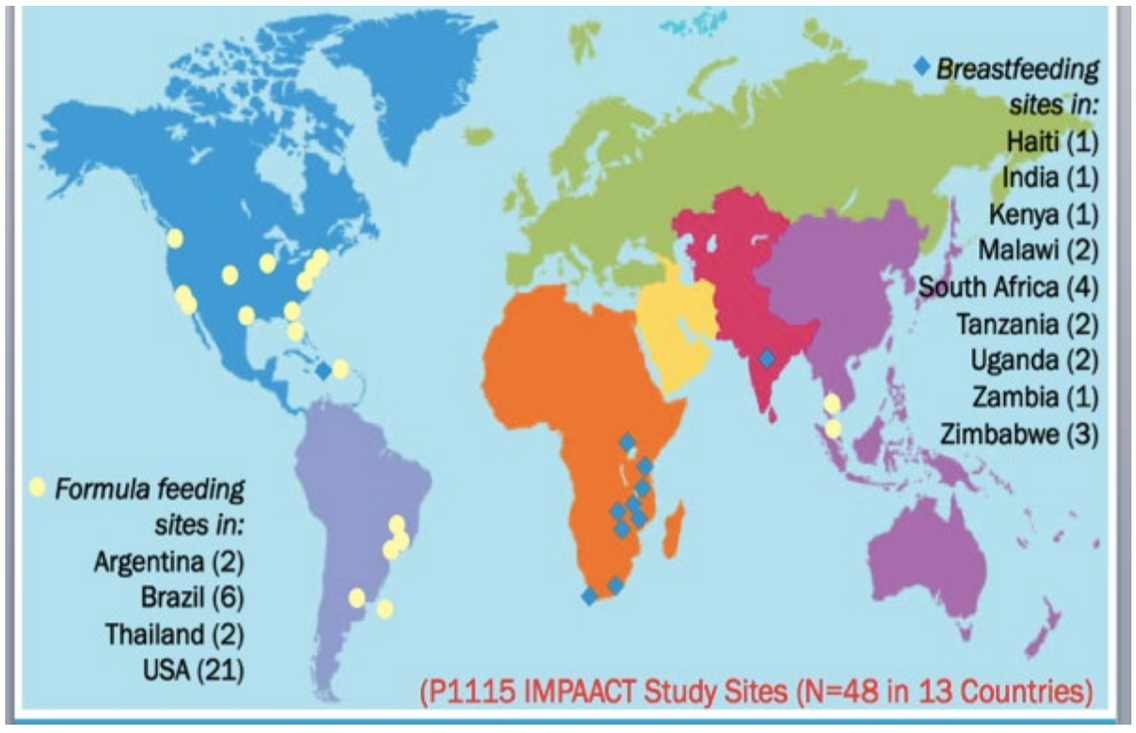
	<200 cp/ml		<LOD (target not detected)	
Cohort 1 (n=32):	24	75% (95% CI 57%,89%)	17	53% (35%,71%)
Cohort 2 (n=17):	15	88% (95% CI 64%,99%)	8	47% (23%,72%)

CROI 2019: IMPAACT P1115: Poster #0799

Probability of Remaining Free of Virologic Failure



IMPAACT P1115
(Version 2.0-Status-At Sites)



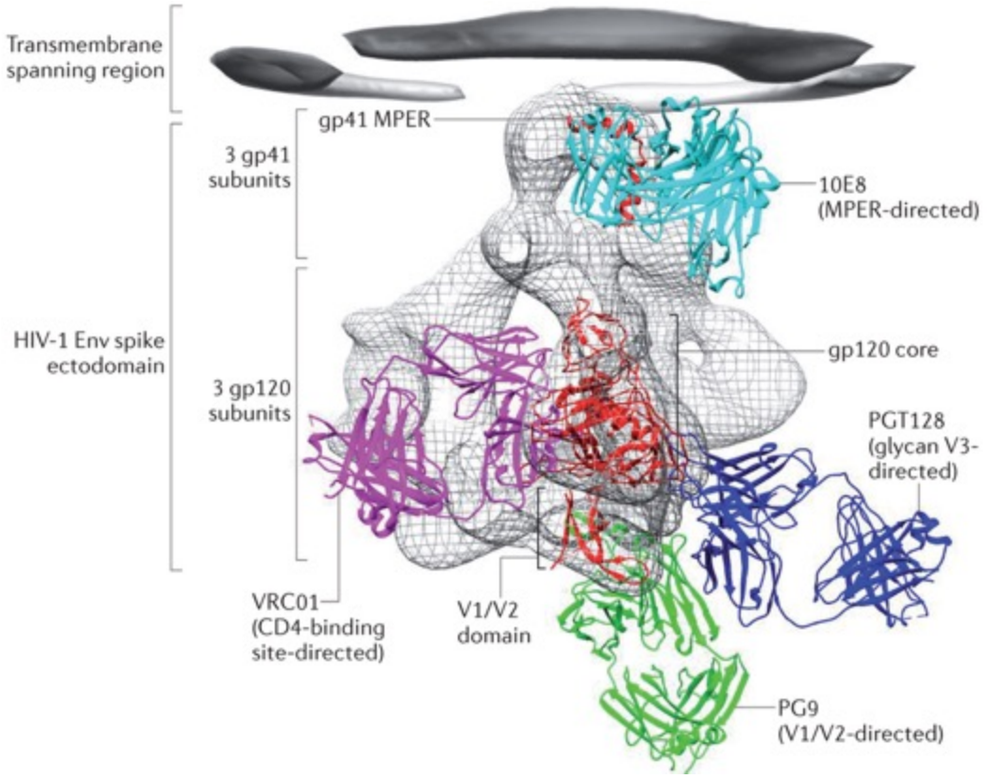
48 clinical trials sites in 13 countries

Cohort 1- 445 mother infant-pairs prospectively enrolled
Raltegravir+ nevirapine –based ART or
Raltegravir+ nevirapine –based ART + VRC01 within 48 hours of life (to enroll 45 infected infants)

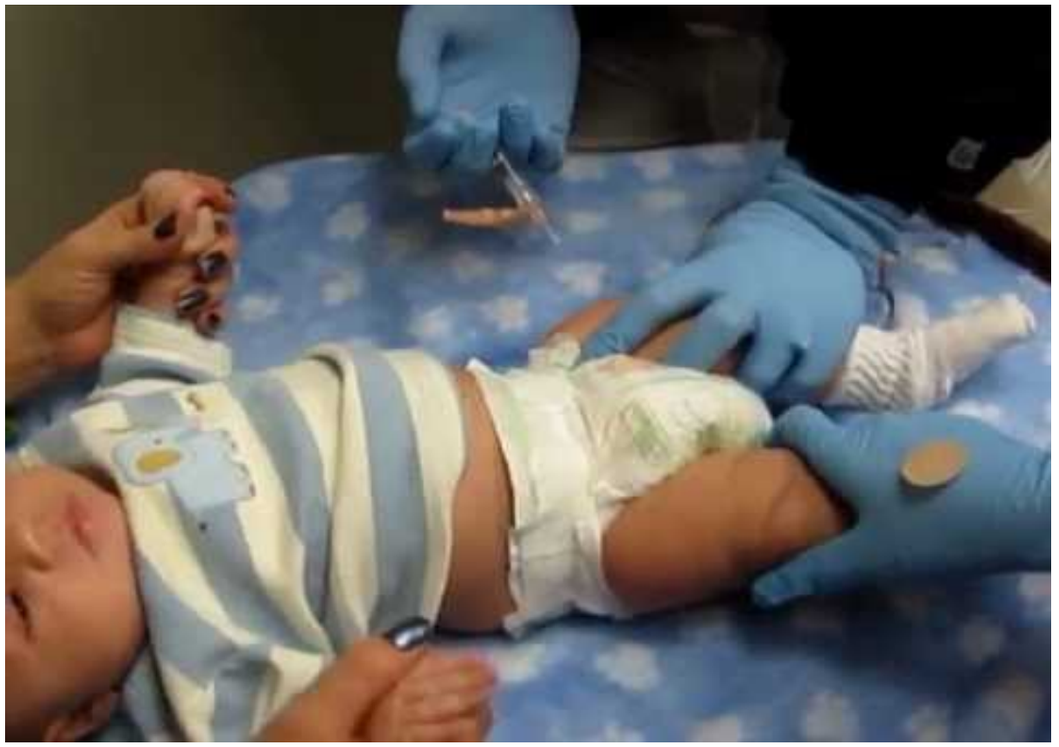
Cohort 2 : Enrolled within 10 days of life but have received very early combination ARV outside the trial

IMPAACT 2008

Phase I/II Multisite, Randomized, Controlled Study of Monoclonal Antibody VRC01 with Combination Antiviral Therapy to Promote Clearance of HIV-1-Infected Cells in Infants



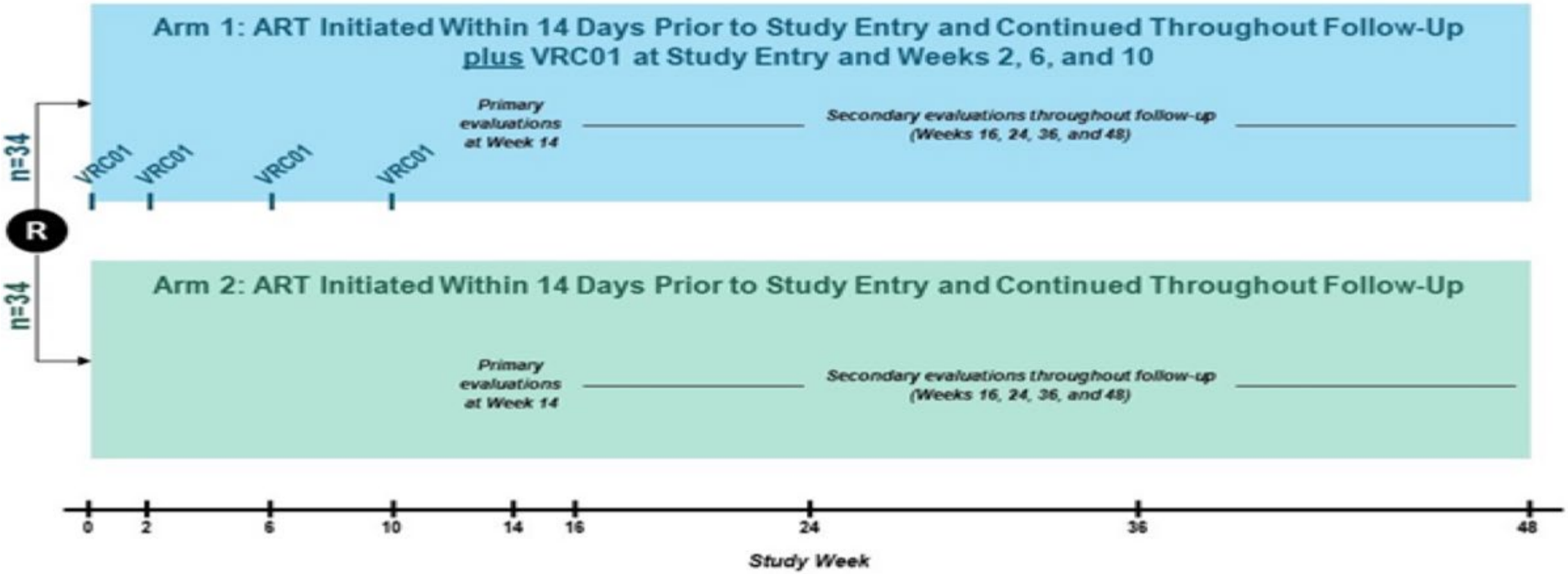
Kwong PD et al. Nature Reviews/Immunology 2013



Hypothesis: Long acting antibody injectables may promote faster clearance of HIV-infected cells, enabling early virologic control and restrict HIV reservoirs

Protocol Chairs: **Betsy McFarland (University of Colorado) and William Borkowsky (NYU);** Collaboration with the Vaccine Research Center at the NIH (Rick Koup; Lucio Gama, Julie Ledgerwood and John Mascola and Barney Graham)

Study Design, Study Population and Study Regimen



Study Design: Two-arm randomized (1:1) to VRC01 or no VRC01, open label study
Study Population: HIV infected infants age 72 hours -<12wks of age
Study Regimen: VRCO1 regimen started within 14 days of initiating ART; four doses (0, 2, 6, 10 weeks)
Accrual and duration: 34 infected infants per arm accrued over approximately 12 months; 48 weeks of follow up

IMPAACT P1112: Safety & Pharmacokinetics of Monoclonal Antibodies VRC01 and VRC01LS in HIV-Exposed Newborns

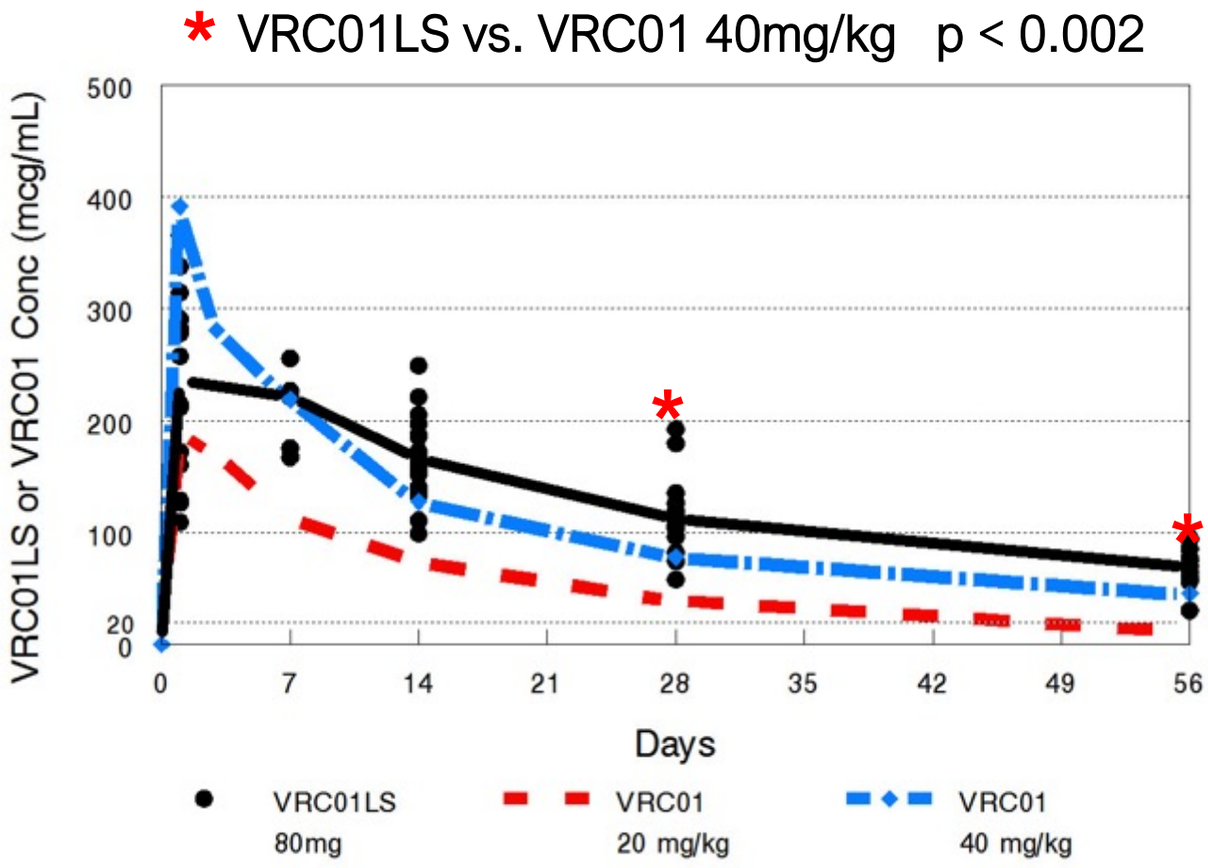
C Cunningham, E McFarland, E Capparelli, P Muresan, C Perlowski, L Morrison, P Morgan, B Smith, J Mascola, B Graham, and the IMPAACT P1112 Team;
Slide Courtesy of E. McFarland; CROI 2019 Abstract #45

Single SC doses of VRCO1 at birth (N=27) or VRC01LS (N=10), or repeated doses of VRC01 (N=13) or VRCO1-LS (N=11) over the period of breastfeeding are well tolerated

A birth dose of 40 mg/kg SC, followed by monthly doses of 20 mg/kg SC of VRCO1 result in levels consistently above 50 mcg/mL

VRC01LS has favorable PK in infants; T1/2 =59±8 days

($T_{1/2}$: 71 ± 18 days) in healthy adults[1]



[1]*Gaudinski et al. Plos Med; 2018*

HIVR4P 2018 Oral Presentation, Madrid, October 2018
CROI 2019, Oral Presentation, Seattle, March 5, 2019

Outcome Measures (P2008)

Primary

Safety: Grade 3 or higher adverse events

Virology: Change in HIV-infected cell concentrations at Week 14 compared with week 0

Secondary

PK of VRC01 in infants initiating ART

- Additional Objectives: Effect on reservoir size

Current Status (P2008)

Non US sites
CRS 5097 – Hosp Geral de Nova Iguacu
CRS 5072 – Hosp dos Servidores
CRS 30301 – JHU Blantyre
CRS 12701 – Gaborone
CRS 12702 – Molepolole
CRS 31890 – Harare Fam Care
CRS 12001 – UNC Lilongwe

US sites
CRS 5112 – David Geffen SoM UCLA
CRS 5092 – JHU
CRS 5052 – U Colorado Denver
CRS 5055 – South Fla CDTC

Non US sites
CRS 8051 – Shandukani
CRS 8052 – PHRU Soweto
CRS 8950 – FAM-CRU
CRS 30022 – Les Centres , GHESKIO
CRS 30300 – CAPRISA Umlazi

US sites
CRS 4601 – UCSD
CRS 5048 – USC

18 sites planned:
11 activated
7 in approval process

Country	Site	Number screened	Number enrolled
Botswana	Gaborone CRS	4	2
Brazil	Hosp. dos Servidores Rio de Janeiro	2	1
	Hosp. Geral De Nova Igqaucu	4	3
Malawi	Malawi CRS	2	2
	Blantyre CRS	28	17
Zimbabwe	Harare Family Care CRS	5	3
Total		**45**	**28**

40 doses VRCO1 given

Summary: Courtesy of Betsy McFarland, MD

IMPAACT 2008 TEAM

Elizabeth McFarland, M.D., Chair
William Borkowsky, M.D., Vice Chair
Deborah Persaud, M.D., Virologist
Sallie Permar, MD, Ph.D. Immunologist
Edmund Capparelli, Pharm.D. Pharmacologist
Mark Cotton, M.Med, Ph.D., Investigator
Jintanat Ananworanich, M.D., Investigator
Jane Lindsey, ScD, SDAC
Camlin Tierney, PhD, SDAC
Betsy Smith, M.D., Med. Officer
Rohan Hazra, M.D., Med. Officer
Lynette Purdue, Pharm.D. Pharmacist
Anne Coletti, MS, CTS
Charlotte Perlowski, MSPH, CTS

Paul Harding, MS, Lab Technician
Chelsea Krotje, MPH, Data Manager
Katelyn Hergott, MLIS, Lab Data Manager
Diane Costello, BS, Lab Specialist
Jonathan Lucas, MPH, Community Associate
Kathryn Myers, Westat
Dichaba Siane, ICAB

VRC Collaborators
Lucio Gama, Ph.D
Alison Taylor
Julie Ledgerwood, D.O.
Richard Koup, M.D.

Clinical Research Sites

Study Participants

Knowledge to be Gained (P2008)

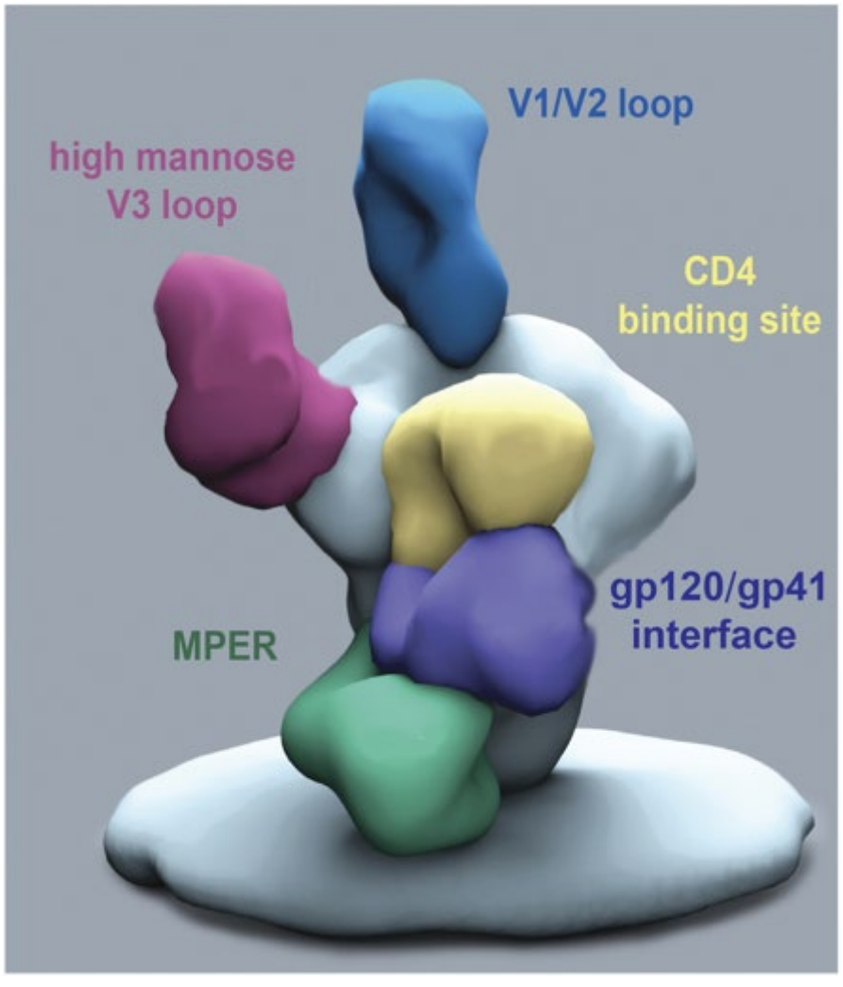
Effect of passive immunity on HIV reservoirs in perinatal infection

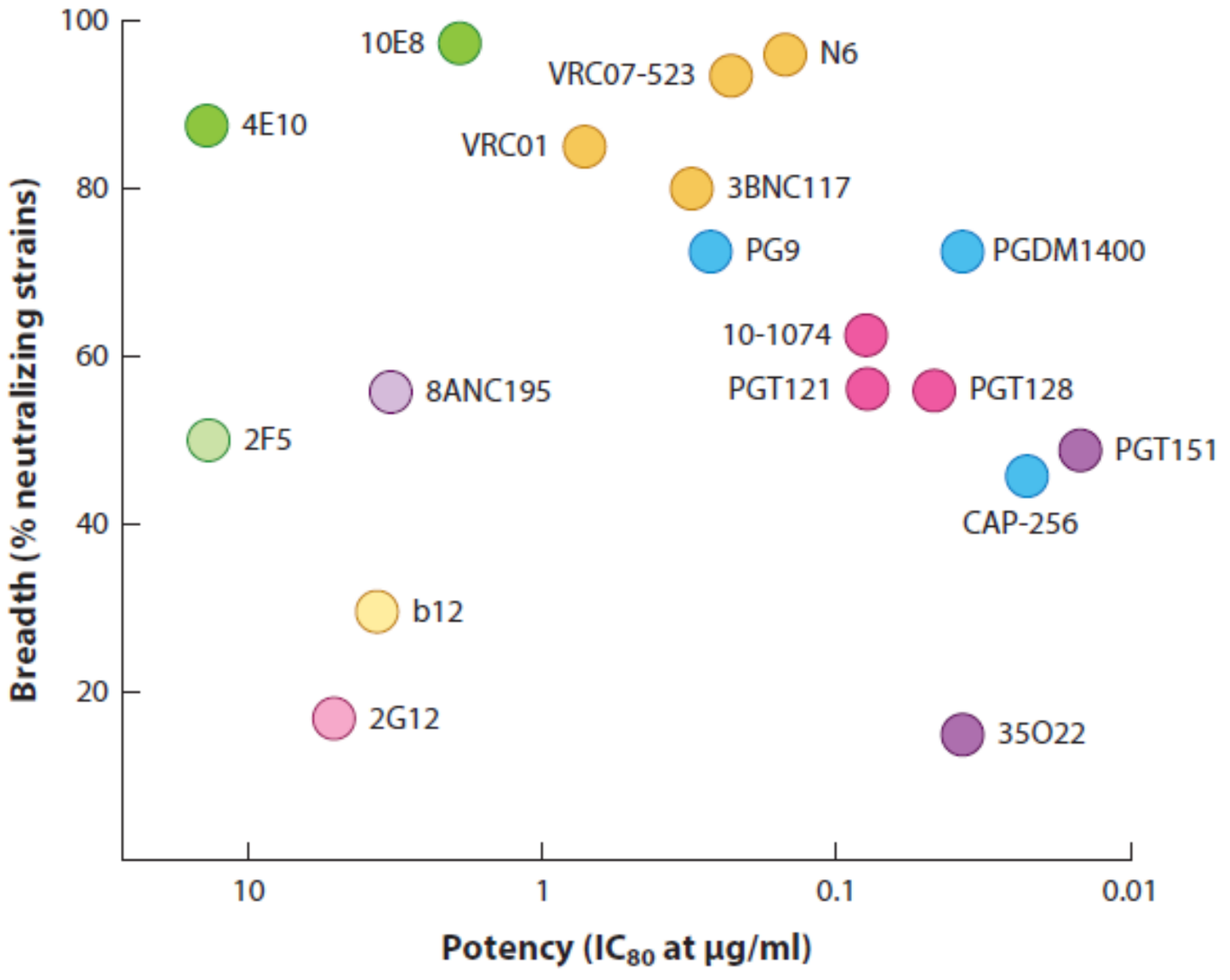
Would addition of bNAbs to ART lead to faster clearance of viremia, and smaller HIV reservoirs in perinatal HIV infection?

Does the addition of bNAbs to early ART enhance HIV-specific immune effector function in perinatal infection?

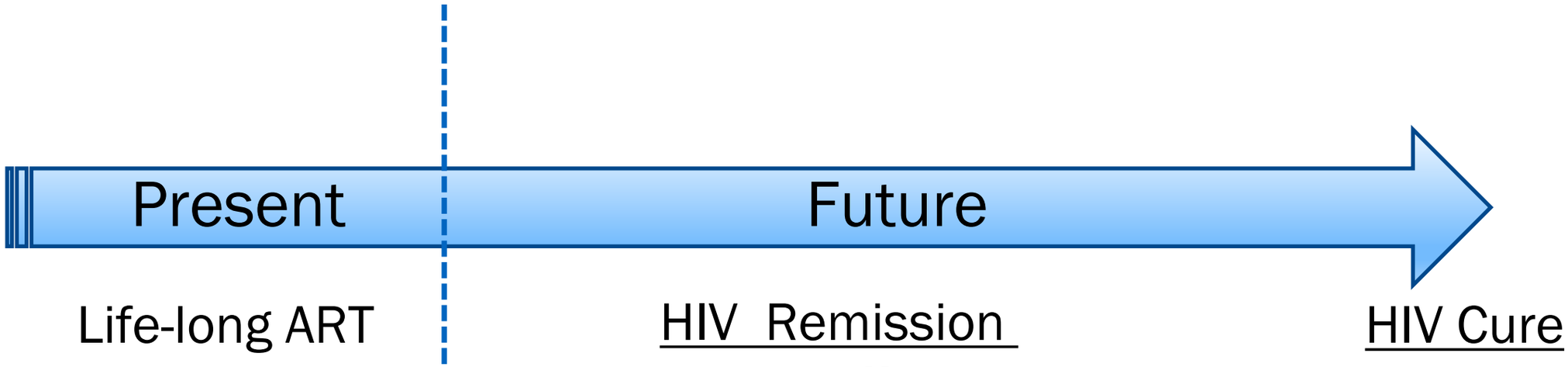
Study provides a framework for combination antibody treatment towards ART-free remission in acute infection in pediatric populations, including in adolescents

HIV Therapeutics with Combinations of Broadly Neutralizing Antibodies: Rapidly Evolving Field in Adult Infections





Shifting the HIV Treatment Paradigm



Undefined HIV Reservoirs

IMPAACT 2015: Evaluation of the HIV-1 Reservoir in the Central Nervous System of Perinatally-Infected Youth and Young Adults with Cognitive Impairment (v1.0)

Ann Chahroudi & Thor Wagner

IMPAACT
International Maternal Pediatric
Adolescent AIDS Clinical Trials Network

IMPAACT 2015
Evaluation of the HIV-1 Reservoir in the Central Nervous System of Perinatally-Infected Youth and Young Adults with a History of Neurocognitive Impairment

PROTOCOL TEAM ROSTER

Protocol Co-Chairs
Ann Chahroudi, MD, PhD
Emory University School of Medicine
Division of Pediatric Infectious Diseases
Department of Pediatrics
2015 Uppergate Drive
Atlanta, GA 30322
Phone: 404-727-5642
Email: ann.m.chahroudi@emory.edu

Thor Wagner, MD
Center for Global Infectious Disease Research
University of Washington
1900 Ninth Avenue
UW Mail Stop 359300
Seattle, WA 98105
Phone: 206-987-3642
Email: thor.wagner@seattlechildrens.org

NIAID Medical Officer
Elizabeth Smith, MD
Pediatric Medicine Branch
NIH, NIAID, DAIDS, TRP
Room 5105
6700-B Rockledge Drive, MSC 7624
Bethesda, MD 20892-7624
Phone: 301-402-3226
E-mail: mesmith@niaid.nih.gov

NICHD Program Officer
Eric Lorenzo, PhD
Maternal and Pediatric Infectious Disease Branch, NICHD
6710B Rockledge Drive
Room 2159C, MSC 7002
Bethesda, MD 20817
Phone: 301-443-4993
Email: lorenzoe@mail.nih.gov

NIMH Program Officer
Jeymohan Joseph, PhD
HIV Neuropathogenesis, Genetics and Therapeutics Branch, DAIDS/NIMH
Room 9G20, MSC 9831
5601 Fishers Lane
Bethesda, MD 20892-9830
Telephone: 240- 627-3869
Email: jjeymoha@mail.nih.gov

Clinical Trials Specialists
JL Ariansen, MS
IMPAACT Operations Center
FHI 360
359 Blackwell Street, Suite 200
Durham, NC 27701, USA
Phone: 919-544-7040 x11185
Email: jariansen@fhi360.org

Anne Coletti, MS
IMPAACT Operations Center
FHI 360
359 Blackwell Street, Suite 200
Durham, NC 27701, USA
Phone: 919-544-7040 x11238
Email: acoletti@fhi360.org

Protocol Statistician
Konstantia Angelidou, MS
Center for Biostatistics in AIDS Research
Harvard T.H. Chan School of Public Health
651 Huntington Avenue
Boston, MA 02115
Phone: 617-432-2524
Email: kangelid@sdac.harvard.edu

Protocol Investigators
Kathleen Malee, PhD
Ann & Robert H Lurie Children's Hospital of Chicago and Northwestern University Feinberg School of Medicine
225 East Chicago Avenue, Box 155
Chicago, IL 60611-2605
Phone: 312-227-8271
Email: kmalee@luriechildrens.org

Sharon Nichols, PhD
University of California, San Diego
Department of Neurosciences
9500 Gilman Drive, MC 0935
La Jolla, CA 92093-0672
Phone: 858-822-6700
Email: slnichols@ucsd.edu

Deborah Persaud, MD
Johns Hopkins University School of Medicine
Division of Infectious Diseases
Department of Pediatrics
PMOB 3-3151
200 North Wolfe Street, Room 3151
Baltimore, MD 21287
Phone: 443-287-3733
Email: dpers@jhmi.edu

Stephen A. Spector, MD
University of California, San Diego
School of Medicine
9500 Gilman Drive, MC 0672
La Jolla, CA 92093-0672
Phone: 858-534-7055
Email: saspector@ucsd.edu

Serena Spudich, MD, MA
Division Chief, Neurological Infections and Global Neurology
Yale University
PO Box 208018
New Haven, CT 06520
Phone: 203-688-4242

Collaborators
Jintanat Ananworanich, MD, PhD
The Henry M. Jackson Foundation for the Advancement of Military Medicine
6720-A Rockledge Dr., Suite 400
Bethesda, MD, 20817
Phone: 301-500-3949
Email: jananworanich@hivresearch.org

Lydie Trautmann, PhD
US Military HIV Research Program
Walter Reed Army Institute of Research
503 Robert Grant Avenue, #1N72
Silver Spring, MD 20910
Phone: 301-319-9704
Email: ltrautmann@hivresearch.org

Protocol Data Managers
Amanda Golner, BA/BS
Frontier Science & Technology Research Foundation
4033 Maple Road
Amherst, NY 14226
Phone: 716-834-0900 x7382
Email: golner@fstrf.org

Chelsea Krotje, MPH
Frontier Science & Technology Research Foundation
4033 Maple Road
Amherst, NY 14226
Phone: 716-834-0900 x7368
Email: krotje@fstrf.org

Protocol Laboratory Data Manager
Kaitley Wozer, BS
Frontier Science & Technology Research Foundation
4033 Maple Road
Amherst, NY 14226
Phone: 716-834-0900 x7224
Email: wozer@fstrf.org

P2015

- **Purpose:** To assess the HIV-1 reservoir in the CNS of perinatally HIV-1-infected youth and young adults. Findings from this study will advance understanding of the role of the CNS in HIV-1 persistence and its implications for future HIV-1 remission research.
- **Design:** Cross-sectional, multi-site, exploratory, observational study.
- **Study Population:** Perinatally HIV-1-infected youth and young adults (13-24 years of age) on suppressive antiretroviral therapy. Participants will be from study sties in the United States and will have a history of neurocognitive impairment
- **Sample Size:** Up to 45 to achieve 30 with plasma HIV-1 RNA <20 copies/mL and the minimum required volume (10 mL) of CSF collected for study purposes.
- **Study Intervention:** not applicable
- **Study Duration:** Approximately 12 months.
  - Accrual is expected to require up to nine months (from the date of first enrollment).
  - Each participant will undergo all required study procedures within a 30-day period*.
  - After all participants have completed the required evaluations, specimen testing is expected to be completed within approximately three months.

P2015

Study Objectives

Primary Objective:

- To assess CSF HIV-1 reservoirs by determining the:
  - Prevalence of quantifiable cell-free HIV-1 RNA in CSF
  - Prevalence of detectable HIV-1 DNA in CSF cell pellets*

Secondary Objective:

- To assess for associations of CSF HIV-1 reservoirs with:
  - Concentration of inflammatory and neuronal injury biomarkers in CSF
  - Concentration of inflammatory and neuronal injury biomarkers in plasma
  - Neuropsychological functioning, based on standardized testing
  - Antiretroviral drug levels in hair

Exploratory Objective:

- To assess for associations of CSF HIV-1 reservoirs with:
  - CD4+ and CD8+ T cell phenotypes in CSF

P2015

Participating Sites

- 5013 Jacobi Medical Center
- 5092 Johns Hopkins
- 5030 Emory
- 5017 Seattle
- 5048 Southern LA
- 5114 Bronx Lebanon Hospital
- 4001 Lurie Children's Hospital
- 6501 St. Jude
- 5112 UCLA
- 4601 UCSD
- 6601 Puerto Rico (pending activation)
- 5052 Colorado (pending activation)

Screening & Enrollment Update

- 13 individuals screened by 7 sites using the NIH toolbox to evaluate Fluid Cognition Composite score (starting in Oct 2018)
  - 5 screen failures (scored too high)
  - 4 screen failures (scored too low)
- 4 participants enrolled (1/mo Feb-May 2019)
  - 0 aged 13-18 years
  - 4 aged 19-24 years
- 9 month accrual window started 2/6/19

IMPAACT
International Maternal Pediatric Adolescent AIDS Clinical Trials Network

Acknowledgements

IMPAACT 2015 Participants!
IMPAACT 2015 Sites!
IMPAACT 2015 Protocol Team

Clinical Trials Specialists:	Anne Coletti	Lab Center Representative: Diane Costello
	Nicole Montanez	Protocol Lab Technologist: Paul Harding
Protocol Statistician:	Nadia Angelidou	
DIADS Medical Officer:	Betsy Smith	
NICHD Program Officer:	Eric Lorenzo	
NIMH Program Officer:	Jemoyhan Joseph	

Overall support for the International Maternal Pediatric Adolescent AIDS Clinical Trials (IMPAACT) Network was provided by the National Institute of Allergy and Infectious Diseases (NIAID) of the National Institutes of Health (NIH) under Award Numbers UM1AI068632 (IMPAACT LOC), UM1AI068616 (IMPAACT SDMC) and UM1AI106716 (IMPAACT LC), with co-funding from the Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD) and the National Institute of Mental Health (NIMH). The content is solely the responsibility of the authors and does not necessarily represent the official views of the NIH.

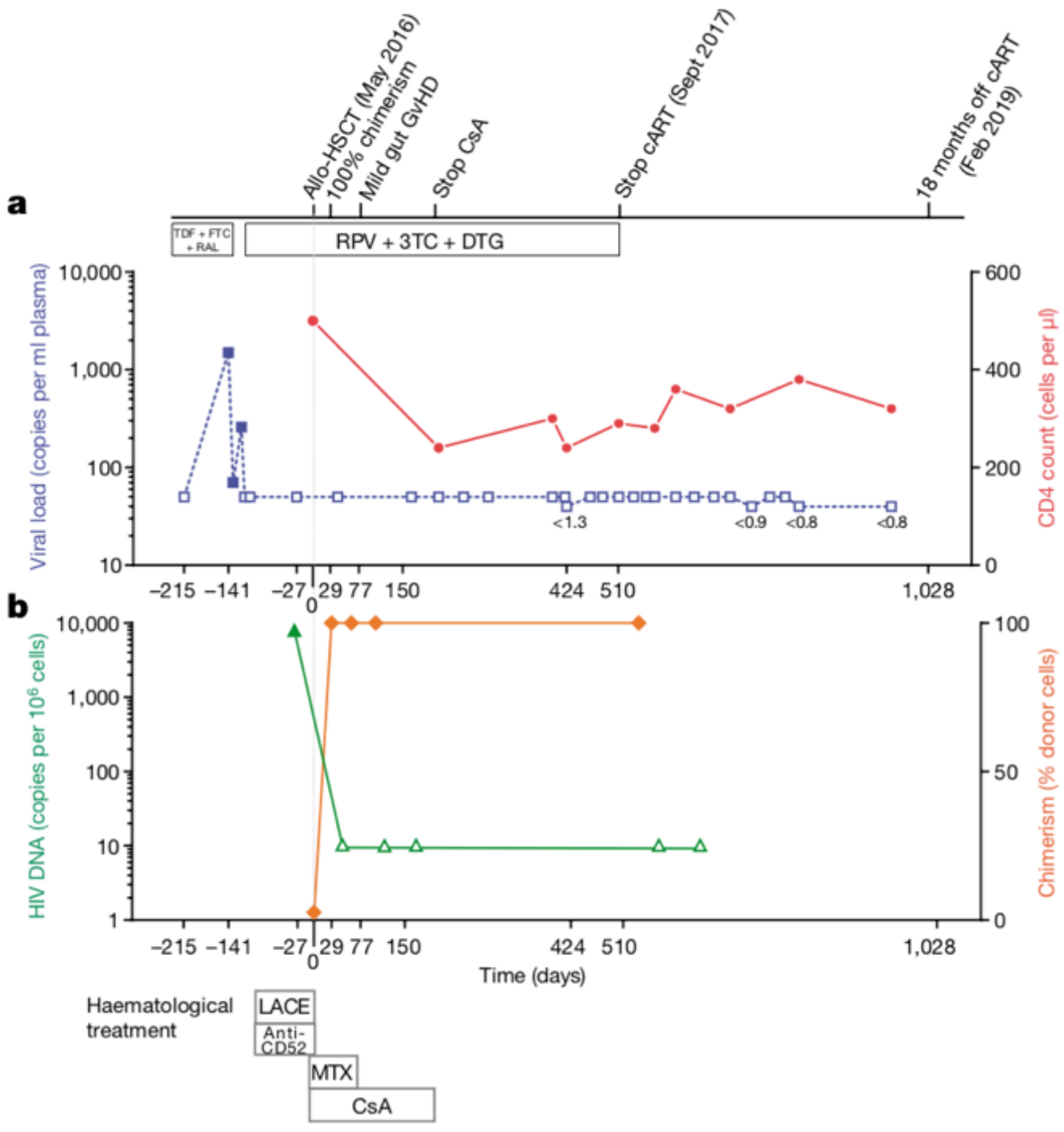
LETTER

https://doi.org/10.1038/s41586-019-1027-4

HIV-1 remission following CCR5Δ32/Δ32 haematopoietic stem-cell transplantation

Ravindra K. Gupta[1,2,3,4,5*], Sultan Abdul-Jawad[1], Laura E. McCoy[1], Hoi Ping Mok[4], Dimitra Peppa[3,6], Maria Salgado[7], Javier Martinez-Picado[7,8,9], Monique Nijhuis[10], Annemarie M. J. Wensing[10], Helen Lee[11], Paul Grant[12], Eleni Nastouli[12], Jonathan Lambert[13], Matthew Pace[6], Fanny Salasc[4], Christopher Monit[1], Andrew J. Innes[14,15], Luke Muir[1], Laura Waters[3], John Frater[6,16], Andrew M. L. Lever[4,17], Simon G. Edwards[3], Ian H. Gabriel[14,15,18,19] & Eduardo Olavarria[14,15,19]

The “London Patient”-18 Months of ART-Free Remission after BMT with CCR5 delta 32 homozygous cells for Hodgkins Lymphoma



IMPAACT P1107

Observational Study of Cord Blood Transplantation Using CCR5Δ32 Donor Cells For The Treatment of Underlying Disease in HIV infected patients and its effect on HIV Disease

A Multicenter, Domestic & International Trial of the International Maternal Pediatric Adolescent AIDS Clinical Trials Group (IMPAACT)/and ACTG

IND# Held by NIAID
DAIDS ES#

The IMPAACT HIV-1 CURE Committee Chair: Deborah Persaud, MD

Protocol Chair: Yvonne Bryson, MD
Protocol Vice Chairs: Deborah Persaud MD
Theodore Moore, MD

NIAID Medical Officer: Renee Browning /, RN MPH
NICHD Medical Officer: Rohan Hazra, MD
Clinical Trials Specialist: Anne Colleti,

The picture can't be displayed.

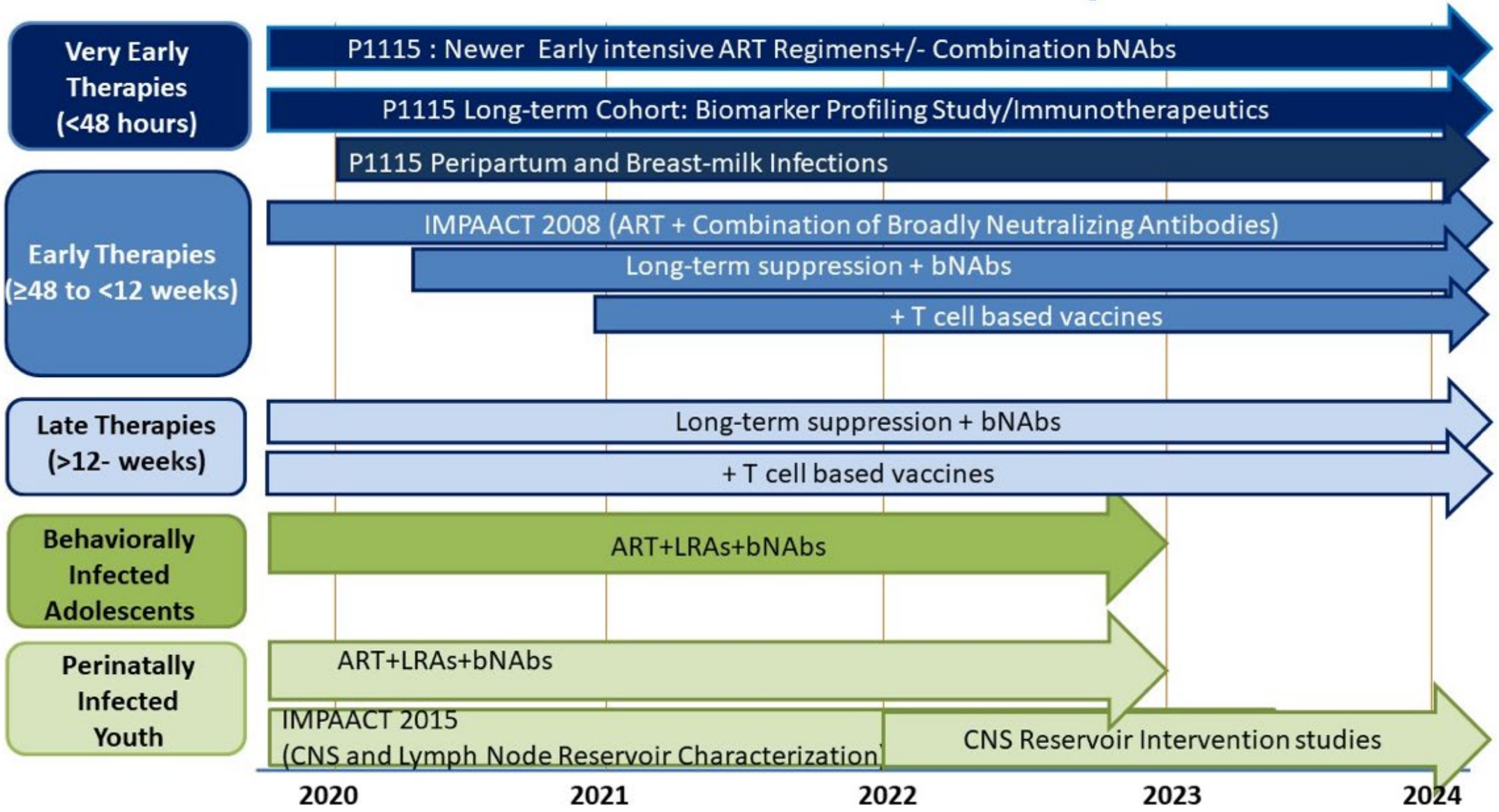
In-Development

- Long-term follow up study of P1115 and P2008 study participants (CAP 546)

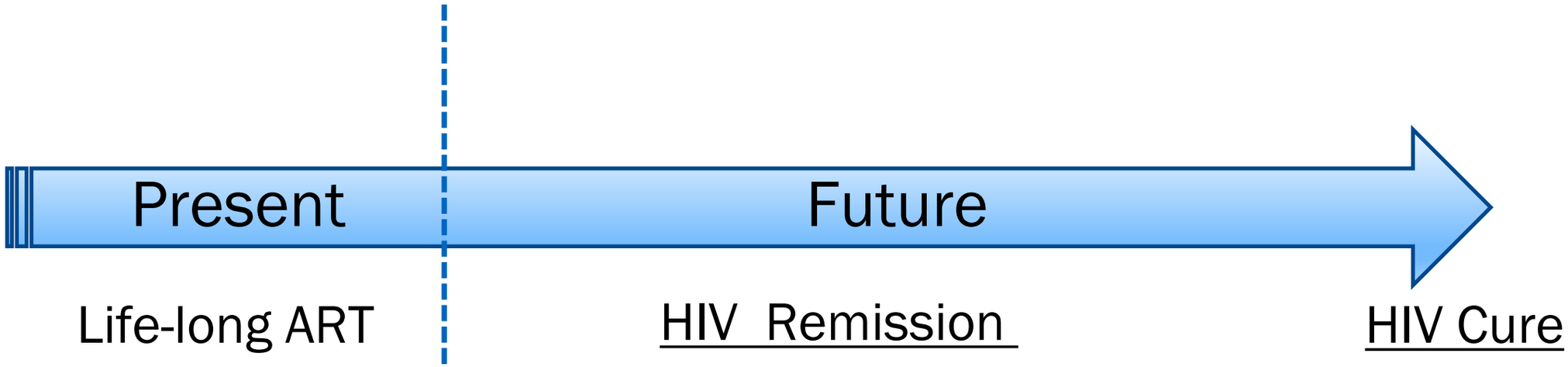
- Therapeutic vaccines in perinatally infected adolescents

- Combination broadly neutralizing antibodies in infants (P2008-version 2)

IMPAACT HIV Cure Roadmap



Shifting the HIV Treatment Paradigm



IMPAACT Leadership: Sharon Nachman and James McIntyre

IMPAACT HIV Cure Scientific Committee Members
Deborah Persaud (Chair) and Ellen Chadwick (Vice-Chair)

Committee Members
Jintanat Ananworanich
William Borkowsky
Yvonne Bryson
Mark Cotton
Katherine Luzuriaga
Betsy McFarland
Steve Spector
Thor Wagner
Dan Barouch
Ann Chahroudi

Community Advisory Board Representatives
Steven Mphonda

Committee Specialists
Anne Coletti and Charlotte Perlowski

NICHD:Rohan Hazra, Eric Lorenzo
NIAID:Patrick-Jean Phillipe, Sarah Read, Judi Miller and Ellen DeCarlo
NIMH: Pim Brouwers

Biostatisticians: Camlin Tierney, Bryan Nelson, Jane Lindsey, Meredith Warshaw

IMPAACT SLG Liason:John Sleasman

IMPAACT International Maternal Pediatric Adolescent AIDS Clinical Trials Network

Clinical Trials Team

Parents, Children and Youth

NIH NIMH

NIH National Institute of Allergy and Infectious Diseases

NIH NICHD