Broadly Neutralizing Antibodies in Oral Secretions After Administration to Newborns Exposed to HIV

793

Elizabeth J McFarland[1], Edmund V Capparelli[2], Mark J Giganti[3], Kelly Seaton[4], Caroline Brackett[4], Emily Brown[5], Charlotte Perlowski[5], Dwight E Yin[6], Hans Spiegel[7], John H Moye, Jr[8], Sai Majji[8], Paul A Harding[1], Richard A Koup[9], Lu Zhang[4], Georgia Tomaras[4], Coleen K Cunningham[10], for IMPAACT P1112 Team

[1]U Colorado Anschutz Medical Campus and Children's Hospital of Colorado, Aurora, CO; [2]UC San Diego, San Diego, CA; [3]Center for Biostatistics in AIDS Research, Harvard T.H. Chan School of Public Health, Boston, MA; [4]Duke U School of Medicine, Durham NC; [5]FHI 360, Durham, NC; [6]DAIDS, NIAID, Bethesda, MD; [7]Kelly Gov Solutions, NIAID, Rockville MD; [8]Maternal & Pediatric ID Branch, Eunice Shriver NICHD, NIH, Bethesda, MD; [9]Vaccine Research Center, NIAID, NIH, Bethesda, MD; [10]UC Irvine and Children's Hospital of Orange County, Irvine, CA

BACKGROUND

Broadly neutralizing antibodies (bNAbs) hold promise for HIV perinatal prophylaxis. Three anti-CD4 binding site bNAbs, VRC01, VRC01LS (longer plasma half-life), and VRC07-523LS (greater potency, longer plasma half-life), have favorable plasma pharmacokinetics (PK) when administered subcutaneously (SC) to newborns exposed to HIV.[1,2,3] Concentrations of bNAbs in oral secretions (OS) may be relevant to protection from HIV mucosal transmission in breastfeeding infants.

METHODS

- Open label study of three bNAbs (VRC01, VRC01LS, VRC07-523LS) administered to HIV-exposed infants at increased risk of HIV infection.
- Infants received a SC dose within 5 days of birth.
  - Dose Group 1 VRC01 20mg/kg
  - Dose Group 2 VRC01 40mg/kg
  - Dose Group 3 VRC01LS 80mg fixed dose (mean 28 mg/kg)
  - Dose Group 4 VRC07-523LS 80mg fixed dose (mean 28 mg/kg)
- Concentrations of bNAb in OS were tested in duplicate by binding antibody multiplex assay using 5-PL logistic regression from individual monoclonal Ab-specific standard curves on the same plate with lower limit of quantitation (LLOQ) of 1ng/mL.
- OS samples with total IgG concentration under 48 ng/mL were excluded (n=2).
- Concentrations of bNAb in plasma, previously reported, were determined by Beckman Biomek-based platform with anti-idiotype mAb.[1,2,3]

TABLE 1. Infant Characteristics.

		Dose Group			
		VRC01 20mg/kg	VRC01 40mg/kg	VRC01LS 80mg	VRC07-523LS 80mg
		N=13	N=12	N=19	N=22
Sex male # (%)		8 (62)	5 (42)	10 (53)	13 (59)
Black race # (%)		6 (46)	11 (92)	18 (95)	19 (86)
Hispanic/ Latino # (%)		5 (38)	2 (17)	0 (0)	2 (9)
Weight grams, mean (SD)	Birth	3185 (704)	3112 (278)	3054 (475)	3029 (482)
	Wk 8	4869 (723)	5256 (760)	4914 (481)	4833 (1263)

bNAbs were detected in oral secretions (OS) within one day and persisted through 8-12 weeks after a SC single dose in some infants, indicating rapid distribution and prolonged secretion of bNAbs at the mucosal surface. Further investigation of mucosal bNAb levels are needed to elucidate the mechanism and implications of differential bNAb PK in OS.

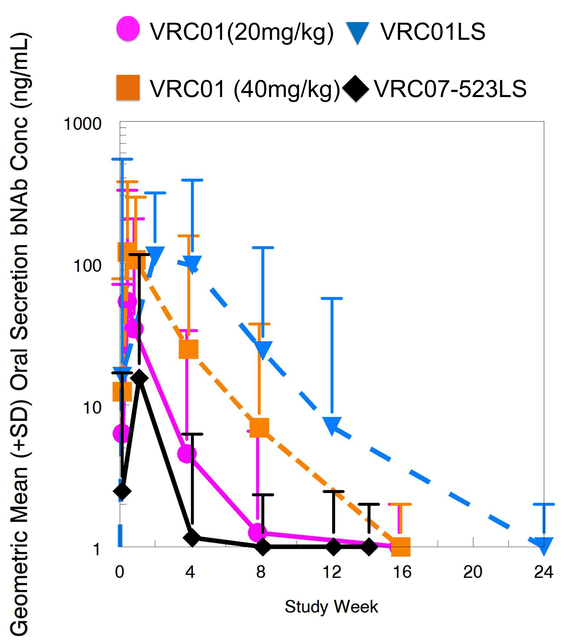
RESULTS

TABLE 2. Concentrations and proportions of infants with detectable bNAb in OS after a single SC dose at birth.

Visit	VRC01 20mg/kg	VRC01 40mg/kg	VRC01LS 80mg	VRC07-523LS 80mg
% of infants with bNAb detected in OS				
Day 1	62%	82%	68%	48%
Wk1/Wk2*	92%	100%	100%*	81%
Wk 4	62%	91%	100%	26%
Wk 8	31%	80%	100%	7%
Wk 12	ND	ND	76%	8%
Geometric mean concentration [10th-90th percentile] (ng/mL)				
Day 1	6 [<1, 125)	12 [2, 104]	16 [<1, 431]	3 [<1, 24]
Wk1/Wk2*	35 [<1,160)	106 [<1, 170]	112 [40, 312]*	15 [<1, 90]
Wk 4	5 [<1, 96)	25 [1, 165]	97 [20, 465]	1 [<1, 13]
Wk 8	1 [<1, 8]	26 [1, 318]	24.1 [5, 120]	<1 [<1, <1]
Wk 12	ND	ND	7 [<1, 55]	<1 [<1, <1]

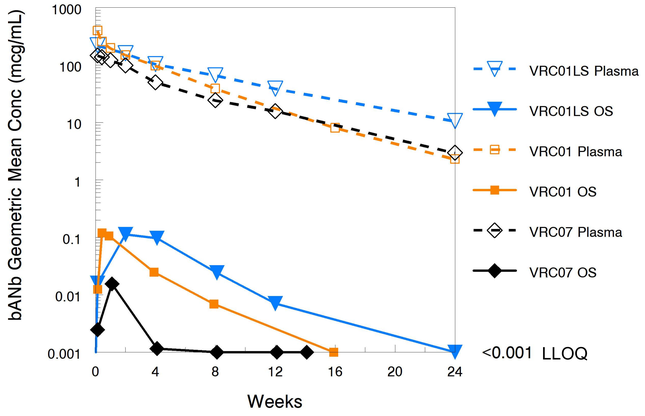
* Specimens from VRC01LS were collected at Wk 2 and not Wk 1; specimens from other dose groups were collected at Wk 1 and not Wk 2; ND = Not done

FIGURE 1. bNAb concentrations in OS after single subcutaneous dose at birth.



Plain Language Summary
Infants received antibodies that are active against HIV injected under the skin at birth. The antibodies were transported into saliva within one day, though the levels were lower than in blood. Antibodies in saliva may help protect from HIV acquired from breastmilk.

FIGURE 2. VRC01, VRC01LS, and VRC07-523LS concentrations in OS and plasma.



	Infant Plasma T1/2 days[1,2,3]
	mean (SD)
VRC01LS	39.2 (5)
VRC07-523LS	39.2 (5)

CONCLUSIONS

- VRC01, VRC01LS, VRC07-523LS were detected in OS by Day 1 post-SC administration in most newborns and persisted until Wk 12 in some infants.
- Antibody-specific differences in OS clearance may not be predicted by plasma clearance. VRC07-523LS had faster clearance in OS than VRC01LS and VRC01
- Although the role of mucosal antibody in prevention of HIV transmission via breastmilk is unknown, these data encourage future trials of more potent bNAbs for infants.

ACKNOWLEDGEMENTS

We thank the parents and infants who participated in the study; protocol team members including Frederic Bone, Benjamin Johnston, Sheetal Sawant; study sites Family Care Unit, Harare Family Care, Bronx-Lebanon Hospital Center, S. Florida CDTC, University of Colorado, David Geffen School of Medicine at UCLA, Pediatric Perinatal HIV, Johns Hopkins Univ, Emory Univ School of Medicine, Jacobi Med Ctr, Univ of Florida, U Puerto Rico, Texas Children's Hosp, San Juan City Hosp Clinical Research sites, and the NIH Vaccine Research Center.

REFERENCES

[1] Cunningham et al. 2020. "Safety, Tolerability, and Pharmacokinetics of the Broadly Neutralizing Human Immunodeficiency Virus (HIV)-1 Monoclonal Antibody VRC01 in HIV-Exposed Newborn Infants". *J Infect Dis*, 222.
[2] McFarland et al. 2021. "Safety, Tolerability, and Pharmacokinetics of a Long-Acting Broadly Neutralizing Human Immunodeficiency Virus (HIV)-1 Monoclonal Antibody VRC01LS in HIV-Exposed Newborn Infants". *J Infect Dis*, 224.
[3] Cunningham et al. 2025. "Safety, Tolerability, and Pharmacokinetics of a Long-Acting Broadly Neutralizing HIV-1 Monoclonal Antibody VRC07-523LS in Newborn Infants Exposed to HIV-1. *JPIDS*, 14.

For more information, visit impaactnetwork.org and follow us:
Facebook: IMPAACTNetwork | X (formerly Twitter): @IMPAACTNetwork | LinkedIn: IMPAACTNetwork

Overall support for the International Maternal Pediatric Adolescent AIDS Clinical Trials Network (IMPAACT) was provided by the National Institute of Allergy and Infectious Diseases (NIAID) 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), all components of the National Institutes of Health (NIH), under Award Numbers UM1AI068632 (IMPAACT LOC), UM1AI068616 (IMPAACT SDMC), and UM1AI106716 (IMPAACT LC), and by NICHD contract number HHSN275201800001I. The content is solely the responsibility of the authors and does not necessarily represent the official views of the NIH.

Presented at the 2026 Conference on Retroviruses and Opportunistic Infections (CROI) 22-25 February 2026 Denver, Colorado, USA