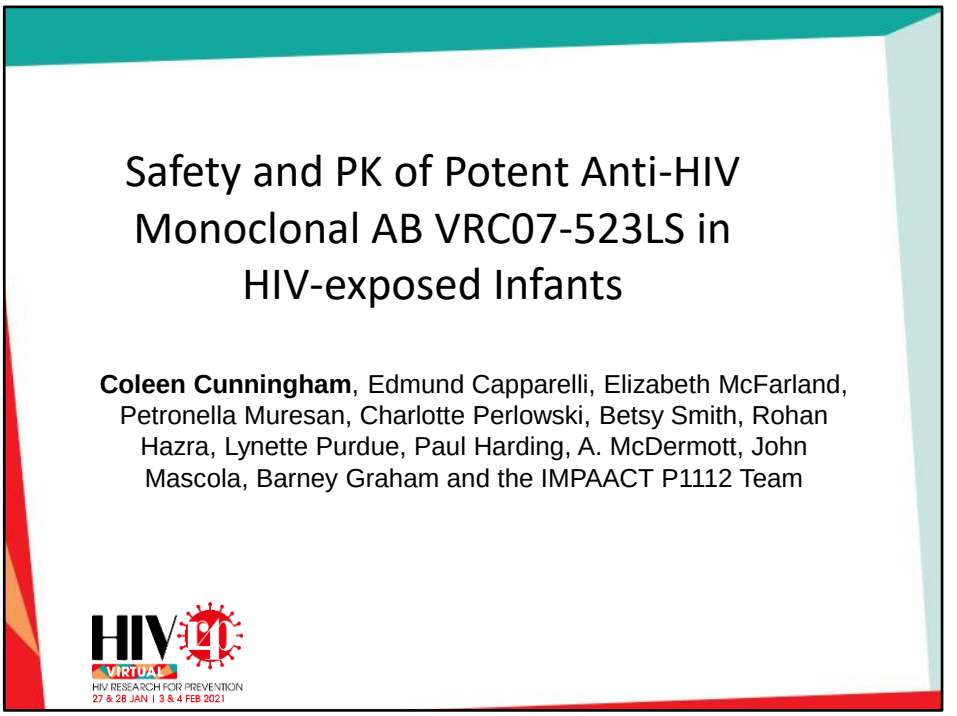
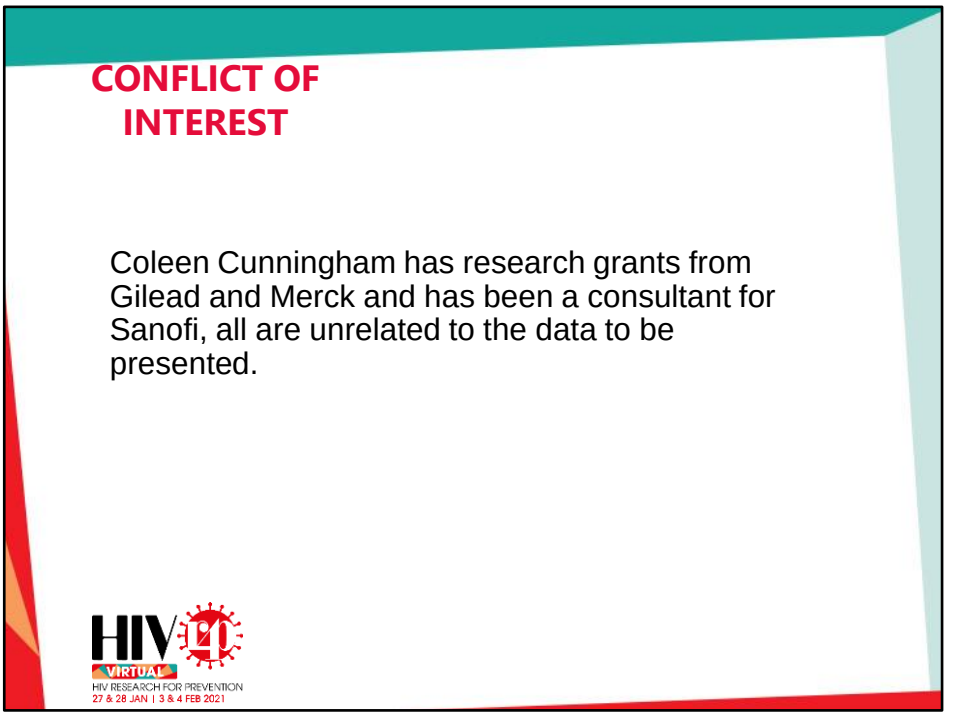


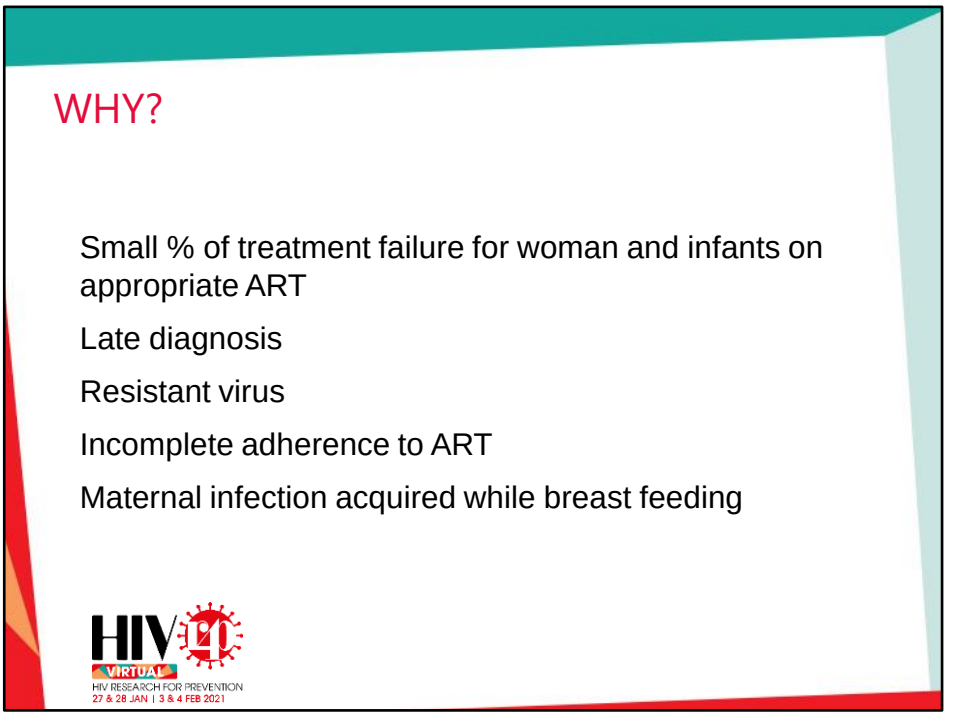
I am pleased to present the safety and PK of VRC07-523LS in HIV-exposed infants on behalf of my co-authors, the study team, and the participants



I have received research funding from Gilead and Merck and I have consulted for Sanofi. This funding is unrelated to the data I will present today.

150,000

It is estimated that 150,000 children were newly HIV infected in 2019. The vast majority of newly infected children are infected through vertical transmission. These children account for 9% of all new HIV infections in 2019!!!



Why are children still infected. Yes, we know how to decrease vertical transmission but it doesn't always work- for a variety of reasons.

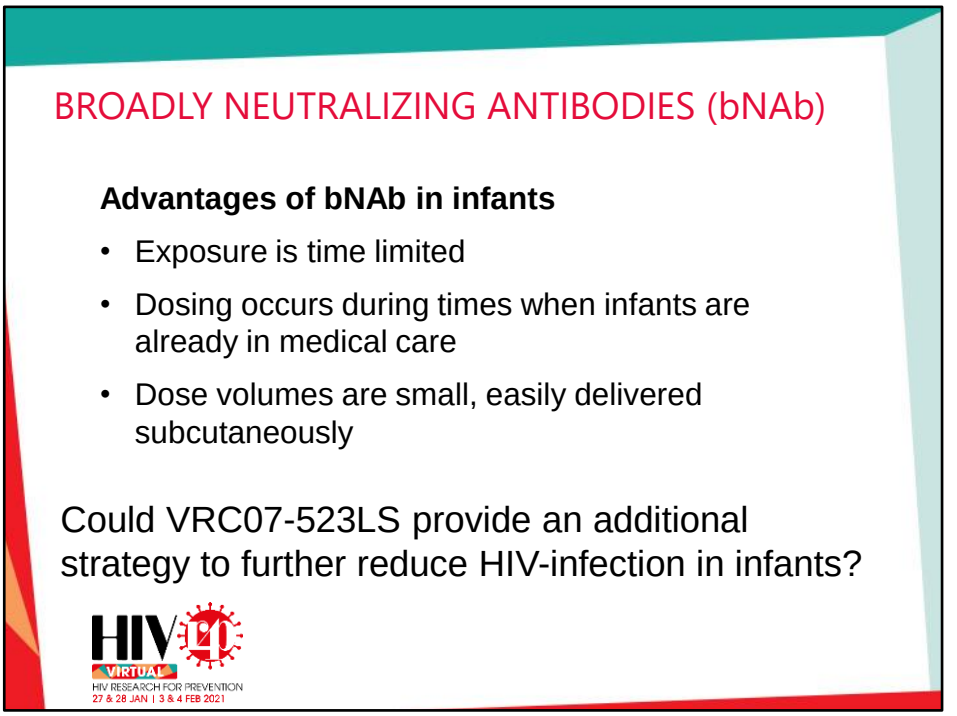
click

First, even when women receive appropriate therapy during pregnancy and during the time of breastfeeding, a small % of their infants will still become HIV-infected

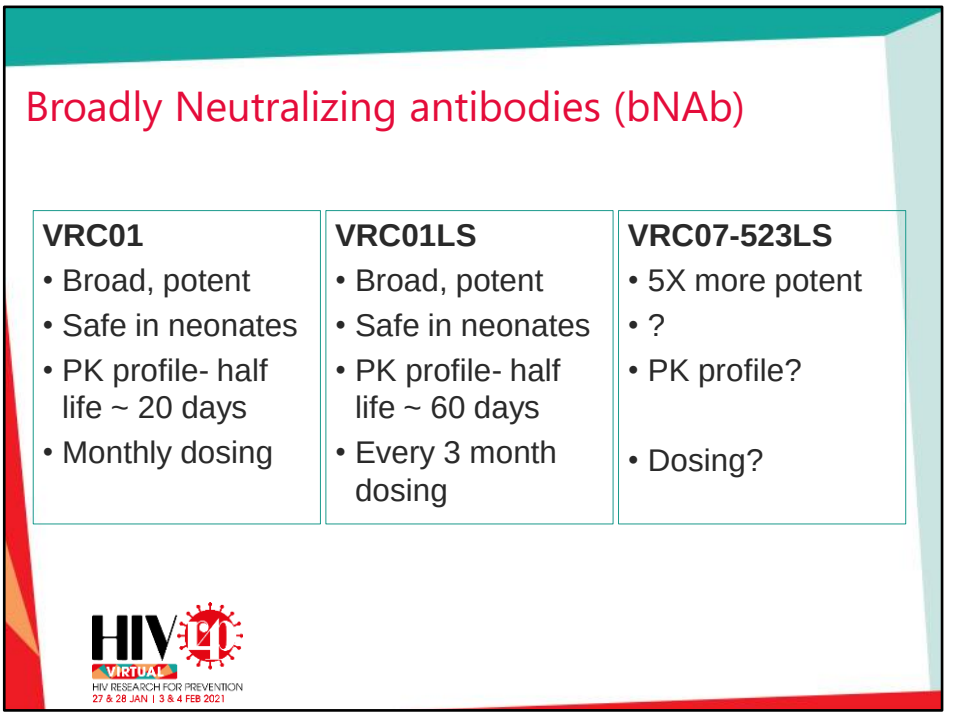
Click

But, more importantly, not all women receive full treatment. Some because of late diagnosis. Or resistant virus or inability to adhere to the treatment regimen. An additional group are infants being breastfed by a woman who is newly HIV infected. We have no antiretroviral strategy for that group.

So, we still need ways to further reduce mother to child HIV transmission



bNAbs have potential to prevent HIV transmission
Infants are the ideal candidates for a bNAb strategy as their exposure is well -defined and time-limited: its either just at delivery or delivery + the time of breast feeding. The times when doses are administered are times when the infants normally in medical care so there are no extra medical visits and the small volume doses can be delivered SC rather than requiring an IV infusion.
Click
Therefore, VRC07-523LS may provide an additional strategy to further reduce HIV infection in infants.



Our group has previously studied VRC01 and VRC01LS in infants and shown those two antibodies to be safe. VRC01LS has a very favourable PK profile. However, VRC07-523LS is 5 times more potent than VRC01 and has a better PK profile in adults compared to VRC01.

Given the potency, breadth and anticipated favourable PK profile of VRC07-523LS, this drug has the potential to be an additional tool in the prevention of infection in children. Therefore, we initiated this open label study of VRC07-523 LS in HIV exposed infants at increased risk of HIV transmission.

Abstract 363

Safety and PK of Potent Anti-HIV Monoclonal AB VRC07-523LS in HIV-exposed Infants

Type: Regular abstract

Topic: Broadly neutralizing antibodies

Authors: C. Cunningham[1], E. Capparelli[2], E. McFarland[3], P. Muresan[4], C. Perlowski[5], E. Smith[6], R. Hazra[7], L. Purdue[8], P. Harding[3], A. McDermott[9], J. Mascola[9], B. Graham[9]; [1]Duke University School of Medicine, NC, United States of America, [2]University of California, San Diego, CA, United States of America, [3]University of Colorado Anschutz Medical Campus, CO, United States of America, [4]Harvard T.H. Chan School of Public Health, MA, United States of America, [5]FHI360, NC, United States of America, [6]NIH, MD, United States of America, [7]National Institute of Child Health and Human Development, MD, United States of America, [8]DAIDS, NIAID, MD, United States of America, [9]Vaccine Research Center, NIAID, MD, United States of America

Background

Despite the effectiveness of antiretroviral therapy, vertical HIV transmission continues. A potent, broadly neutralizing, monoclonal antibody (bNAb) administered to HIV-exposed infants might reduce transmission. VRC07-523LS is 5-fold more potent and has a prolonged half-life compared to VRC01. VRC07-523LS may provide therapeutic levels over the duration of breastfeeding with infrequent doses.

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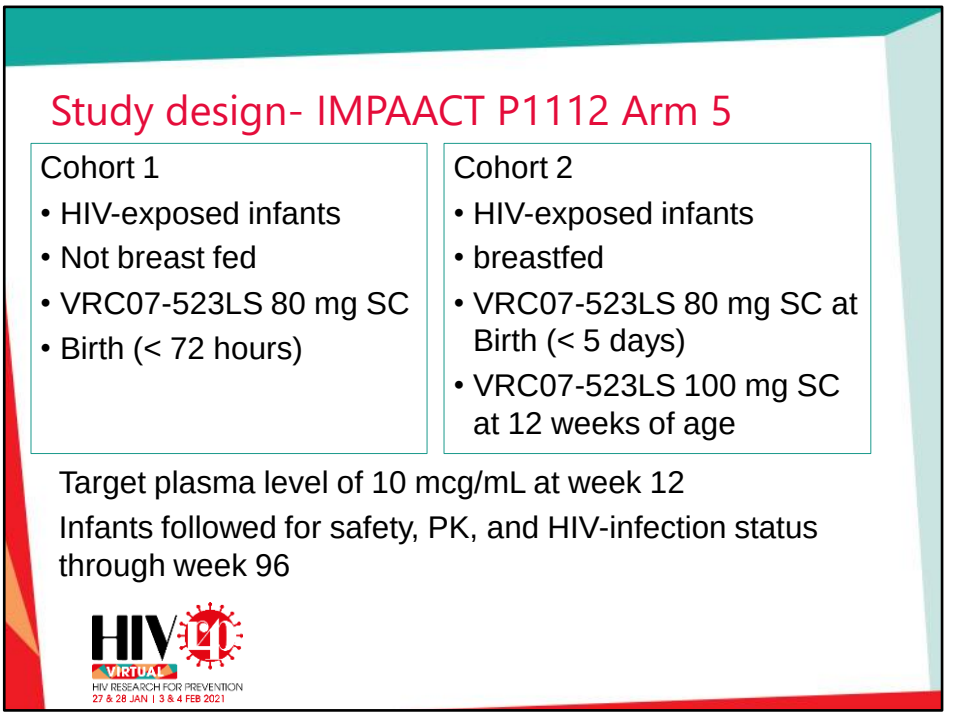
The submitted abstract describes the first cohort enrolled. This cohort included infants who were not receiving breastmilk and they received a single dose of study product at birth. Since abstract submission, we completed enrolment of a second cohort. Infants in the second cohort were breastfed as that is the standard of care at the sites where they were born. These infants received 2 doses of VRC07-523LS- one at birth and the second at 12-weeks of life.

Since we now have data on the additional cohort, today I will present safety data for both cohorts. The pharmacokinetics are only available for the first dose.



Cohort 1 infants were not breastfed and received a single SC dose of 80 mg VRC07-523LS within 72 hours of birth.
Cohort 2 infants were breastfed and received the same dose at birth, followed by a week 12 dose of 100 mg SC.
Click
The target week 12 plasma level was 10 mcg/mL: the level needed to neutralize >90% of tier II viruses in a multiclade panel.
Infants in both groups were followed for safety, PK and HIV-infection status through week 96

STUDY DESIGN

- Born to women living with HIV
- Healthy, but at increased risk of HIV-acquisition
- > 36 weeks gestational age
- > 2.0 kg birth weight
- Hb >12 g/dL, platelets >100,000

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infants enrolled were born to a woman living with HIV, were healthy but at increased risk of HIV infection, > 36 weeks gestational age and > 2.0 kg birth weight. There met several laboratory criteria as well.

RESULTS

Baseline Characteristics		VRC07-523LS single dose	VRC07-523LS 2-dose	Total
Study site	USA	11	0	11
	Africa	0	11	11
Race/Ethnicity	Black non-Hispanic	7 (64%)	11 (100%)	18 (82%)
Infant ARV	NVP	0	10 (91%)	10 (45%)
	ZDV	5 (45%)	0	5 (23%)
	3TC, ZDV, NVP	3 (27%)	0	3 (14%)
	ZDV, NVP	2 (18%)	1 (9%)	3 (14%)
	3TC, ZDV	1 (9%)	0	1 (5%)
Age Days Mean- (SD)		1.5 (0.7)	3.4 (1.5)	2.5 (1.5)
Birth Weight Grams- Mean (SD)		2830 (272)	3228 (571)	3019 (482)

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Baseline characteristics are shown. All infants in the single dose cohort were enrolled in USA and all in the 2-dose cohort were enrolled in Zimbabwe and S Africa. All infants received standard of care treatment to reduce the risk of vertical transmission of HIV, though the regimens varied between sites and between cohorts. Infants in Africa primarily received NVP alone while infants in the US received ZDV or combinations that included ZDV.
All infants received study drug within the specified protocol window

RESULTS

Local reactions		VRC07-523LS single dose	VRC07-523LS 2-dose	Total
		N= 11	N=11	N=22
Dose 1	Erythema	1	3	4
	Pain/Tenderness	1	1	2
	Edema	0	4	4
	Induration	0	5	5
			N=8	N=8
Dose 2	Erythema	NA	4	4
	Pain/Tenderness	NA	2	2
	Edema	NA	4	4
	Induration	NA	3	3

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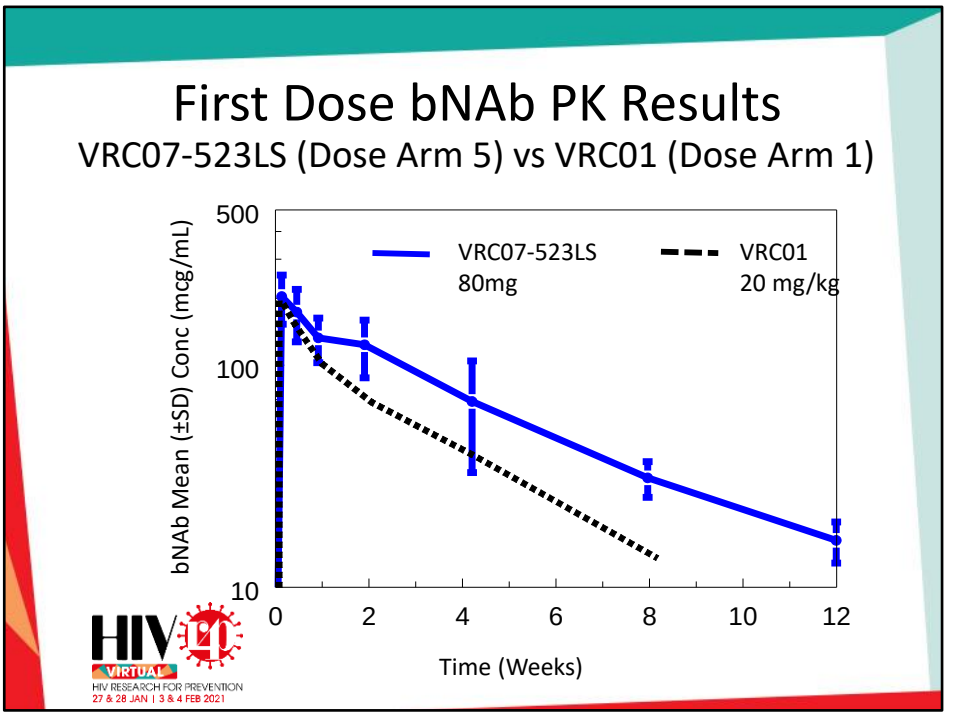
This table describes the local reactions for the single dose and 2-dose cohorts. The lower portion describes reactions after the second dose. Please note that infants in the 2-dose cohort did not receive a second dose if the infant was no longer being breastfed at week 12; therefore, only 8 received dose 2.

Local reactions were rare in the group enrolled in the US but common among the infants enrolled in Africa. Regardless of cohort, local reactions were mild and most resolved on the same day. Only one event lasted until day 2 and that was grade 1 pain. The most severe local reaction was grade 2.

Other vaccine-related reactions reported included grade 1 “sleeping less than usual” in 3 infants, grade 1 irritability in 2 infants, and grade 1 vomiting in 1 infant

Five infants developed Grade 3 or 4 events within 28 days of receipt of study drug including vomiting in 2, and neutropenia, hyperkalemia, and parainfluenza sepsis in 1 each, none considered related to study treatment.



Pharmacokinetic measures are available through week 12 in the single dose cohort. The blue line shows the results for VRC07-523LS and the dotted black line shows VRC01 levels from a previous cohort. The average levels of VRC07-523LS at weeks 4, 8 and 12 are 68.7, 31.1, 16.3 mcg/mL, respectively.

This is favorable compared with VRC01 but lower compared with VRC01LS; however, levels remain >10 mcg/mL, our target, at week 12 in all infants.

CONCLUSIONS

VRC07-523LS 80 mg SC at birth and 100 mg SC at 12 weeks

- Is safe and well-tolerated
- Is rapidly absorbed and maintains concentrations >10 mcg/mL for at least 12 weeks after 80mg in all infants

VRC07-523LS, with its enhanced potency and extended half-life, could achieve target levels for the duration of breastfeeding with dosing every 3 months

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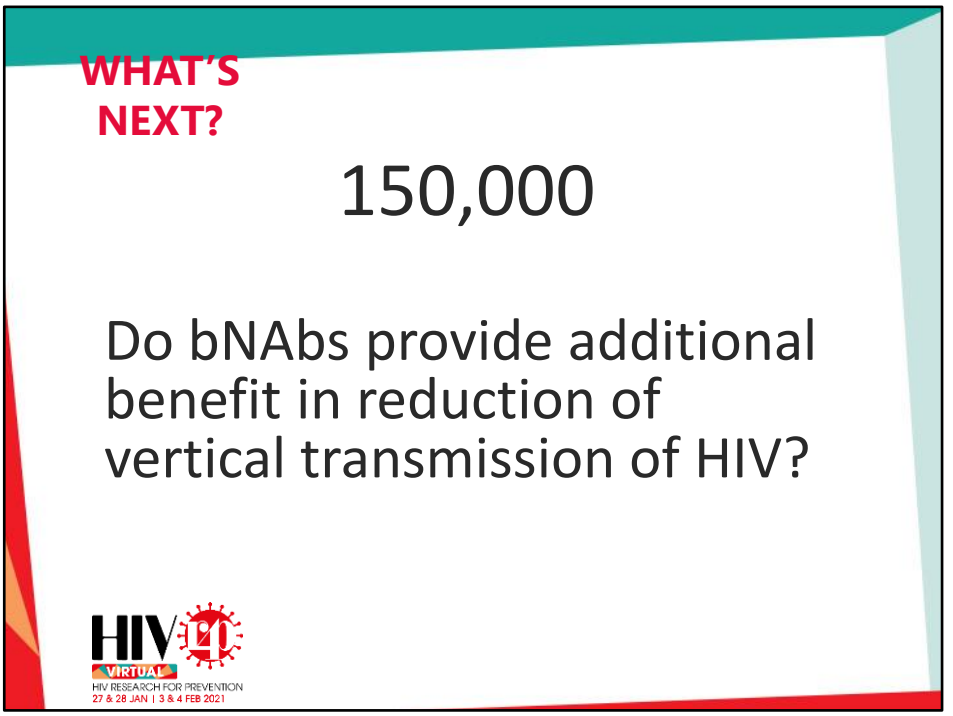
In conclusion……



Remember, 150,000 newly infected children in 2019. Can we do better?
click
We now have a pressing question- do bNAbs, including VRC07-523LS, provide additional benefit in reduction of vertical transmission of HIV
Further studies are needed to answer this question

Acknowledgements -Thanks to:

The IMPAACT P1112 Team (an awesome team)

Thanks to: Vaccine Research Center: Barney Graham, John Mascola, Julie Ledgerwood

Sites

Cape Town, S. Africa
Harare Family Care
Bronx-Lebanon Hospital, NY
University of California, LA
Emory University
University of Puerto Rico
Jacobi Med. Ctr., NY
Johns Hopkins University
San Juan, Puerto Rico
South Florida, Ft Lauderdale
Texas Children's Hospital
University of Colorado
University of Florida

The parents and infants

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