Predictive markers for sustained viral suppression on dual bNAbs during ART interruption in children

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Jaspreet Banga[1,2], Bryan S. Nelson[3], Gbolahan Ajibola[4], Terence Mohammed[4], Comfort Maphorisa[4], Correttah Boleo[4], Oganne Batlang[4], Maureen Sakoi-Mosetlhi[4], Kenneth Maswabi[4], Molly Pretorius Holme[2], Kathleen M. Powis[2,4,5], Shahin Lockman[2,4,6], Michael D. Hughes[3], Joseph Makhema[4], Daniel R. Kuritzkes[6], Mathias Litcherfeld[7], Roger Shapiro[2,4]

1.Beth Israel Deaconess Medical Center, Division of Infectious Diseases, Boston, United States, 2. Harvard T.H. Chan School of Public Health, Department of Immunology and Infectious Diseases, Boston, MA, United States, 3. Harvard T.H. Chan School of Public Health, Department of Biostatistics, Boston, MA, United States, 4. Botswana Harvard Health Partnership, Gaborone, Botswana, 5. Massachusetts General Hospital, Departments of Internal Medicine and Pediatrics, Boston, MA,, United States, 6. Brigham and Women's Hospital, Boston, MA, United States, 7. Ragon Institute of Mass General, MIT, and Harvard, Cambridge, MA, United States

BACKGROUND

- Simple clinical markers to predict success of bNAb-only treatment (or during any ART interruption) are needed
- The combination of a negative qualitative HIV DNA and negative enzyme immunosorbent assay (EIA) at study entry was previously reported to correlate with success in the Tatelo Study in Botswana
- We now report findings for additional biomarker combinations, including HIV RNA target detection at study entry and during the bNAb-only step of the Tatelo Study

METHODS

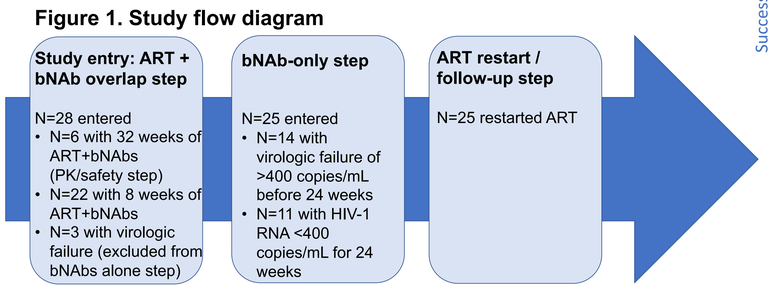
- Twenty-five children received up to 24 weeks of bNAb-only treatment (VRC01LS+10-1074) following ART interruption (Figure 1)
- Enrolled children were on ART since birth in a previous study, were virally suppressed for at least 24 weeks prior to study entry, and were ≥96 weeks and <5 years of age at enrollment
- HIV qualitative DNA and HIV RNA were performed every 1-2 weeks and EIA every 4-8 weeks.

Table 1. Birth and enrollment characteristics of Tatelo participants who interrupted ART (N=25)

At birth	
Female Sex (%)	16 (64)
Median HIV-1 RNA, log_{10} copies/mL (IQR)	3.5 (2.5-4.4)
Median HIV DNA, copies per million cells (IQR)	465 (100-1129)
At time of enrollment	
Median HIV DNA, copies per million cells (IQR)	31.9 (25.8-42.2)
Median age, years (IQR)	3.7 (3.1-4.4)
ART regimen at time of enrollment[a]	
ZDV + 3TC + LPV/r	23
ABC + 3TC + LPV/r	1
ZDV + ABC + 3TC + LPV/r	1

a. ZDV=zidovudine; 3TC=lamivudine; LPV/r=lopinavir/ritonavir; ABC=abacavir

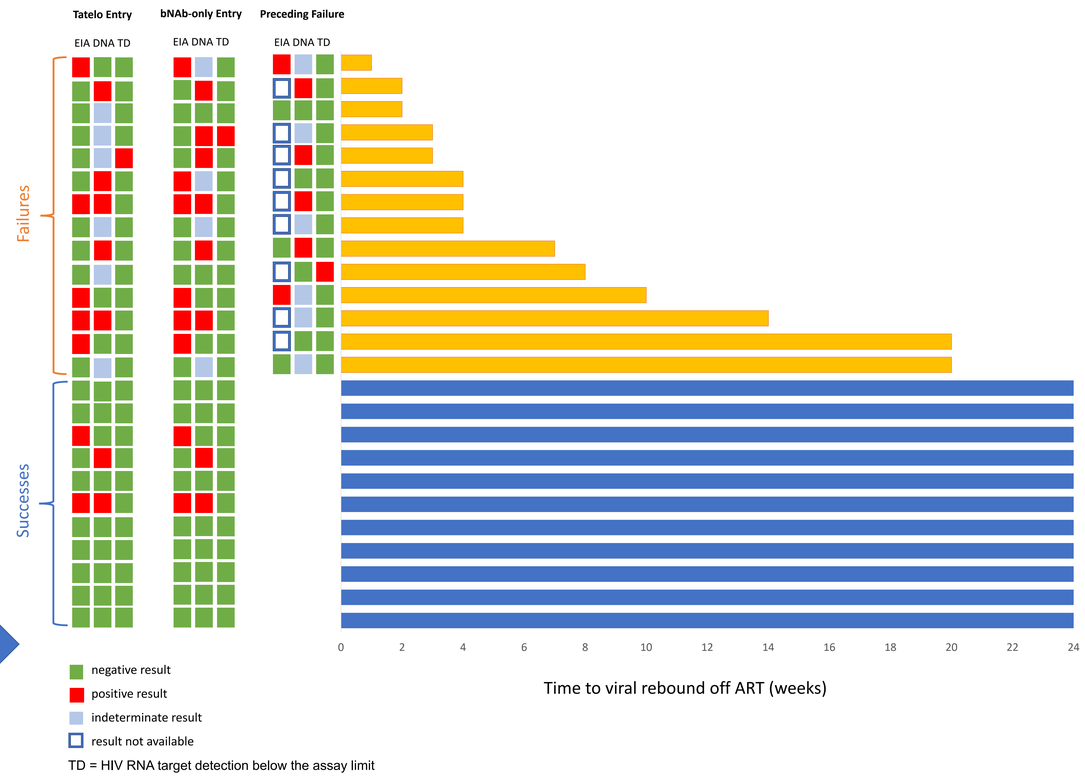
Figure 1. Study flow diagram



Negative/negative qualitative DNA and EIA at start of bNAb-only treatment predicted maintenance of viral suppression among children

No biomarker combination was clinically useful in predicting virologic rebound in the three visits preceding failure

Figure 2: bNAb treatment success and biomarker patterns at study entry and start of bNAb-only step in the Tatelo Study, Botswana



RESULTS

Table 2. Biomarker results at start of bNAb-only step and successful maintenance of viral suppression

Biomarker	N (%) with 24-wk viral suppression if marker **negative**	N (%) with 24-wk viral suppression if marker **non-negative**	p-value (Fisher's test)
At Study Entry			
Qualitative DNA	9/12 (75%)	2/13 (15%)	**0.005**
EIA	9/18 (50%)	2/7 (29%)	0.41
Both DNA and EIA	8/8 (100%)	3/17 (18%)	**0.0002**
RNA Target Detected	11/24 (46%)	0/1 (0%)	>0.99
At bNAb-only Step Entry			
Qualitative DNA	9/13 (69%)	2/12 (17%)	**0.02**
EIA	9/17 (53%)	2/8 (25%)	0.23
Both DNA and EIA	8/10 (80%)	3/15 (20%)	**0.005**
RNA Target Detected	11/24 (46%)	0/1 (0%)	>0.99

- All 8 with negative/negative qualitative DNA and EIA at study entry and 8/10 with negative/negative at bNAb-only step entry succeeded
- In the visit immediately prior to rebound, HIV RNA target detection occurred in only 1/14 (7%) of participants (Figure 2)
- No marker or combination of markers reliably changed in the 3 visits prior to rebound (Figure 2)
- Throughout the study period, indeterminate DNA did not reliably predict a subsequent negative or positive DNA result (unable to distinguish HIV qualitative DNA assay failure vs. trace of contamination vs. very low level virus detection which may all be read as indeterminate)

CONCLUSIONS

- Negative/negative DNA and EIA at start of bNAb-only treatment predicted maintenance of viral suppression
- HIV-1 RNA target detection below the assay limit did not prove to be a predictive biomarker
- No biomarker combination was clinically useful in the visits preceding failure – frequent HIV RNA monitoring should continue to be used
- Our study is limited by small sample size and pre-specified study population (treated since birth, virally suppressed before entry), further study is needed to evaluate additional potential biomarkers

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