

Viral Control among Children in Botswana Receiving Combination Broadly Neutralizing Antibodies

Preliminary Findings from the Tatelo Plus Study (IMPAACT 2042)

Phase I/II Trial to Evaluate the Impact of Three Broadly Neutralizing Antibodies or Analytic Treatment Interruption on Viral Reservoir, Immune Function, and Maintenance of HIV Suppression in Early-Treated Children in Botswana

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Introduction

- 1.4 million children aged 0-14 years are living with HIV
 - ~4,200 in Botswana
- Children on ART have lower rates of viral suppression than adults
 - Only 46% with sustained viral suppression
- Daily adherence to oral ART is especially challenging in children
- **There is a need for long-acting treatment options for children living with HIV, and for strategies that promote post-treatment viral control**

Combination bNAbs offer long-acting treatment for children living with HIV

- Monthly combination bNAbs can maintain viral suppression in children started on ART very early in life
 - **Tatelo Study:** without phenotypic pre-screening, 44% of children who had started ART near birth maintained HIV-1 RNA <40 copies/mL through 24 weeks while receiving 10-1074 + VRCO1LS bNAb-only treatment
- **In the current Tatelo Plus / IMPAACT 2042 study, we are evaluating whether pre-screening children for bNAb susceptibility or biomarkers for HIV replication, and using broader and more potent bNAbs, can maintain viral control in a higher percentage of children**

Adult data support combination bNAbs to promote drug-free HIV remission

- Clinical trials in adults, such as the RIO Study support the use of bNAbs to promote drug-free HIV remission
 - bNAbs may reduce the intact HIV viral reservoir
 - bNAbs may impact immune responses against HIV
- **Unknown if bNAbs can promote post-treatment control in children. This is being evaluated in the next phase of the Tatelo Plus Study**

Tatelo Plus Study Design

Initial eligibility criteria:

- Children receiving ART since birth
- HIV RNA <40 copies/mL for >24 weeks prior to entry

Step 1: Combination bNAbs added to ART

- All received intravenous VRC07-523LS, PGDM1400LS, PGT121.414.LS
 - VRC07-523LS every 4 weeks
 - PGDM1400LS / PGT121.414.LS every 8 weeks, alternating
- Safety and PK evaluated

Step completed. See poster #843 by Capparelli et. al. for detailed safety and PK results

Step 2: bNAb-only treatment

- Participants were pre-screened, eligible if:
 - Susceptible to at least 2 bNAbs (early-life samples)
 - If no susceptibility data: negative/negative biomarker status (neg qual HIV DNA + neg serostatus)

Step completed for the first group and the focus of this presentation.

Step 3: Analytic Treatment Interruption (ATI)

- Evaluating viral control without ART or bNAbs, eligible if:
 - Negative/negative biomarker status

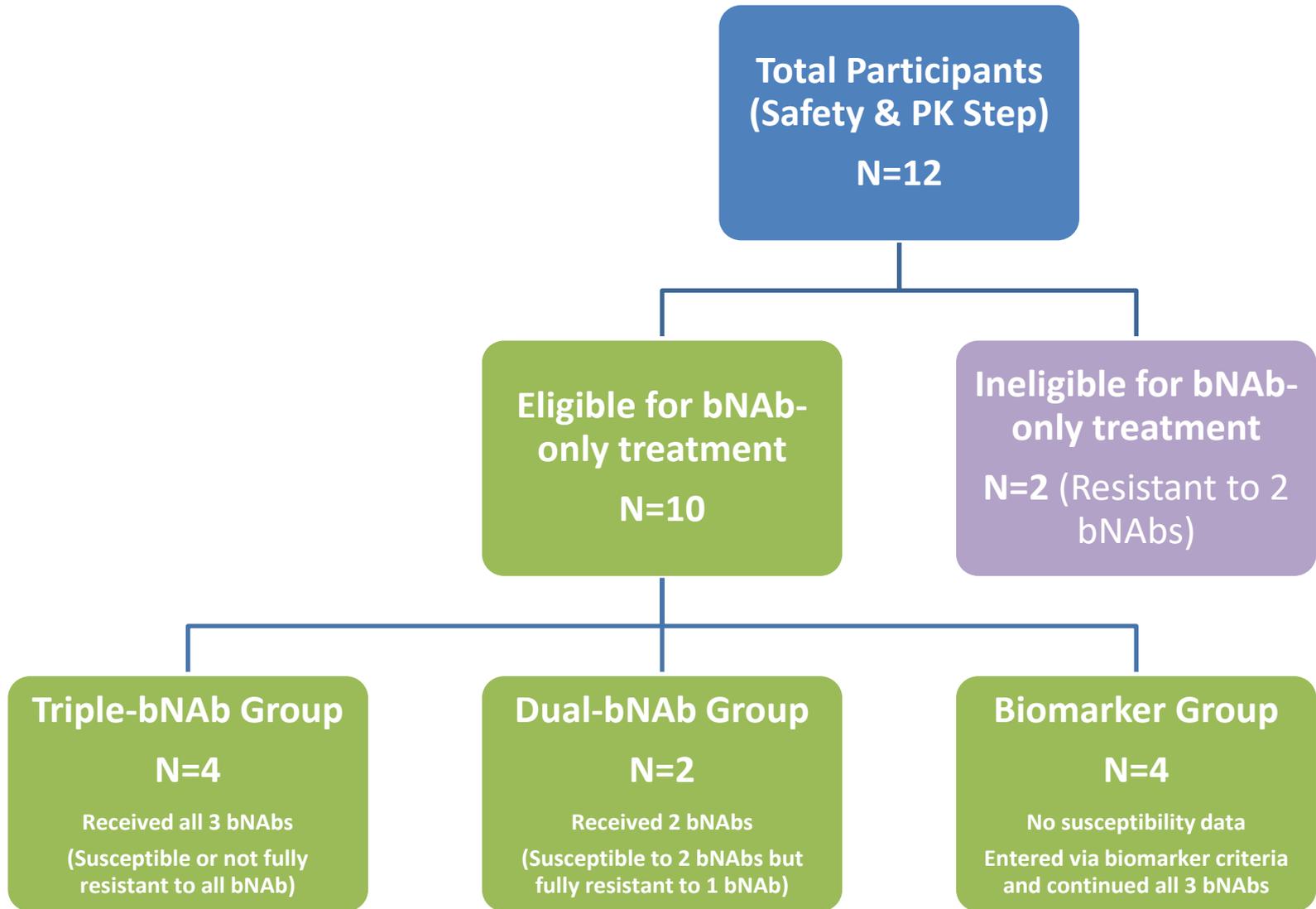
Ongoing

Step 4: ART restart and study exit

- Long-term safety assessment, including development of bNAb resistance and anti-drug antibodies to bNAbs

Ongoing

Eligibility for bNAb-only Treatment



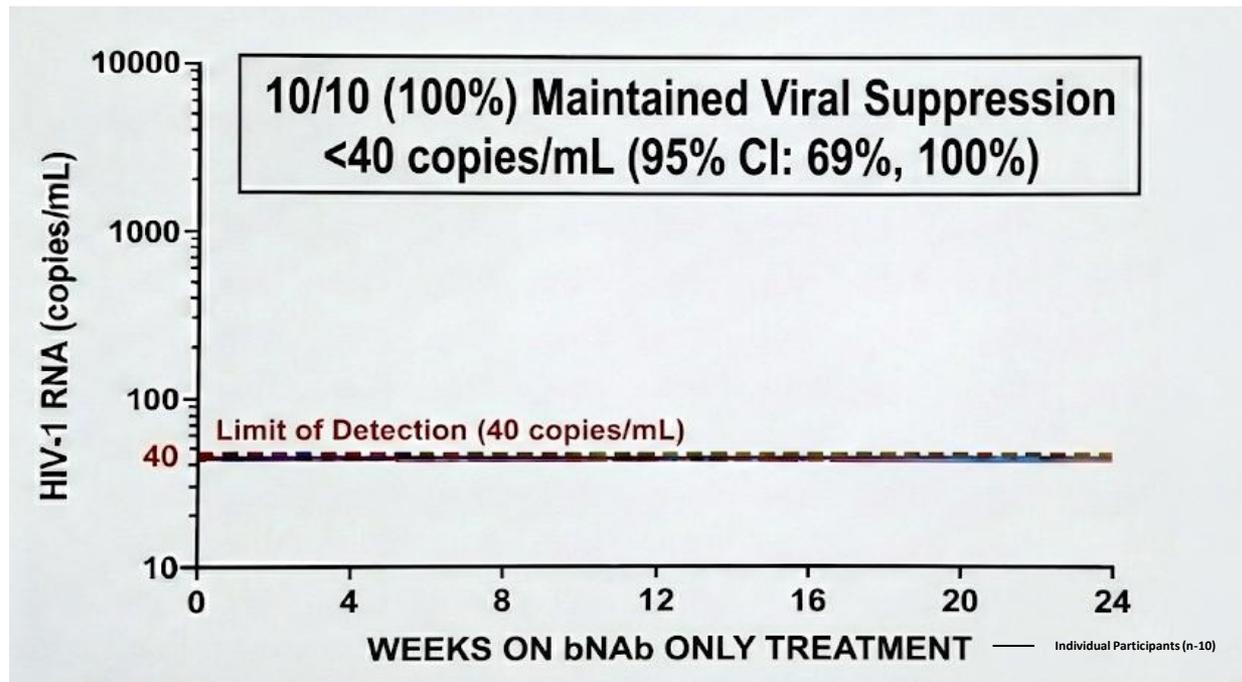
See poster #844 by Moraka-Mankge et al. for complete bNAb susceptibility data

Baseline Characteristics of Participants on bNAb-Only Treatment

Baseline Characteristics at Step 2 Entry	Step 2 Participants (N=10) <i>bNAb-only treatment</i>
Female sex	8 (80%)
Median age in days at ART initiation (range)	3 days (2 – 5)
Median age in months at last detectable virus >40 copies/mL (range)	1 month (0 – 90)
Median age in years at Step 2 entry (range)	9 years (2 – 10)
ART regimen prior to Step 2	
ABC/3TC/DTG	7 (70%)
TAF/FTC/DTG	2 (20%)
TDF/3TC/DTG	1 (10%)
Negative HIV DNA PCR	10 (100%)
Negative HIV EIA	9 (90%)
Prior receipt of bNAbs in Tatelo Study	9 (90%)

Main Results for bNAb-only Treatment

- All 10 participants completed 24 weeks of bNAb-only treatment following scheduled ART interruption (no missed doses)
- No Grade 3 or 4 adverse events during bNAb-only treatment
- Virologic findings:
 - **HIV-1 RNA remained < 40 copies/mL in all 10 participants throughout the 24 weeks of bNAb-only treatment**



Study Limitations

- Only 8 of 12 children had successful phenotyping
 - Early-treated children may have limited intact virus
- Participants were selected based on receipt of early ART and other favorable characteristics
 - May not be generalizable to other children with HIV
- bNAb-only step used a non-randomized design
 - Some children may control virus without need for bNAbs

Conclusion

- All of the first 10 Tatelo Plus participants maintained complete viral suppression for 24 weeks during treatment with triple- or dual-bNAbs following scheduled ART interruption
- The triple-bNAb regimen was well tolerated with no Grade 3 or 4 adverse events
- A combined approach using phenotypic screening and biomarker criteria offers a practical first step for trials of bNAbs to promote drug-free remission in children

Acknowledgments

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