Susceptibility Patterns for VRC07-523LS, PGDM1400LS, and PGT121.414.LS Among Children in Botswana

Natasha O. Moraka-Mankge,[1] Gbolahan Ajibola,[1] Melanie Lancien,[2] Jacqueline D. Reeves,[3] Timothy Persyn,[3] Molly Pretorius Holme,[4] Bryan S. Nelson,[5] Michael D. Hughes,[5] Dwight E. Yin,[6] Patrick Jean-Philippe,[6] Kathleen M. Powis,[1,4,7] Sikhulile Moyo,[1,4,8] Sharon Nachman,[10] Daniel R. Kuritzkes,[10] Mathias Lichterfeld,[2] Roger L. Shapiro[1,4]

1. Botswana Harvard Health Partnership, Gaborone, Botswana, 2. Ragon Institute of MGH, MIT and Harvard, Cambridge, MA, USA , 3. Labcorp-Monogram Biosciences, Inc., South San Francisco, CA, USA, 4. Department of Immunology and Infectious Diseases, Harvard T.H. Chan School of Public Health, Boston, Massachusetts, USA, 5. Department of Biostatistics, Harvard T.H. Chan School of Public Health, Boston, Massachusetts, USA , 6. Division of AIDS, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, Maryland, USA, 7. Department of Internal Medicine and Pediatrics, Massachusetts General Hospital, Boston, MA, USA, 8. Division of Medical Virology, Faculty of Medicine and Health Sciences, Stellenbosch, South Africa , 9. Department of Pediatrics, Stony Brook Medical Center, Stony Brook, NY, 10. Division of Infectious Diseases, Brigham and Women's Hospital, Harvard Medical School, Boston, Massachusetts, USA

844

- Broadly neutralizing antibodies (bNAbs) are being investigated as part of HIV remission strategies in children
- We examined baseline bNAb neutralization profiles in participants from the Tatelo Plus (IMPAACT 2042) study, which is evaluating combined infusions of VRC07-523LS, PGDM1400LS, and PGT121.414.LS among early-treated children living with HIV in Botswana

METHODS

- Twelve children who initiated ART within 7 days of life participated in the safety and pharmacokinetic study phase (age at study entry: 1.5-9.5 years)
- Envelopes from intact virus obtained from stored plasma near birth (N=11) or at viral rebound in the prior Tatelo Study (N=1) were tested for susceptibility to VRC07-523LS, PGDM1400LS, and PGT121.414.LS using the PhenoSense Monoclonal Antibody Assay (Labcorp-Monogram Biosciences)
- Nine children enrolled in the prior Tatelo study previously received 10-1074 and VRC01LS (all but one sample was prior to this exposure)
- Each bNAb was classified as: full susceptibility (inhibitory concentration [IC] 90 ≤1.0 µg/mL and maximum percent inhibition [MPI] ≥98%), partial susceptibility (IC90 >1.0 µg/mL but ≤10 µg/mL and MPI ≥98%), partial resistance (either IC90 >1.0 µg/mL but ≤10 µg/mL with MPI <98%, or IC90 >10 µg/mL but ≤20 µg/mL with MPI ≥98%), and full resistance IC90 >20 µg/mL regardless of MPI) (Fig 1)

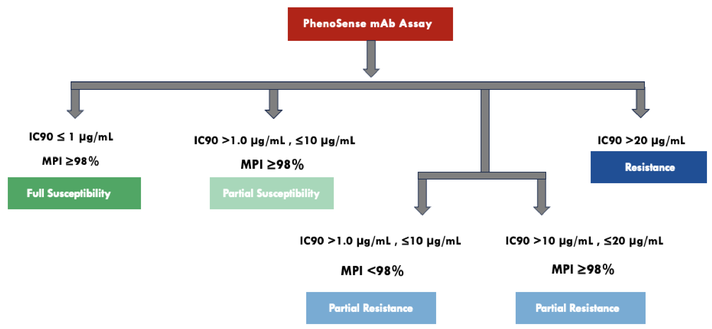


Fig 1: Classification of HIV-1 susceptibility to bNAbs

RESULTS

Children with early antiretroviral treatment who were sampled near birth had variable susceptibility patterns to VRC07-523LS, PGDM1400LS and PGT121.414.LS. Pediatric bNAb susceptibility testing remains important even with combination therapy and broadly acting agents.

- Stored samples were available from all 12 participants (3 male, 9 female), median sampling time was at 3 days of life (range 2 days, 212 weeks)
- Eight (66.7%) participants had successful bNAb phenotypes (Figure 2)

VRC07-523LS: 4 (50%) fully susceptible, 4 (50%) partially susceptible
PGDM1400LS: 2 (25%) fully susceptible, 1 (12.5%) partially resistant, 5 (62.5%) fully resistant
PGT121.414.LS: 4 (50%) fully susceptible, 1 (12.5%) partially susceptible, 3 (37.5%) fully resistant

- One participant fully susceptible to all three bNAbs
- Two participants resistant to both PGDM1400LS and PGT121.414.LS
  -- both children in youngest age group
- Virus from one child sampled at Tatelo virologic failure (rather than birth) was partially susceptible to VRC07-523LS and PGDM1400LS
- **In total, 6 (75%) of 8 participants with results were fully or partially susceptible to ≥2 bNAbs, allowing entry into the bNAb-only phase of the Tatelo Plus study by bNAb susceptibility criteria**

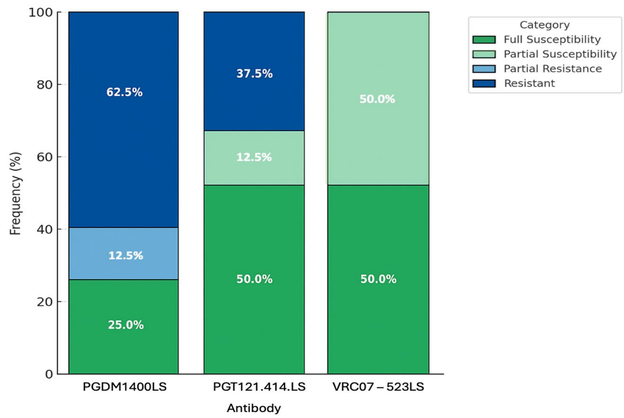


Fig 2: Susceptibility Patterns for VRC07-523LS, PGDM1400LS, and PGT121.414.LS

LIMITATIONS

- Only 8 of 12 children had successful phenotyping (early treated children may have limited intact virus)
- The first 12 participants were chosen for favorable characteristics (most without viral rebound in early life, had succeeded in prior Tatelo study, had loss of HIV DNA PCR positivity, and negative HIV serostatus) which may correlate with baseline bNAb susceptibility
  -- Susceptibility patterns may not reflect those of other children with HIV

CONCLUSIONS

- In early-treated children sampled primarily near birth in Botswana, participants had variable susceptibility patterns to VRC07-523LS, PGDM1400LS and PGT121.414.LS
- Phenotypic susceptibility testing remains an important component of current research trials using bNAbs in children, even with combination therapy and broadly acting agents

ACKNOWLEDGEMENTS

We would like to thank the Tatelo Plus Study participants and their families. We thank the Tatelo Plus study teams and collaborators, including D. Babuile, O. Batlang, J. Beck, F. Bone, C. Brackett, L. Bunhu, E. Capparelli, N. Cleland, A. Coletti, K. Colsh, L. Colson, J. Dziedzic, O. Elias, T. Frank, C. Gaetsaloe, B. Heckman, L. Hovind, M. Kasongo, G. Kenyaditse, S. Kgosiemang, C. Koofhethile, S. Lee, L. Lotsweletse, L. Mabe, J. Makhema, C. Maphorisa, K. Powis, G. Masheto, O. Masuku, K. Matsagopane, L. Melton, T. Mohammed, T. Mokane, W. Mokganedi, O. Mokgatle, O. Moloi, O. Pule, W. Motlhagodi, A. Motlhanka, T. Moyo, J. Mpolokang, M. Oabona, G. Pelontle, O. Pule, M. Sakoi-Mosetlhi, K. Seaton, T. Sekoto, N. Seonyatseng, K. Stephenson, C. Stotz, M. Tabona, D. Thebe, G. Tlhabano, G. Tomaras, X. Yu. We also thank collaborators at Labcorp-Monogram Biosciences, including C. Petropoulos, K. Strommen, Y. Lie and the Clinical Reference Lab. We also thank the Botswana Ministry of Health and Wellness and the IMPAACT 2042 Safety Monitoring Committee. The Tatelo Plus Study is funded by NIH/NIAID (U01 AI17956). 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. We would like to also thank the Sub-Saharan Network for TB & HIV research excellence (SANTHE) which is funded by the Science for Africa Foundation to the Developing Excellence in Leadership, Training and Science in Africa (DELTAS Africa) programme [Del-22-007] with support from Wellcome Trust and the UK Foreign, Commonwealth & Development Office and is part of the EDCPT2 programme supported by the European Union; the Bill & Melinda Gates Foundation [INV-033558]; and Gilead Sciences Inc., [19275] for postdoctoral support of the presenting author. The content is solely the responsibility of the authors and does not necessarily represent the official views of the NIH. Study products were provided by the Dale and Betty Bumpers Vaccine Research Center and by NIH Division of AIDS.

Presented at the 2026 Conference on Retroviruses and Opportunistic Infections (CROI 2026) February 22 to February 25, Colorado Convention Center in Denver, Colorado, USA.

Email: natasha.o.moraka@gmail.com