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

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BACKGROUND

- 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)

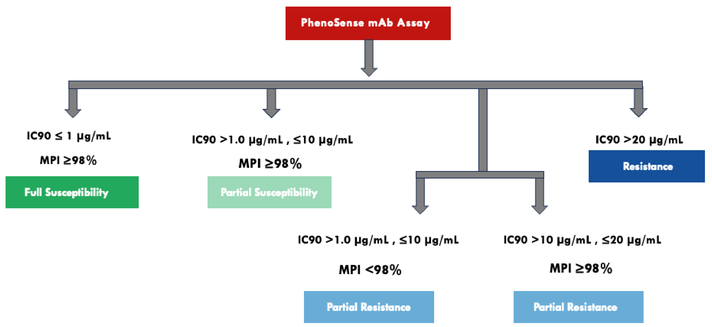

Fig 1: Classification of HIV-1 susceptibility to bNAbs

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**

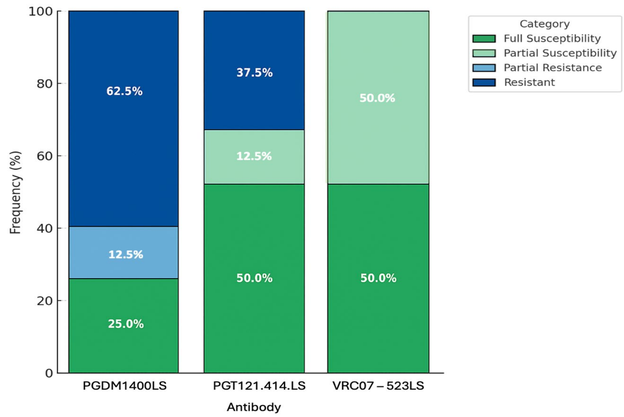

Fig 2: Susceptibility Patterns for VRC07-523LS, PGDM1400LS, and PGT121.414.LS

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

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