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SAFETY & PHARMACOKINETICS OF MONOCLONAL ANTIBODY, VRC01LS, IN HIV-EXPOSED NEWBORNS

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Background:

Vertical HIV transmission occurs despite use of antiretroviral therapy (ART). A broadly neutralizing monoclonal antibody, administered to HIV-exposed infants might further prevent transmission. VRC01LS, modified from VRC01, has an extended half-life and may be a feasible adjunct to ART prophylaxis.

Methods:

This is an open label safety and pharmacokinetic study of VRC01LS administered to HIV-exposed infants. Cohort 1 infants (non-breastfeeding) receive subcutaneous (SC) Dose 1 (80mg for birth weights 2.0 to <4.5kg) within 72 hours of birth. Cohort 2 (breastfeeding) receive Dose 1 within 5 days of birth and Dose 2 (100mg SC) at Week 12, if still breastfeeding. All infants and their mothers receive ART to prevent HIV transmission. Safety is assessed post vaccination at 4 hours, Day 1, 14, 28, 56, Week 12, and then every 12 weeks through Week 96. Cohort 2 also has safety assessments at Week 14 and 16. Preliminary VRC01 pharmacokinetic parameters are determined through Week 12.

Results:

Cohort 1 (n=10) and 2 (n=11) fully accrued from 8 sites (6 in the US, 1 site each in Zimbabwe and South Africa) with no HIV transmissions. All infants received Dose 1. Ten in Cohort 2 received Dose 2, as of the April 2018 safety analysis. Birth weight ranged from 2.5-4.1kg. VRC01LS was well tolerated with no treatment related toxicities >grade 2. Local reactions (all grade 1 or 2; 95% resolved by 24 hr) were common after Dose 1, occurring in 5/10 (50%) and 9/11 (82%) infants in Cohort 1 and 2, respectively, but less frequent after Dose 2, occurring in 2/10 (20%) infants. Plasma VRC01LS levels for Dose 1 (Cohorts combined) are available at Days 1 (n=14), 7 (n=5), 14 (n=20), 28 (n=20), 56 (n=17), and Week 12 (n=12) and compared to previously reported levels at Day 28 (n=13) and Day 56 (n=12) for 20mg/kg and 40mg/kg VRC01 given SC at birth (Figure). VRC01LS was rapidly absorbed following SC administration, with all Day 1 levels >100mcg/mL. VRC01LS levels were significantly greater than VRC01 levels at Day 28 (p=0.0018) and Day 56 (p=0.0019) despite the lower weight-band dosing (VRC01LS 20-32mg/kg vs. VRC01 40mg/kg). At Week 12, the median VRC01LS level was 39.1mcg/mL and all infants' levels were >20mcg/mL.

Conclusion:

Preliminary results indicate that VRC01LS administered to neonates via the SC route at birth and age 12 weeks is well tolerated with mild-moderate transient local reactions. VRC01LS with its extended half-life could achieve target levels for the duration of breastfeeding with infrequent dosing.