VERY EARLY ART WITH OR WITHOUT VRC01 FOR *IN UTERO* HIV: VIROLOGIC OUTCOMES AT 2 YEARS OF AGE IN IMPAACT P1115

#839

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BACKGROUND

- Neonatal ART has enabled virologic control and remission in children with *in utero* HIV.
- We report viral suppression outcomes through 2 years of age in neonates treated with very early ART with or without VRC01 and the prospect for analytic treatment interruption to assess remission.

METHODS

Study Design: Phase I/II non-randomized, open-label study

Study Population: Infants with *in utero* HIV acquisition≥36 weeks (wks) gestation and ≥2 kg who initiated treatment within 48 hours (hrs) of life

Very Early Treatment Regimens:

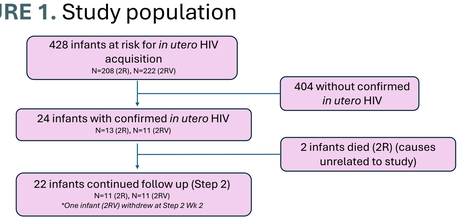
- *Regimen 2R:* 2 NRTIs + nevirapine (NVP) + raltegravir (RAL)
  Regimen 2RV: 2 NRTIs + NVP + RAL +VRC01 (40 mg/kg) initiated within 72 hrs of birth and at 2, 6, and 10 wks of age
- NVP was stopped 12 wks after 2 consecutive HIV-1 RNA levels <lower limit of quantification (<20 or <40 copies/mL).
- Sites were selected to provide either Regimen 2R or 2RV; all 2RV infants were enrolled at a single site in Zimbabwe.

Outcomes:

- Plasma HIV-1 RNA at 24 and 96 wks.
- Virologic failure was defined as RNA≥200 copies/mL at wk 24 or confirmed (two consecutive measurements) detected thereafter.
- Initial (strict) virologic criteria for consideration of possible treatment interruption at ≥wk 96:
  - No confirmed RNA ≥200 c/mL from wk 24 up to wk 48
  - No RNA detected at wk 48 and thereafter.

Statistical Analysis: Probabilities at each timepoint were described with 2-sided exact 95% binomial confidence intervals (CI) by regimen. Cumulative incidence of time until first instance of confirmed no RNA detected through week 96 was estimated with 95% CIs. Kaplan-Meier survival curves with 95% CIs were used to describe time until virologic failure.

FIGURE 1. Study population



The probability of achieving initial virologic control in infants with *in utero* HIV infection receiving very early RAL-based ART with or without VRC01 was 81%. Approximately 25% of infants had sustained virologic control to meet strict virologic criteria for consideration of possible analytic treatment interruption to assess remission.

FIGURE 2. HIV-1 RNA over 96 weeks in each participant

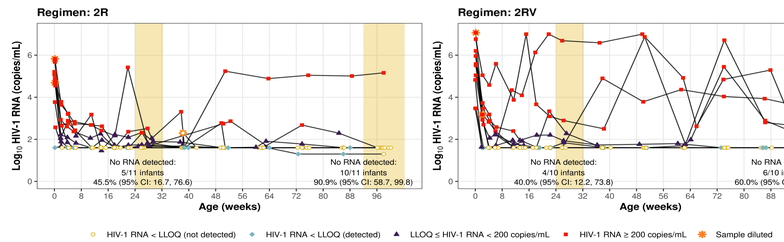
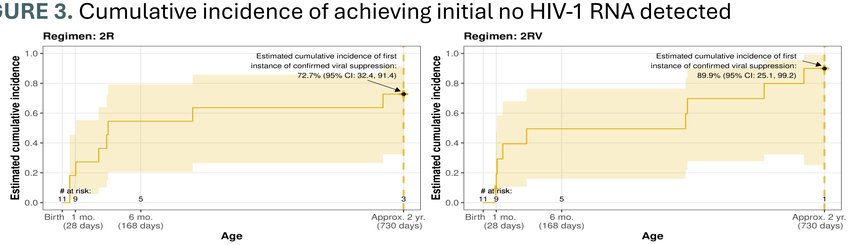


FIGURE 3. Cumulative incidence of achieving initial no HIV-1 RNA detected



Event is defined as the time of the first of two consecutive measurements where HIV-1 RNA is less than the assay lower limit of quantification and not detected. Plus signs indicate censoring times.

RESULTS

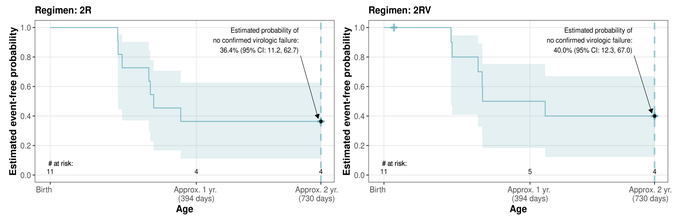
- The proportion [95% (CI)] of infants with no RNA detected were:
  - At wk 24, 5/11 on 2R [45.5% (16.7, 76.6%)] and 4/10 on 2RV [40.0% (12.2, 73.8%)]
  - At wk 96, 10/11 on 2R [90.9% (58.7, 99.8%)] and 6/10 on 2RV [60.0% (26.2%, 87.8%)]
- Among 11/11 infants on 2R and 8/10 infants on 2RV with RNA <200 copies/mL at wk 24 up to wk 48, 4/11 (2R) and 2/8 (2RV) infants had no RNA detected thereafter through wk 96.
- Overall, cumulative incidence (95% CI) of first instance of confirmed viral suppression was: 52.0% (28.5, 71.1%) at wk 24 and 81% (54.3, 92.8%) at wk 96
- Overall, 5 infants (23%) had a ≥ Grade 3 adverse event deemed possibly, probably, or definitely related to study product (rash, hematologic and hepatic abnormalities, and drug-induced liver injury).

TABLE. Characteristics of mother/infant pairs at enrollment

	Total (n=22)	Child Regimen 2R (n=11)	Child Regimen 2RV (n=11)
Maternal			
Age, years	28 (25, 33)	29 (26, 34)	26 (24, 31)
Singleton gestation	21 (95.5%)	10 (90.9%)	11 (100%)
No ART during pregnancy and delivery	15 (68.2%)	8 (72.7%)	7 (63.6%)
HIV RNA at enrollment, copies/mL			
<LLOQ detected	1 (4.5%)	1 (9.1%)	0 (0%)
>LLOQ - <1000	0 (0%)	0 (0%)	0 (0%)
1000 - <2000	1 (4.5%)	0 (0%)	1 (9.1%)
2000 - <10,000	1 (4.5%)	1 (9.1%)	0 (0%)
10,000 - <100,000	10 (45.5%)	3 (27.3%)	7 (63.6%)
Child			
Age at enrollment, hours	21.2 (14.3, 26.3)	23.4 (13.73, 7.4)	20.9 (14.3, 26.0)
Female sex	15 (68.2%)	7 (63.6%)	8 (72.7%)
Gestational age, weeks	38 (38, 40)	38.5 (37.3, 40.0)	38 (38, 40)
Age at first ARV, hours	16.2 (2.2, 23.9)	9.5 (0.9, 16.9)	20.3 (11.7, 27.8)
Age at first NAT, hours	21.9 (14.9, 27.1)	24.1 (14.3, 38.3)	21.8 (14.9, 27.1)
HIV-1 RNA at enrollment, copies/mL			
<LLOQ, detected	1 (4.5%)	1 (9.1%)	0 (0%)
200 - <1000	1 (4.5%)	1 (9.1%)	0 (0%)
1000 - <10,000	3 (13.6%)	1 (9.1%)	2 (18.2%)
10,000 - <100,000	5 (22.7%)	4 (36.4%)	1 (9.1%)
≥100,000	12 (54.5%)	4 (36.4%)	8 (72.7%)
Median CD4, cells/mm^3 (CD4 %)	1937 (51.1%)	1961 (48%)	1824 (54.3%)
Birth WAZ	-0.7 (-1.3, -0.5)	-0.7 (-1.4, -0.2)	-0.7 (-1.3, -0.5)
Birth LAZ	0.0 (-0.9, 0.4)	-0.8 (-1.4, -0.0)	0.3 (-0.1, 0.7)

ART=antiretroviral therapy, ARV=antiretroviral, LAZ=length for age INTERGROWTH Z score, LLOQ=lower limit of quantification, NAT=nucleic acid test, WAZ=weight for age INTERGROWTH Z score. All continuous variables expressed as median (interquartile range) and categorical variables as n (%)

FIGURE 4. Probability of remaining free from virologic failure



Event is defined as either plasma HIV-1 RNA level ≥ 200 cp/mL at 24 weeks or confirmed detected thereafter based on two consecutive measurements with HIV-1 RNA quantified or below the assay quantification limit with target detected. The event is a composite outcome of time until virologic failure or death; however, no deaths were observed. Plus signs indicate censoring times.

CONCLUSIONS

- The probability of achieving initial virologic control in infants with *in utero* HIV infection receiving very early RAL-based ART with or without VRC01 was 81%.
- 6/22 had sustained virologic control through wk 96 that met strict virologic criteria for consideration of possible treatment interruption to assess remission.

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Plain Language Summary
A large majority of infants with HIV at birth who got HIV treatment in the first 2 days of life had an undetectable viral load by about 2 years old. About one quarter of these infants were able to keep their viral load undetectable for a long period of time, making them potentially eligible to stop treatment to see if their HIV is in remission.

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