# Is Routine PCP Prophylaxis Needed in Very Early-Treated Infants with HIV?

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Bryan S. Nelson[1], Camlin Tierney[1], Deborah Persaud[2], Jennifer Jao[3,4], Mark F. Cotton[5], Yvonne Bryson[6], Kira Bacon[7], Diane Costello[8], Charlotte Perlowski[9], Maria Leticia Santos Cruz[10], Josphat Kosgei[11], Sai Majji[12], Dwight Yin[13], Ellen G. Chadwick[3,4], for the IMPAACT P1115 Team

[1]Harvard T.H. Chan School of Public Health, Boston, MA, USA, [2]Johns Hopkins University School of Medicine, Baltimore, MD, USA, [3]Northwestern University Feinberg School of Medicine, Chicago, IL, USA, [4]Ann & Robert H. Lurie Children's Hospital of Chicago, Chicago, IL, USA, [5]Stellenbosch University, Tygerberg, South Africa, [6]University of California Los Angeles David Geffen School of Medicine, Los Angeles, CA, USA, [7]Frontier Science and Technology Research Foundation, Amherst, NY, USA, [8]IMPAACT Laboratory Center, University of California Los Angeles, Los Angeles, California, USA, [9]FHI 360, Durham, NC, USA, [10]Hospital Federal dos Servidores do Estado, Rio de Janeiro, Brazil, [11]Kenya Medical Research Institute/Walter Reed Project, Kericho, Kenya, [12]Eunice Kennedy Shriver National Institute of Child Health and Human Development, National Institutes of Health, Bethesda, MD, USA, [13]National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, MD, USA

## BACKGROUND

- Global guidelines recommend routine cotrimoxazole (CTX) prophylaxis for the first year of life to prevent *Pneumocystis jirovecii* pneumonia (PCP) in infants with HIV.
- Infants with HIV are increasingly diagnosed and given antiretroviral therapy (ART) shortly after birth, preserving CD4 cell counts and likely reducing risk of PCP.

## METHODS

- 54 infants with *in utero* HIV infection followed in the IMPAACT P1115 study of very early ART:
  - **Cohort 1 (N=34)** born to high-risk (no ART) mothers enrolled and started nevirapine (NVP)-based ART within 48 hours of birth.
  - **Cohort 2 (N=20)** enrolled within 10 days of birth, having been diagnosed with HIV and started an NVP-based regimen outside the study within 48 hours of birth.
- **Study ART:** Lopinavir (LPV/r) added when age-appropriate. NVP discontinued 12 weeks after confirmed viral load (VL) below the limit of detection (<LOD).
- CTX given per local guidelines.
- Infants not achieving VL <200 c/mL at 24 weeks or with VL ≥200 c/mL after 24 weeks discontinued from follow-up.
- **Virologic Suppression**: VL <200 c/mL at 24 weeks and no confirmed detectable VL thereafter.

**TABLE 1.** Participant Characteristics

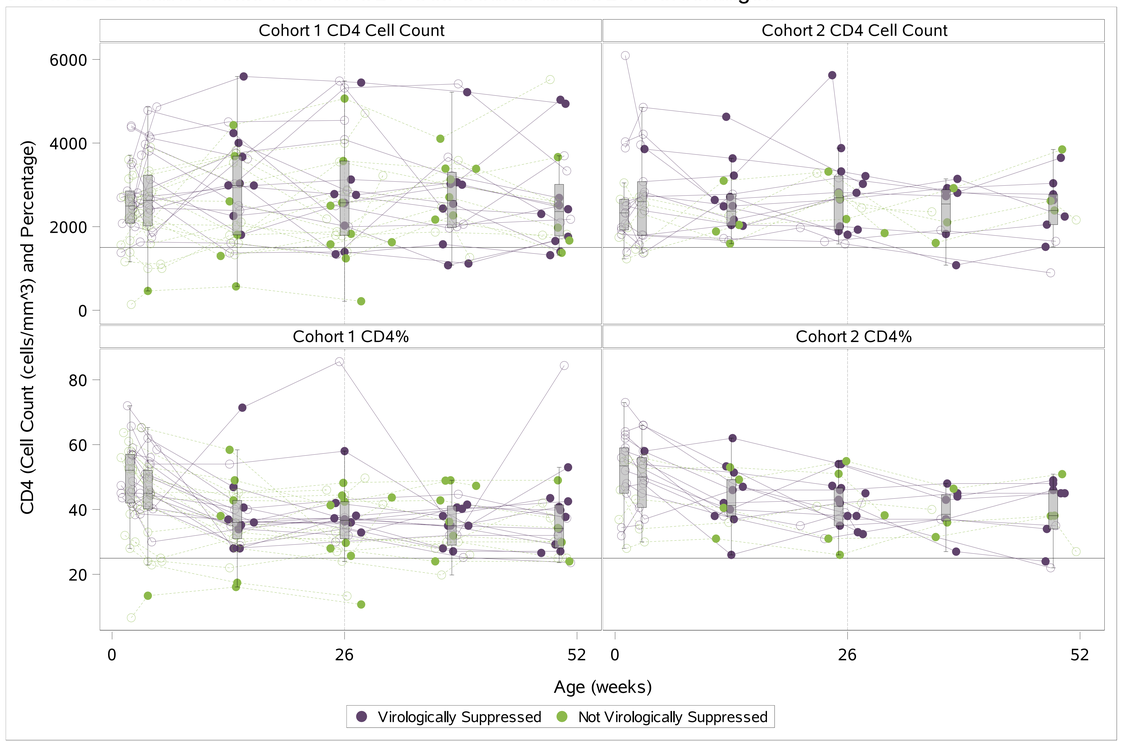
| | Cohort 1 (N=34) | Cohort 2 (N=20) |
|---|---|---|
| | Median (Q1-Q3) or n (%) | |
| Female Sex | 23 (68%) | 10 (50%) |
| Region | | |
| Africa | 33 (97%) | 14 (70%) |
| Asia | 1 (3%) | – |
| North America | – | 2 (10%) |
| South America | – | 4 (20%) |
| Age at Study Entry | 22.2 (12.6-32.6) hours | 8 (5.5-8) days |
| Premature (34-<37 weeks Gestational Age) | 4 (12%) | 2 (11%) |
| Earliest Weight (kg) (1) | 2.7 (2.5-3) | 2.7 (2.3-3.3) |
| Small for Gestational Age (2) | 9 (27%) | N/A |
| Earliest VL ($log_{10}$ c/mL) (3) | 4.9 (4-5.3) | 4.1 (3.2-5.2) |
| Earliest CD4 Cell Count (cells/mm$^3$) (4) | 2458.5 (2080-2789.5) | 2330 (1923-2654) |
| Earliest CD4% (4) | 50.4 (42-57.5) | 53.5 (45-59) |

*(1)1 (0-1) days in Cohort 1 and 8 (5.5-8) days in Cohort 2. (2)below INTERGROWTH 10th %ile for sex and gest age (N/A in Cohort 2 due to entry age). (3)1 (0-1) days in Cohort 1 and 6.5 (2-8) days in Cohort 2. (4)15 (13-16) days in Cohort 1 [N=32] and 8 (5-8) days in Cohort 2 [N=18].*

**Most infants with HIV receiving very early ART and achieving viral suppression maintained high CD4 cell count and CD4% through age 1 year.**

**Guidelines for routine PCP prophylaxis through 1 year of life where malaria or severe bacterial infections are not prevalent warrant re-evaluation.**

**FIGURE 1.** Infant Profile Plots of CD4 Cell Counts and CD4 Percentages




*The dashed vertical line corresponds to the week 24 visit, at which point only infants with HIV plasma viral load <200 c/mL continue to be followed. Horizontal lines at 1500 cells/mm$^3$ and 25%. Filled circles indicate participant was on CTX at the time of CD4 measurement. Virologically Suppressed = HIV plasma viral load <200 c/mL at 24 weeks and no confirmed detectable viral load thereafter.*

**TABLE 2.** Proportion of Infants at Each Study Visit with both CD4 Cell Count ≥1500 cells/mm$^3$ and CD4% ≥ 25%

| | Cohort 1 (N=34) | Cohort 2 (N=20) |
|---|---|---|
| **Entry** | 29 / 33 (88%) | 16 / 18 (89%) |
| **Week 2** | 26 / 29 (90%) | 16 / 19 (84%) |
| **Week 12** | 27 / 33 (82%) | 18 / 18 (100%) |
| **Week 24** | **24 / 32 (75%, 95%CI* 57%-89%)** | **18 / 18 (100%, 95%CI* 81%-100%)** |
| **Week 36**** | 22 / 26 (85%) | 11 / 12 (92%) |
| **Week 48**** | **18 / 23 (78%, 95%CI* 56%-93%)** | **10 / 12 (83%, 95%CI* 52%-98%)** |

**Clopper-Pearson Exact Confidence Interval (CI).*
***Only infants maintaining VL<200 c/mL remained on study after week 24.*

## RESULTS

- The 10th percentile for CD4 cell count (CD4%) ranged from 1340 to 1592 cells/mm$^3$ (24% to 32%) in Cohort 1 and 1390 to 1665 cells/mm$^3$ (24% to 34%) in Cohort 2 over the first year of life (**Figure 1**).
- At weeks 24 and 48, ≥75% in Cohort 1 and ≥83% in Cohort 2 had both CD4 cell count ≥1500 cells/mm$^3$ and CD4% ≥25% (**Table 2**).
- 71% in Cohort 1 and 80% in Cohort 2 initiated CTX and continued for a median of 29.1 and 40.7 weeks.
- There were no cases of PCP.
- 91% in Cohort 1 and 80% in Cohort 2 had ≥1 adverse event on study: primarily infections, anemia or neutropenia; 15% in Cohort 1 and 55% in Cohort 2 had hospitalizations; and 1 death occurred in Cohort 1 due to probable bacterial pneumonia (last CD4 cell count (CD4%) was 3621 cells/mm$^3$ (40%) and last VL was undetectable).

## CONCLUSIONS

- Most infants with HIV receiving very early ART and achieving viral suppression maintained high CD4 cell count and CD4% through age 1 year.
- Guidelines for routine PCP prophylaxis through 1 year of life for infants with consistently high CD4 cell count and CD4% in settings where malaria or severe bacterial infections are not prevalent warrant re-evaluation.

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