HIV-1 VIRAL REBOUND AND SAFETY OUTCOMES OF POSTPARTUM TREATMENT INTERRUPTION IN WOMEN

Catherine N. Le1, Paula Britto2, Sean S. Brunmire1, Risa M. Hoffman1, Patricia M. Flynn1, Taha E. Taha3, Anne Coletti4, Mary Glenn Fowler5, Karin Klingman1, James A. McIntyre6,8, Jonathan Z. L10, Judith S. Currier1

1University of California Los Angeles, Los Angeles, CA, USA, 2Harvard T H Chan School of Public Health, Boston, USA, 3St. Jude Children’s Research Hospital, Memphis, TN, USA, 4Johns Hopkins Bloomberg School of Public Health, Boston, MA, USA, 5PHI, Durham, NC, USA, 6Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, USA, 7D4DIS, MAFD, Bethesda, MD, USA, 8Annie E. Casey Foundation, Baltimore, MD, USA, 9Johns Hopkins School of Medicine, Baltimore, MD, USA, 10Division of AIDS, National Institute of Allergy and Infectious Diseases (NIAID), National Institutes of Health (NIH), Bethesda, MD, USA

Department of Women’s Health, University of Cape Town, Cape Town, South Africa, Brigham and Women’s Hospital, Boston, MA, USA

Introduction

Structured, temporary treatment interruptions are a necessary aspect of cure studies and eventually, cure therapies. However, CD4-guided analytic treatment interruption (ARTIs) have been associated with poor outcomes and increased mortality.1

In contrast, short-term ART interruptions with intensive viral load monitoring are designed to minimize potential risks by using time to first detectable viremia as the primary outcome, but safety data are limited.1,2 Such data are very limited in women, who make up greater than 50% of the global HIV burden yet are included in only 18% of current cure studies.1,3

Here, we describe safety events and viral rebound kinetics data from asymptomatic, virologically suppressed, HIV-infected women with CD4 counts >350 cells/mm³ in the PROMISE trial who were randomized to discontinue ART postpartum.4

Methods

This study included 1,076 HIV-infected women who participated in the PROMISE Study (1077BF/1077FF/1077HS). Women were included in this analysis if they were randomized to discontinue ART at the end of risk for perinatal transmission, had an HIV-1 viral load below the limit of detection on the day of randomization, met the inclusion/exclusion criteria as described below, and had post-randomization viral load measurements. Follow-up time was censored at the time of ART re-initiation. Baseline was defined as the last measurement 30 days prior to or at the time of randomization.

Viral load and safety events through week 24 (measurement 30 days prior to or at the time of randomization) were censored at the time of ART re-interruption. Women who discontinued ART would remain virally suppressed through 24 weeks (Figure 1).

Results

Women were recruited from Argentina, Botswana, Brazil, China, Haiti, India, Malawi, Peru, South Africa, Tanzania, Thailand, USA, Uganda, Zambia and Zimbabwe. Median age was 28 years, CD4 count 766 cells/mm³ (IQR 418, 577). Median duration on ART before discontinuation was 17 weeks (IQR 11-12). At baseline, 97.6% of participants were classified as WHO Stage I (Table 1).

Overall, <1% of patients progressed from WHO Stage I to Stage 2 or higher after discontinuing ART. 3.6% of participants experienced a decline in CD4 count to levels meeting country-specific treatment criteria. While off ART, 1% of participants experienced any HIV/AIDS-related or WHO Stage II/III clinical event (Table 2). 10% experienced grade 2 or higher sign/symptom or laboratory event (Figure 2).

Conclusion

In this large, international cohort of young, postpartum women with high CD4 cell counts, we estimated that 6% of participants would remain virally suppressed through 24 weeks in the absence of ART re-initiation. Overall, less than 1% of participants progressed from WHO Clinical Stage 1 to Stage 2 or higher, and approximately 4% of patients experienced a decline in CD4 count to country-specific treatment criteria during this study. In women who experienced viral rebound, serious adverse events during the first 24 weeks off ART were rare.

These data suggest that short treatment interruptions in HIV-cure related studies can be done safely in young women with nadir CD4 cell counts above 350 cells/mm³. Such strategies need to be explored further in other populations but should be considered for use in cure-related study protocols.

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