AUTHOR CONTACT INFORMATION
Carlo Sacdalan MD-MBA, MSc
carlo.s@searchthailand..org

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RV550: Safety and virological outcomes in blood and lymph nodes of N-803 with ART in acute infection

Carlo Sacdalan[1,2], Eugene Kroon[1], Meera Bose[3,4], Shida Shangguan[3,4], Nicole Dear[3,4], Pathariya Promsena[1,2], Nicha Tulmethakaan[1], Anchalee Avihingsanon[5], Jeffrey Safrit[6], Somchai Sriplienchan[1], Morgane Rolland[3,4], Lydie Trautmann[3,4], Kiat Ruxrungtham[5,7], Sandhya Vasan[3,4], on behalf of the RV550 Study Group

BACKGROUND

- We conducted a Phase 2, open-label study to evaluate the safety of **N-803** with ART in **acute HIV infection (AHI)** and evaluated the **impact** on HIV viral load (VL), levels of vDNA and vRNA in CD4 T cells and lymph nodes (LN).

METHODS

- We randomized **12 participants** in AHI to receive **immediate ART** (n=4, Fiebig 1-2) or **ART + N-803** (n=8, Fiebig 1-4) at **6 mcg/kg** SC abdominally at weeks 0, 3, and 6 then followed to week 12. **HIV VL** was measured at weeks 2, 3, 6, 8 and 12 and 4 days after each N-803 dose.

- All participants had inguinal LN biopsy at **week 0** and **week 6.5.** Blood was drawn for VL, CD4 and CD8 count. **Adverse events (AEs)** were solicited every N-803 injection.

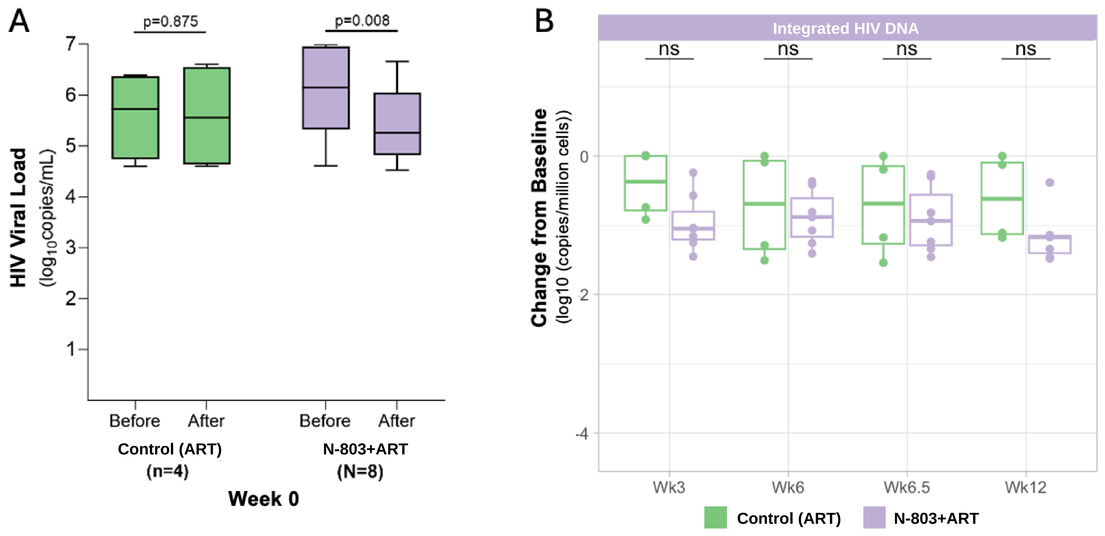
- **CD4** T cells and **LN vRNA and vDNA** were compared using nonparametric Wilcoxon signed rank, Mann-Whitney U and Kruskal-Wallis tests and Spearman correlations.

RESULTS

- Median (IQR) age **was 32 (26-35)** years in the N-803 arm, 24 (21-28) years in the controls. All N-803 recipients reported **injection site redness** at all time-points (n=24) with 4 mild, 3 moderate and 17 severe. For **injection site swelling** (n=23), 6 were mild, 9 moderate and 8 severe. Despite this, **injection site AEs resolved in 7 days** and all participants consented to continued N-803 administration.

N-803 with ART during acute HIV infection was safe and resulted in a more rapid plasma HIV VL decline from the time of infection compared to ART alone.

Figure Effect of N-803 on plasma VL (**A**) and on vDNA in CD4+ T cells (**B**)



RESULTS continued

- There was **no significant difference** at baseline for CD4 (300 vs 548 cells/mm^3), HIV VL (6.15 vs 5.73 $\log_{10}$) and CD4 count increase over time between groups. While VL was overall comparable across groups, **VL significantly declined (p=0.008)** after the first dose of N-803 compared to ART-only (**Figure A**).

- vRNA and vDNA were obtained from CD4 T cells and LN from 7 ART + N-803 participants and 4 ART participants. vRNA (LTR-Gag, Tat-Rev) and vDNA (total, integrated, 2-LTR circles) levels **declined** for all participants in CD4 T cells in 12 weeks and LN in 6.5 weeks. There was **no significant difference** in the decline of vRNA and vDNA between groups for LN (adjusted p≥0.545) and CD4 T cells (adjusted p≥0.218) from baseline (**Figure B**).

CONCLUSIONS

- N-803 with ART was **safe and resulted in a rapid plasma HIV VL decline** from study baseline compared to ART alone.

- While there was **some evidence of a faster decline** in viremia immediately post N-803 injection, differences in reservoir measurements were overwhelmed by the large fluctuations that occur over the first weeks of ART in acute infection, inter-host variability, and the small number of participants.

- To further explore the impact of N-803 on viral reservoirs, **all eligible and consenting study participants will receive an additional single dose of N-803 followed by ATI** until HIV viral load >1,000 copies/ml for a maximum of 4 weeks.

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DISCLAIMER
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AUTHOR AFFILIATIONS

[1] SEARCH Research Foundation, Bangkok, Thailand
[2] Research Affairs, Faculty of Medicine, Chulalongkorn University
[3] U.S. Military HIV Research Program, Center for Infectious Diseases Research, Walter Reed Army Institute of Research, Silver Spring, MD, USA
[4] Henry M. Jackson Foundation for the Advancement of Military Medicine, Inc., Bethesda, MD, USA
[5] HIV-NAT, Thai Red Cross AIDS Research Centre, Bangkok, Thailand
[6] ImmunityBio Inc., Los Angeles, California, USA
[7] School of Global Health, Chulalongkorn University, Bangkok, Thailand