RV550: Analytic Treatment Interruption After N-803 in Participants on ART Since Acute HIV

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BACKGROUND

N-803, a clinically licensed **IL-15 receptor superagonist**, is safe in humans and showed potential for HIV remission in non-human primates.

We evaluated the **safety** and **impact** on HIV reservoir of N-803 administered during acute HIV infection (AHI) in combination with ART in a Phase 2, open-label study, followed by evaluating the impact of N-803 on HIV remission through an **analytic treatment interruption (ATI)**.

METHODS

RV550 is a 3-step clinical trial that enrolled participants in AHI. In Step 1, participants received ART alone or ART + N-803 (**6 mcg/kg every 3 weeks for 3 doses**). Whole lymph node biopsies were obtained at baseline and two weeks post final N-803 administration during Step 1.

Step 2 added one dose of N-803 regardless of randomization, followed by ATI with weekly HIV viral load (VL) rebound monitoring up to 12 weeks. VL restart criteria were **≥1,000 copies/ml for 4 weeks** or **confirmed ≥100,000 copies/ml**. Step 3 monitored viral re-suppression on ART.

Endpoints:

- Step 1: Safety, vDNA/vRNA in blood and lymph node (LN) tissue, reservoir analyses, and quantification of vRNA in LN.
- Step 2: ATI time to VL > 1,000 copies/ml plus VL AUC for 4 weeks thereafter.
- Step 3: HIV re-suppression

N-803 was safe but did not significantly alter viral rebound kinetics during ATI. However, N-803 decreased viral RNA in lymph nodes by 50-fold and may be effective in future combinatorial strategies.

RESULTS

Twelve participants completed Step 1 of whom 7 consented to continue to Step 2 ATI. **No difference** in age, sex, Fiebig stage, CD4 or CD8 between groups at either entry into Step 1 or Step 2.

As previously reported, N-803 injection site reactions resolved within 7 days. No ATI-related adverse events or discontinuations were observed. N-803 + ART resulted in a **faster VL decline** compared to ART alone, but **no difference in vDNA** in blood.

Fig. 1A:
Lymph Node HIV RNA Cells pre-ATI

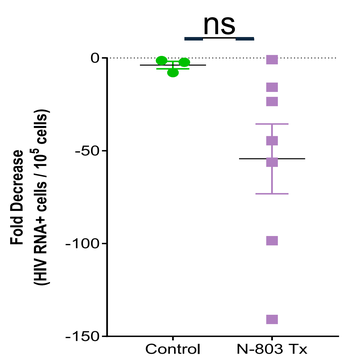
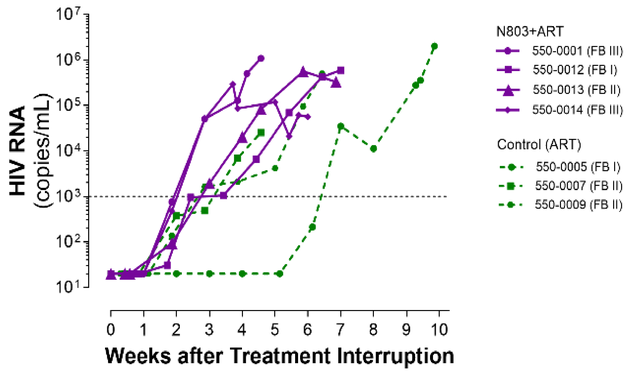


Fig. 1B:
HIV VL Rebound post ATI



RESULTS continued..

Additional LN tissue analysis now demonstrates a non-significant **50-fold decrease in vRNA** in the N-803 group (**Fig.1A**).

In Step 2, median ATI duration was **45 (32-69) days**. There were no significant differences between groups in time to viral rebound, peak viral load, or time to ART re-initiation (**Fig.1B**) nor in time to viral re-suppression in Step 3. Median time to viral re-suppression was 45 (26-82) days.

CONCLUSIONS

N-803 was **safe** but did not significantly alter viral rebound kinetics during ATI. Although a trend toward reduced HIV reservoir size in LN was observed, **N-803 alone was insufficient to achieve sustained HIV remission**. These findings support further investigation of N-803 in combination strategies.

ADDITIONAL KEY INFORMATION

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DISCLAIMER
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