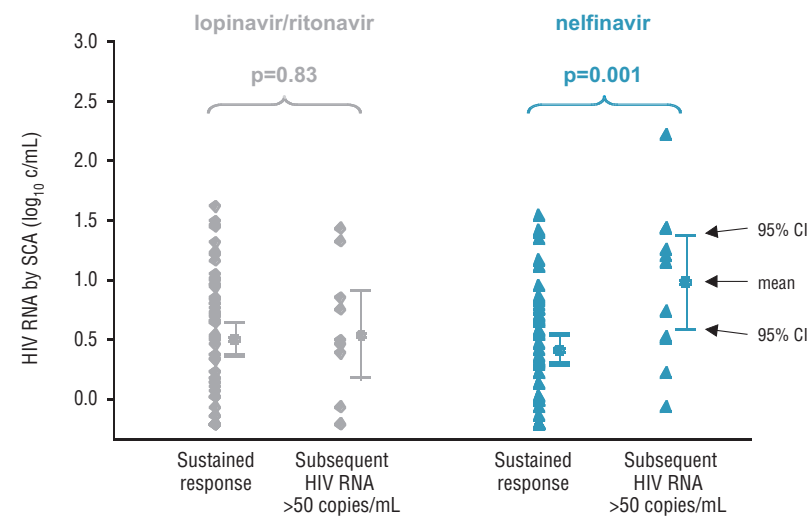


Association Between Week 60 HIV RNA Level and Virologic Outcomes

- For NFV-treated subjects, those with subsequent detectable HIV RNA >50 copies/mL (n=11) had significantly higher week 60 HIV RNA values compared to those (n=60) with sustained response (0.98 vs. 0.41 log₁₀ copies/mL, p=0.001, Figure 5). The effect remained statistically significant (p=0.01) if a lone outlying value in the detectable HIV RNA group was excluded.
- In contrast, LPV/r-treated subjects with subsequent detectable HIV RNA >50 copies/mL (n=10) had similar mean week 60 HIV RNA values compared to those (n=58) with sustained response (0.53 vs. 0.50 log₁₀ copies/mL, p=0.83).

Figure 5. Association Between Week 60 HIV RNA and Subsequent Virologic Outcome



CONCLUSIONS

- Among subjects with HIV RNA <50 copies/mL consistently for at least 36 weeks who had samples tested by SCA at week 60, a trend toward higher risk of subsequent virologic failure (confirmed rebound >400 copies/mL) was observed among NFV-treated subjects compared to LPV/r-treated subjects. This suggests that a LPV/r-based regimen continues to show superior long-term virologic efficacy compared to a NFV-based regimen even among patients achieving undetectable viral load (<50 copies/mL) for an extended duration of time.
- Week 60 SCA values were significantly associated with subsequent HIV RNA rebound >50 copies/mL for NFV-treated subjects, but not for LPV/r-treated subjects, suggesting that the clinical significance of very low level viremia may be different for regimens containing different protease inhibitors.

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Abstract 34

XIV International HIV Drug Resistance Workshop
June 7-10, 2005, Quebec City, Quebec, Canada

The Level of Persistent Viremia Below 50 copies/mL Is Associated with Subsequent Rebound to Above 50 HIV RNA copies/mL for Nelfinavir-Treated Subjects, But Not Lopinavir/Ritonavir-Treated Subjects

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BACKGROUND

The clinical significance of persistent viremia below 50 copies/mL in subjects on suppressive antiretroviral therapy is not known.

In Study 863, antiretroviral-naïve subjects were treated with stavudine, lamivudine, and lopinavir/ritonavir (LPV/r, n=326) or nelfinavir (NFV, n=327). At week 60, HIV RNA was <50 copies/mL in 64% of subjects receiving LPV/r and 52% of subjects receiving NFV, by intent-to-treat, noncompleter=failure analysis (p<0.01, Figure 1).¹

In a subset of the subjects with sustained HIV RNA <50 copies/mL, we examined the relationship between the level of plasma HIV RNA, measured using a real-time RT-PCR assay with single-copy sensitivity, and subsequent virologic outcomes beyond the week 60 evaluation.

METHODS

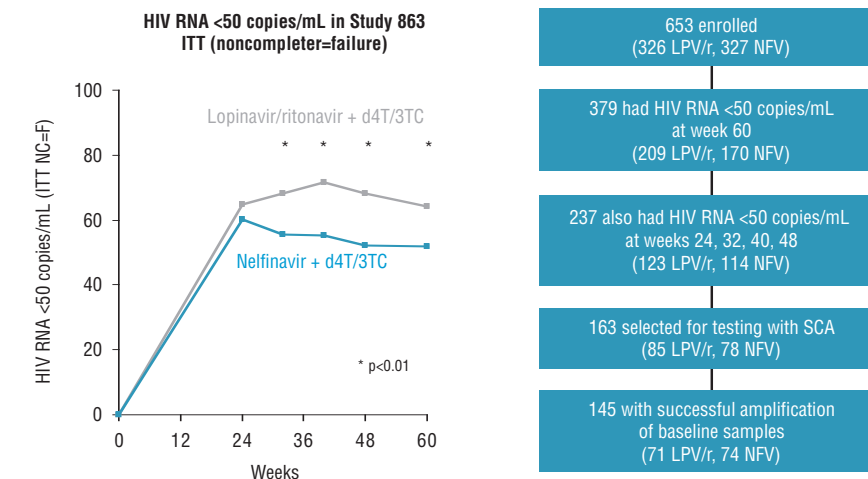
Assay

- An internally controlled real-time RT-PCR assay with single-copy sensitivity (single-copy assay, SCA)² was used to test all samples.
- Based on sample volumes available in this study, the lower limit of assay sensitivity was 0.63 copies/mL.

Subjects

- Samples were selected from among subjects with HIV RNA <50 copies/mL at all visits from week 24 to week 60 (Figure 1). Among 237 such subjects, we selected a convenience sample of 163 subjects (85 LPV/r, 78 NFV), representing those with archive samples in storage in North America.
- Baseline samples were tested with the single-copy assay to ensure suitability of primers and probes. 145 of 163 subjects (71 LPV/r, 74 NFV) with successful amplification of baseline samples had week 60 samples tested by SCA.

Figure 1. Sample Selection for Single-Copy Assay Testing in Study 863



Outcomes After Week 60

- Sustained response: HIV RNA <50 copies/mL at all subsequent visits beyond week 60.
- Subsequent HIV RNA >50 copies/mL.
 - Virologic failure: confirmed HIV RNA rebound >400 copies/mL or a single HIV RNA rebound >400 copies/mL followed by discontinuation.
 - “Blips”: subsequent HIV RNA >50 copies/mL without meeting virologic failure criteria.

Analysis

- Among subjects with HIV RNA <50 copies/mL for weeks 24–60, the association between week 60 HIV RNA value by SCA and subsequent virologic outcomes was assessed by one-way analysis of variance.

RESULTS

Week 60 Results

- As shown previously,³ no difference between treatment groups in week 60 HIV RNA level by SCA was observed, with a mean value of 0.51 log₁₀ copies/mL (p>0.9) in each treatment group.
- However, week 60 HIV RNA value was significantly associated with baseline HIV RNA level (p<0.001 for each group, Figure 2a).
- In an analysis based on combined treatment groups, a slow (slope of decline: –0.004 log₁₀ copies/mL/week), but statistically significant (p=0.04) decline in persistent viremia was observed over the period from weeks 60–110 (Figure 2b).

Figure 2a. Baseline vs. Persistent Viremia at Week 60

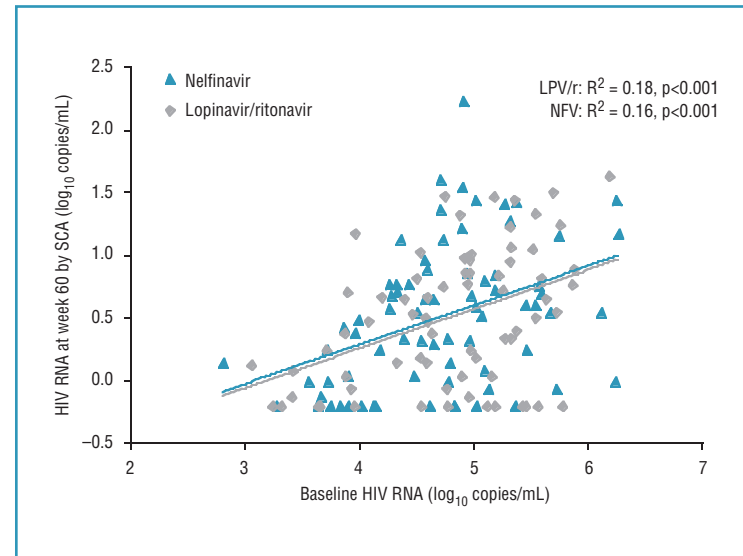
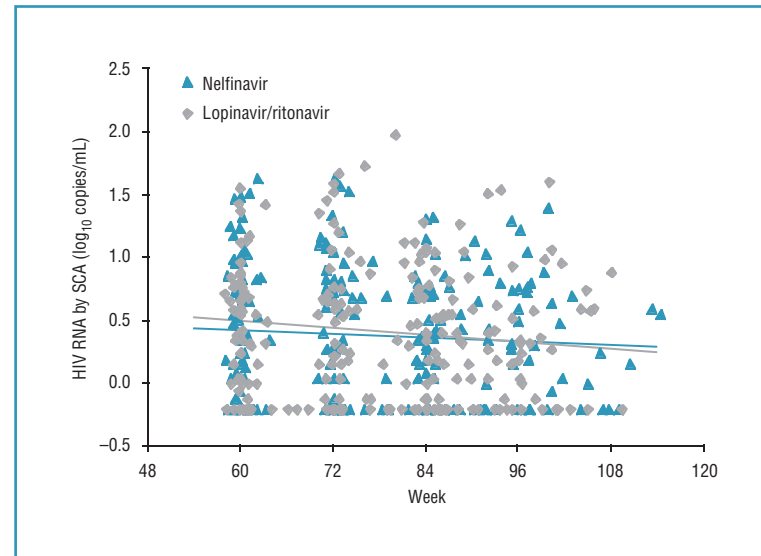


Figure 2b. Slow Decline of Persistent Viremia Over Weeks 60–110



Virologic Outcomes Beyond Week 60

- Median (range) total follow-up was 95 (60–114) weeks for the LPV/r group (n=71) and 95 (60–109) weeks for the NFV group (n=74).

- Virologic outcomes beyond week 60 are summarized in Figure 3.

- 3 subjects in each group had no data available after week 60 and were excluded.
- 118 subjects (58 LPV/r, 60 NFV) maintained HIV RNA <50 copies/mL at all subsequent visits (median 32 additional weeks, range 9–54).
- 6 subjects (1 LPV/r, 5 NFV) met criteria for virologic failure (p=0.076 for the difference between groups). In 4/5 NFV-treated subjects, lamivudine and/or PI resistance was observed (Figure 4).
- 15 subjects (9 LPV/r, 6 NFV) had “blips” >50 copies/mL. Subjects with blips had isolated values between 50–400 copies/mL (7 LPV/r, 3 NFV), multiple values between 50–400 copies/mL (1 NFV), or single values >400 copies/mL followed by resuppression (2 LPV/r, 2 NFV).

Figure 3. Virologic Outcomes Beyond Week 60

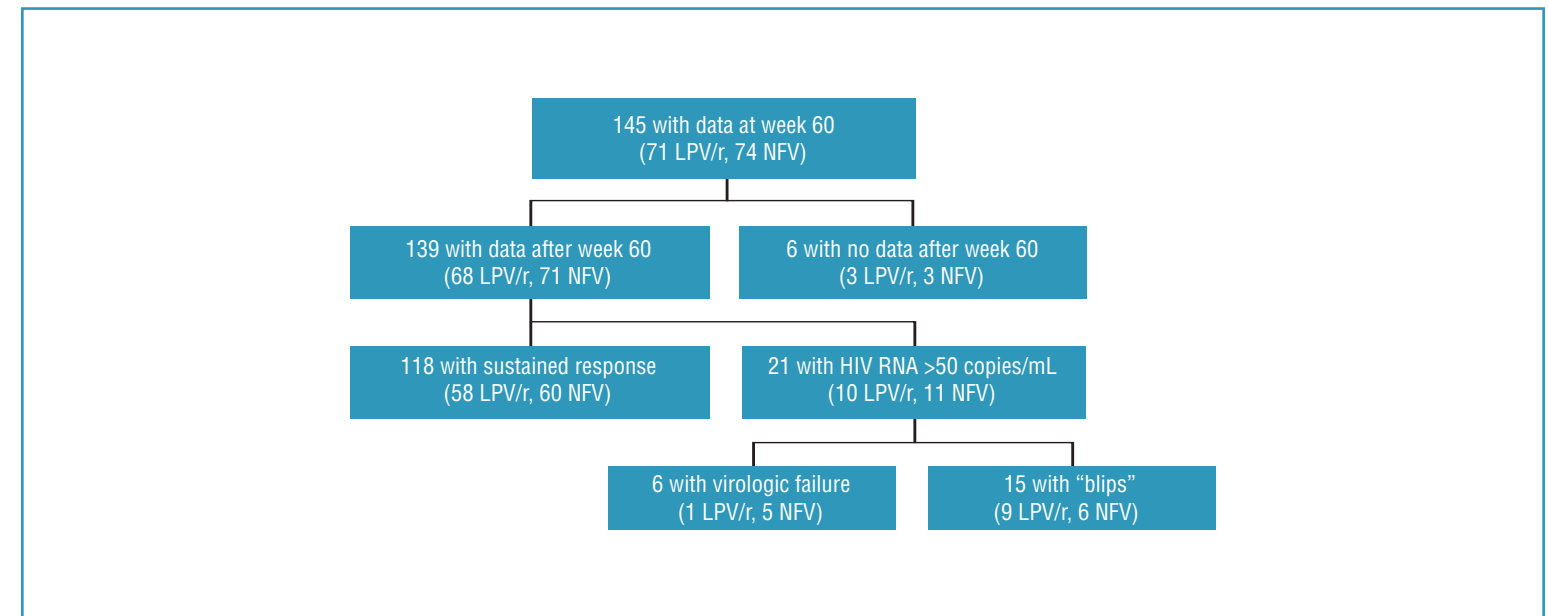


Figure 4. Kaplan-Meier Estimates of Time to Virologic Failure After Week 60

