Antiretroviral Therapy (ART) in Clinical Practice: Effectiveness and Tolerability of Necvirapine (NVP), Stavudine (d4T) and Lamivudine (3TC)

Joseph L. Yozviak DO, FACP
Lehigh Valley Health Network, joseph.yozviak@lvhn.org

R Eric Doerfler NP, CCH
Bornemann Internal Medicine

William C. Woodward DO
Bornemann Internal Medicine

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Jody L. Yozviak
Philadelphia College of Osteopathic Medicine
Philadelphia, PA
E-mail: **joyoz@erols.com**

ANTIRETROVIRAL THERAPY (ART) IN CLINICAL PRACTICE: EFFECTIVENESS AND TOLERABILITY OF NEVIRAPINE (NVP), STAVUDINE (d4T), AND LAMIVUDINE (3TC)

J. L. Yozviak,[1] R. E. Doerfler,[2] and W. C. Woodward[2]*
[1]Philadelphia College of Osteopathic Medicine, Philadelphia, PA, USA, [2]Bornemann Internal Medicine, Reading, PA, USA

ABSTRACT

Background: Recent studies reveal that viral suppression in clinical practice is achieved less frequently than in clinical trials. This study examines the effectiveness and tolerability of an NVP/d4T/3TC ART regimen in an urban HIV clinical practice. **Methods:** A retrospective review of patients (N = 536) from 9/96 to 4/00 yielded 73 patients on NVP/d4T/3TC. Abstracted data: demographics, viral load (VL), CD4+, previous regimen, and adverse events (AE). VL was evaluated by percentage of patients <400 copies/mL by week 16 and <50 copies/mL by week 24. Other studies have suggested that this predicts long-term durability. Analyses performed: intent-to-treat (ITT) (prescription written), and as-treated (AT). **Results:** Study patients were similar to practice demographics; 12/73 (16.4%) were ART-naive. Common reasons for choosing NVP/d4T/3TC: low baseline VL (BLVL), avoidance of PI-associated AEs, and fewer pills/doses. ITT: Week 16: 57/73 (78.1%) had VL <400. Week 24: 33/73 (45.2%) had VL <50. AT: Week 16: 66 patients had follow-up data; 57/66 (86.4%) had VL <400. Week 24: 39 patients had ultrasensitive results; 33/39 (84.6%) had VL <50. Beyond 48 weeks: 13/14 (92.9%) were <50. Mean CD4+ increase was 170 (95% CI: 122, 218). Discontinuations (d/c): 4/73 (5.5%) due to rash, 10/73 (13.7%) due to other AEs, 19/73 (26.0%) for other reasons (nonadherence, illicit drug use, STI), and 8/73 (11.0%) due to virologic failure; 4/8 reported nonadherence. **Conclusions:** Despite a low genetic barrier, NVP/d4T/3TC is effective and tolerable. Virologic success was higher than expected in an urban clinic. There was a low incidence of d/c due to rash or virologic failure. Most d/c were not ART-related. The low pill burden, ease of administration, and lack of AEs make this regimen suitable and effective in clinical practice.

BACKGROUND

In clinical practice, patients on protease inhibitor (PI)-based regimens achieve viral suppression less frequently than in randomized, double-blinded, placebo-controlled, clinical trials.[1,2,3] Many factors influence this discrepancy, including adherence and the use of HAART in heavily treatment-experienced patients. To avoid the complex dosing schedules and side effects of PI therapy, the non-nucleoside reverse transcriptase inhibitors (NNRTIs) have been utilized as an alternative in patients with lower baseline viral loads (BLVL). Recent data suggest that the potency of NNRTI-based regimens in patients with a BLVL greater than 100,000 copies per mL plasma is sufficient to result in long-term viral suppression.[4] When this feature is combined with simple dosing schedules and fewer side effects, the use of NNRTIs can result in the design of highly efficacious, tolerable, and convenient (ETC) regimens. This study examines the ETC of nevirapine (NVP), stavudine (d4T), and lamivudine (3TC) in patients in an urban HIV practice.

METHODS

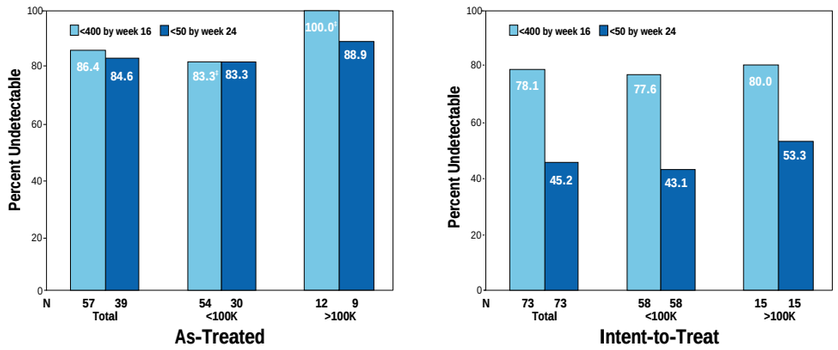
- A retrospective chart review of all patients (N = 536) seen from 9/96 to 4/00 was conducted at Bornemann Internal Medicine (BIM), an urban HIV clinic
- Charts were abstracted for the following: demographics, viral load (VL), CD4+ cell count, previous regimen, adverse events (AEs), and reasons for discontinuation
- Viral load response was evaluated by the percentage of patients <400 copies/mL by 16 weeks and <50 copies/mL by 24 weeks, for those with ultrasensitive (UQ) data. Other studies have suggested that this is predictive of long-term success.[5,6] Patients who discontinued the regimen due to AEs before the week of analysis were considered failures for that time period
- Intent-to-Treat (ITT) (prescription written, no data = failure) and As-Treated (AT) analyses were performed. Patient questioning and self-report determined noncompliance

Table 1. Study patient demographics

Number of patients		73
Mean age		35.2 years
Sex:	Male	63.0% (46)
	Female	37.0% (27)
Race:	White	26.0% (19)
	Black	24.7% (18)
	Hispanic	47.9% (35)
	Asian	1.4% (1)
Previous regimen:	Naive	16.4% (12)
	NsRTI	27.4% (20)
	PI	54.8% (40)
	NNRTI	1.4% (1)
BLVL:	Mean	140,956 copies/mL
	Median	26,871 copies/mL
Mean CD4+ nadir:	All patients	285 cells/mm^3
	BLVL <100,000*	320 cells/mm^3
	BLVL >100,000*	154 cells/mm^3

*P = 0.003

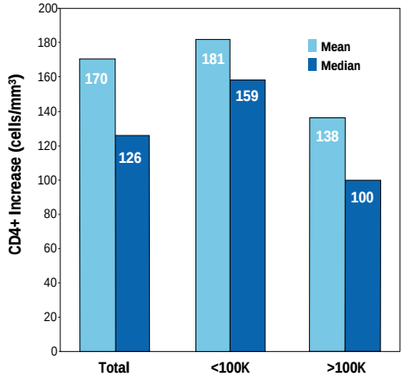
Figure 1. Plasma HIV-1 RNA <400 by week 16 and <50 by week 24†



†Week 24 results are based only on patients with ultrasensitive results.
‡P = 0.001. All other differences between the high and low BLVL subsets were not significant (P >0.05).

• Patients with HIV-1 RNA <50 at >48 weeks = 92.9% (13/14)

Figure 2. CD4+ response§



§Difference between VL subsets was not statistically significant (P = 0.22).

Table 2. Reason for choice of regimen

Low BLVL	53.4% (39)
Fewer pills	16.4% (12)
Avoid PI-related AEs	15.1% (11)
Fewer doses	12.3% (9)
Maintenance ART	8.2% (6)

Table 3. Adverse events

Rash	13.7% (10)
HA	12.3% (9)
N/V	11.0% (8)
Neuropathy	9.6% (7)
Fatigue	6.8% (5)
Methadone withdrawal	5.5% (4)
Other‖ (N = 1)	6.8% (5)

‖Other: itching, diarrhea, constipation, vertigo, decreased appetite

Table 4. Reasons for discontinuation

Failure	11.0% (8)	Illicit drug use	4.1% (3)
N/V	6.8% (5)	Neuropathy	2.7% (2)
Rash	5.5% (4)	Methadone interaction	2.7% (2)
Noncompliance	5.5% (4)	STI	2.7% (2)
Change NsRTI	4.1% (3)	Other¶ (N = 1)	11.0% (8)

¶Other: headache, vertigo, fatigue, embarrassment, stress, depression, lost insurance, prison.
34 patients discontinued; 7 patients discontinued for more than one reason.

CONCLUSIONS

- The use of the NNRTI-based regimen of nevirapine, stavudine, and lamivudine resulted in virologic success rates similar to or better than what would be expected based on previous studies of other NVP-containing regimens [4,7]
- Although the high BLVL group had a lower baseline CD4+ count (P = 0.003), virologic success rates were similar to the low BLVL group. In fact, the only significant difference was a higher percentage of patients in the *high BLVL group* who were <400 copies/mL at 16 weeks in the AT analysis (P = 0.001). The week 24 ITT results are deceptively low in each group due to a large number of patients (34) who did not have ultrasensitive results available for analysis. Although only 14 patients had been taking the regimen for >48 weeks (mean = 98.0 weeks) at the time of submission, the results suggest the potential for long-term durability. No statistically significant differences in immunologic response were noted
- In our practice, patients choose the regimen that is most appropriate for their lifestyle after discussion of all efficacious HAART options and the consequences of each. Most patients (53.4%) chose NVP/d4T/3TC due to a low BLVL. However, the underlying logic was still the avoidance of PI-related AEs and complex dosing since the "extra" potency of PIs was not indicated. The remaining patients chose the regimen directly to avoid PI-based HAART. This suggests a patient preference for NVP-based HAART due to its potential increased tolerability and convenience of dosing
- Although rash was the most common AE reported, the incidence was low (13.7%). Only 4 patients (5.5%) discontinued the regimen due to severe NVP-related rash
- Most discontinuations were not due to AEs, but to external factors. Of those patients with virologic failure (11.0%), 50% reported poor medication adherence. This reminds providers of the importance of adherence in the execution of the treatment plan
- **This result is in agreement with Raffi et al,[4] suggesting that NVP/d4T/3TC has high potency regardless of BLVL**
- **In summary, NVP/d4T/3TC appears to be an effective, tolerable, and convenient regimen for both treatment-naive and treatment-experienced patients regardless of BLVL. Additional prospective examination of the use of NVP-based regimens in such patient groups is warranted**

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