# Antiretroviral Therapy (ART) in Clinical Practice: Ethnic Variability in Effectiveness and Tolerability of Nelfinavir and Two Nucleoside Reverse Transcriptase Inhibitors

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# Antiretroviral Therapy in Clinical Practice: Ethnic Variability in Effectiveness and Tolerability of Nelfinavir and Two Nucleoside Reverse Transcriptase Inhibitors

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## ABSTRACT

*Background*: Recent studies reveal patients in clinical practice achieve viral suppression less frequently than those in clinical trials[1,2,3]. Many variables influence the discrepancy, including patient ethnicity. This study examines ethnic variability in the effectiveness and tolerability of nelfinavir (NFV) and two nucleoside reverse transcriptase inhibitors (NsRTI) in an urban HIV practice.

*Methods*: Retrospective chart review of all patients (N=504) seen at Bornemann Internal Medicine (BIM) after April 1997 yielded 57 patients on NFV and two NsRTIs. Viral load response was evaluated by percentage of patients <400 (copies/mL) by week 16 and <50 (copies/mL) by week 24, of those with ultrasensitive (UQ) data. Other studies have shown this to be predictive of long term durability [4,5].

*Results*: Patients analyzed (n=57) were: White = 18 (31.6%); Black = 22 (38.6%); Hispanic = 17 (29.8%). Most patients were on BID NFV and: d4T/3TC (59.6%), AZT/3TC (26.3%) and d4T/ddI (14.0%).

*Table 1: Summary of Results*

| Ethnicity | Evaluable data | <400 by week 16 | Pts. with UQ data | <50 by week 24* | Mean CD4 | Failure d/t non-compliance |
|---|---|---|---|---|---|---|
| White | 13 (72.7%) | 10 (76.9%) | 6 | 5 (83.3%) | +151 | 0 |
| Black | 17 (77.3%) | 14(82.4%) | 8 | 7 (87.5%) | +206 | 1 |
| Hispanic | 11 (64.7%) | 5(45.5%) | 2 | 2 (100%) | +119 | 3 |

*% of patients <50 by week 24 is based only on patients with UQ results.

Most discontinuations were not due to AEs. Only 5 of 37 discontinued because of intolerable diarrhea.

*Conclusions*: NFV and dual NsRTIs appears to be an effective and tolerable combination regardless of ethnicity examined in this typical treatment setting. The higher prevalence of noncompliance in Hispanic patients suggests the need for adherence interventions. The low incidence of disabling diarrhea was encouraging; most patients were able to control diarrhea with simple measures. Reasons for lower success rates in clinical practice vs. clinical trials should be further examined.

## BACKGROUND

The frequency with which patients achieve viral suppression in clinical practice is often overestimated by the randomized, double blinded, placebo-controlled, clinical trial[1,2,3]. Many variables influence decision making for provider and patient in the selection of a proper regimen that is compatible with a patient's lifestyle. The fear of possible adverse events as well as cultural and ethnic considerations also play a role. A recent study has shown that patients of different ethnicity within the same clinical practice differ in their response to HAART[2]. This study examines variability based on ethnicity in the effectiveness and tolerability of Nelfinavir (NFV) and two nucleoside reverse transcriptase inhibitors (NsRTIs) in an urban HIV practice.

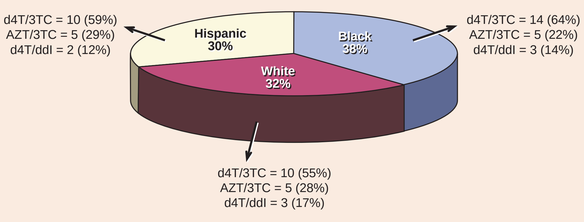
## METHODS

- A retrospective chart review of all patients (N = 504) seen after April 1997 was conducted at Bornemann Internal Medicine (BIM), an urban HIV clinic.
- Charts were abstracted for the following: viral load (VL), CD4, NFV regimen, demographics, adverse events (AEs), and reasons for discontinuation.
- Viral load response was evaluated by the percentage of patients <400 by 16 weeks and <50 by 24 weeks, of those with ultrasensitive (UQ) data. Other studies have shown this to be predictive of long-term success [4,5].
- Intent to Treat (ITT) (prescription written, no data = failure) and As Treated (AT) analyses were performed.

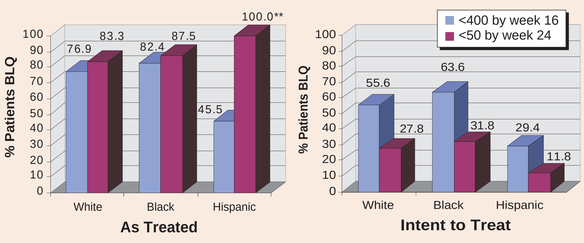
## RESULTS

- Chart Review yielded 57/504 patients on NFV (most BID) and two NsRTIs. Most patients were HAART experienced: 14/57 were treatment naïve; 25/57 were PI-experienced; 11/57 were NVP experienced; 7 patients had dual/mono NsRTI experience.
- The demographics of BIM are as follows: 40% women, 14% gay men, and an equal distribution among White, Black and Hispanic patients.

### Figure 1: Study Patient Demographics and NFV Regimens (n=57)

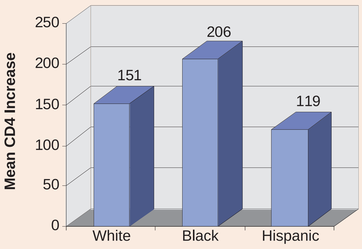



### Figure 2: Plasma HIV-1 RNA <400 (copies/mL) by week 16 and <50 (copies/mL) by week 24*




*Week 24 Results are based only on patients with ultrasensitive results.
** Only two Hispanic patients had UQ results. Both were BLQ.

### Figure 3: Mean CD4 Response




## RESULTS (cont.)

### Table 2: Patient Compliance With Treatment Plan

| | White | Black | Hispanic |
|---|---|---|---|
| Poor Medication Adherence | 0 | 4 | 7 |
| Subsequent Failure | 0 | 1 | 3 |
| Lost to Follow Up | 2 | 4 | 3 |
| No labs | 2 | 2 | 2 |
| No Return Visits | 0 | 2 | 1 |

### Table 3: Adverse Events

| | White | Black | Hispanic | Total |
|---|---|---|---|---|
| Diarrhea* | 55.6% | 36.4% | 29.4% | 40.4% |
| Nausea/Vomiting | 27.8% | 13.6% | 11.8% | 17.5% |
| Abdominal Pain | 16.7% | 0.0% | 11.8% | 8.8% |
| Other GI | 0.0% | 27.3% | 11.8% | 8.8% |
| Headache | 11.1% | 18.2% | 29.4% | 19.3% |
| Fatigue | 11.1% | 18.2% | 17.6% | 15.8% |
| Neuropathy** | 11.1% | 22.7% | 11.8% | 15.8% |
| Lipodystrophy | 11.1% | 13.6% | 0.0% | 8.8% |
| Other Non-GI | 11.1% | 18.2% | 5.9% | 17.5% |
| No AEs | 16.7% | 18.2% | 17.6% | 17.5% |

** Four of seven patients in d4T/ddI subgroup reported diarrhea.*
*** All patients reporting neuropathy were in the d4T/3TC subgroup.*

### Table 4: Reasons for Discontinuation†

| | White | Black | Hispanic | Total |
|---|---|---|---|---|
| Diarrhea | 16.7% | 4.5% | 5.9% | 8.8% |
| Jaundice | 5.6% | 9.1% | 0.0% | 5.3% |
| Other AE | 5.6% | 4.5% | 11.8% | 7.0% |
| Non-compliance | 0.0% | 9.1% | 17.6% | 8.8% |
| Illicit Drug Use | 5.6% | 9.1% | 5.9% | 7.0% |
| Change in ART | 11.1% | 9.1% | 0.0% | 7.0% |
| Virologic Failure | 5.6% | 0.0% | 5.9% | 3.5% |
| Other Non-AE | 5.6% | 18.2% | 29.4% | 19.3% |

† *37 out of 57 (64.9%) patients discontinued.*

## CONCLUSIONS

- All ethnic subgroups in this study exhibited virologic success rates (ITT) much lower than would be expected, based on previous data from clinical trials.
- The Black and White subgroups did not differ significantly in virologic and immunologic response to HAART. However, Hispanic patients had a lower mean CD4 response and very poor virologic success rates (AT and ITT). This may be due to a higher rate of early discontinuation (<16 weeks) and noncompliance to the treatment plan.
- Black and Hispanic patients were less adherent with poor follow-up. In particular, the high rate of noncompliance in Hispanics (59%) on NFV regimens reflects a current trend in the Hispanic population in our practice. A few years ago, this population was more adherent with a better response to HAART than other ethnic groups in our practice[6]. Further investigation of this trend, including specific adherence interventions, is needed for this population.
- Although diarrhea was the most common AE reported (affecting White patients twice as frequently as Hispanic patients), it was easily controlled. Only five patients discontinued due to intolerable diarrhea. Two of these five were also taking ddI.
- The majority of discontinuations were not due to AEs, but to external factors. This reminds providers, once more, of the importance of the patient's psychosocial well-being and lifestyle in the development and execution of a treatment plan.
- Clinical trials often exclude patients with past HAART experience or prior patterns of noncompliance. Although this selection allows for a better representation of the performance of a HAART regimen, the results do not necessarily correlate with the general patient population in a clinical practice. Based on our findings, we believe that lifestyle and psychosocial factors play the most important role in this discrepancy.
- In summary, nelfinavir and two NsRTIs appears to be an effective and tolerable regimen in patients with good compliance, regardless of race. The discrepancies between success rates in clinical practice vs. clinical trials should be further examined.

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