

Impact of Race on the Efficacy and Occurrence of Nervous System Symptoms (NSS) in HIV-Infected Subjects Following a Switch from a Protease Inhibitor (PI) to an Efavirenz (EFV)-Based Regimen

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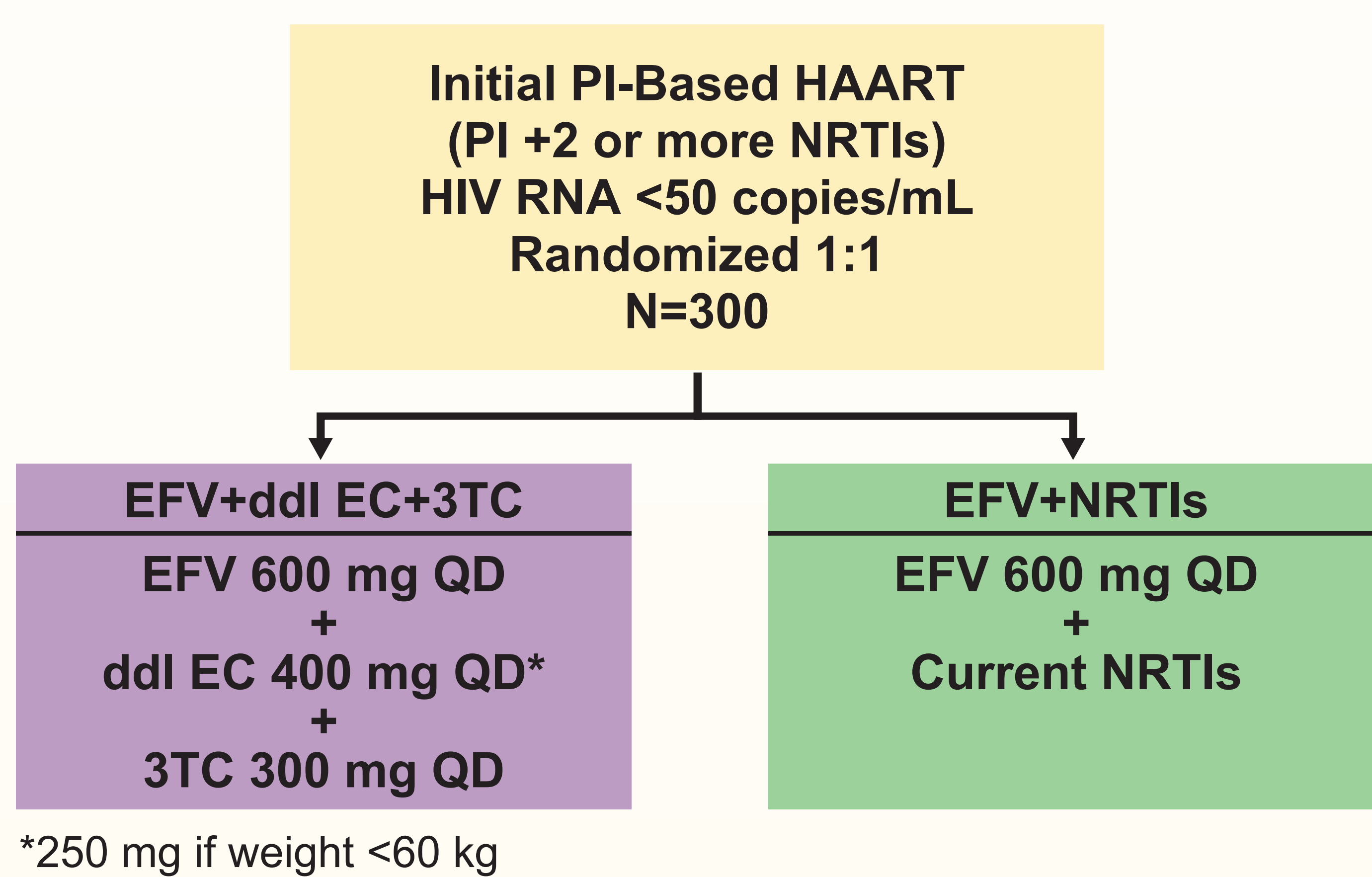
Introduction

Recent data have suggested decreased efavirenz (EFV) clearance rates in Black and Hispanic patients. The clinical impact of this decrease is unclear. This post-hoc analysis of the Week 24 interim results of the VEST-QD study evaluates the impact of race on the efficacy and occurrence of new onset nervous system symptoms (NSS) in subjects receiving an EFV-based antiretroviral regimen.

Methods

- VEST-QD (AI266-406) is a Phase IV, open-label, randomized, multi-center, 48-week study assessing efficacy, safety, adherence, and quality of life in HIV-infected subjects without previous virologic failure who are virologically suppressed on an initial protease inhibitor (PI)-based regimen.

Figure 1: VEST-QD Study Design



- A planned analysis was conducted on the first 186 enrolled subjects at Week 24.¹ Data from these 186 subjects were considered for this post-hoc analysis to evaluate the impact of race on the efficacy and occurrence of new onset NSS in subjects receiving an EFV-based antiretroviral regimen.
- For purposes of this analysis, data from both EFV-based regimen were pooled.
- Seven subjects belonging to racial groups other than White, Black, and Hispanic were excluded from this current analysis.
- New onset NSS included confusion, dizziness, stupor, agitation, amnesia, depersonalization, euphoria, hallucinations, insomnia, somnolence, abnormal thinking, impaired concentration, abnormal dreaming and other related terms.
- A chi-square test was used for categorical data analysis. A log-rank test was used for the analysis of group difference in Kaplan-Meier estimates of onset of NSS.

Results

- A total of 179 enrolled White, Black and Hispanic subjects were analyzed.

Table 1: Baseline Characteristics by Race

	White (n=86)	Black (n=59)	Hispanic (n=34)
Median Age, (years)	45	42	38
Male, (%)	93%	75%	94%
Median CD4 (cells/mm ³) (lower, upper quartile)	553 (373,886)	526 (325,668)	573 (416,792)

Table 2: Week 24 Efficacy Results by Race

	White (n=86)	Black (n=59)	Hispanic (n=34)
CD4 (cells/mm ³) Median Change from Baseline	+6	+55	-11
HIV RNA % <400 copies/mL (ITT, NC=F)	89.5%	89.8%	88.2%
HIV RNA % <50 copies/mL (ITT, NC=F)	88.4%	81.4%	88.2%

- Similar efficacy results were observed in each racial group for both CD4 and HIV RNA through Week 24 ($p>0.05$).

Figure 2: Onset of New NSS All Grades Through Week 24

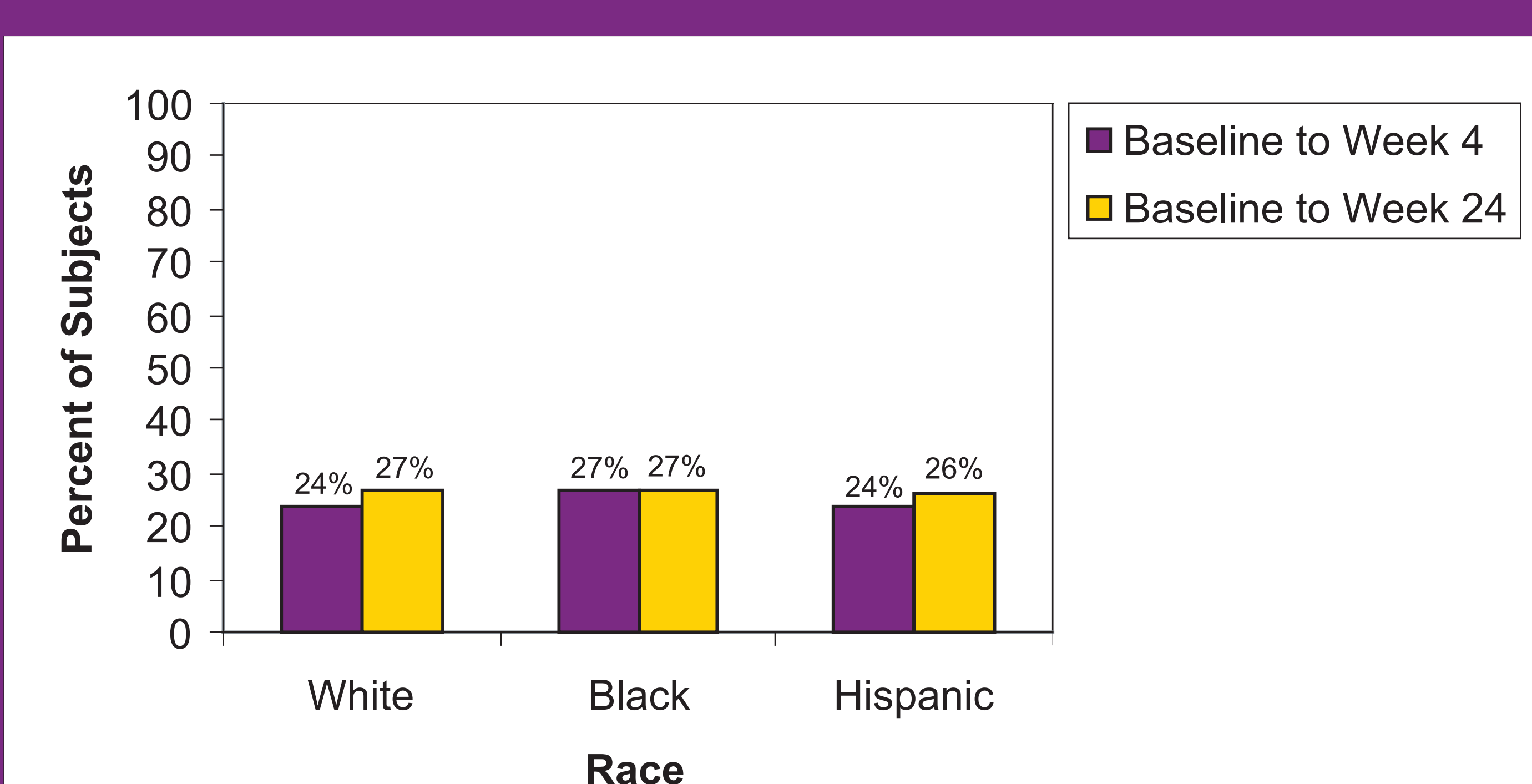
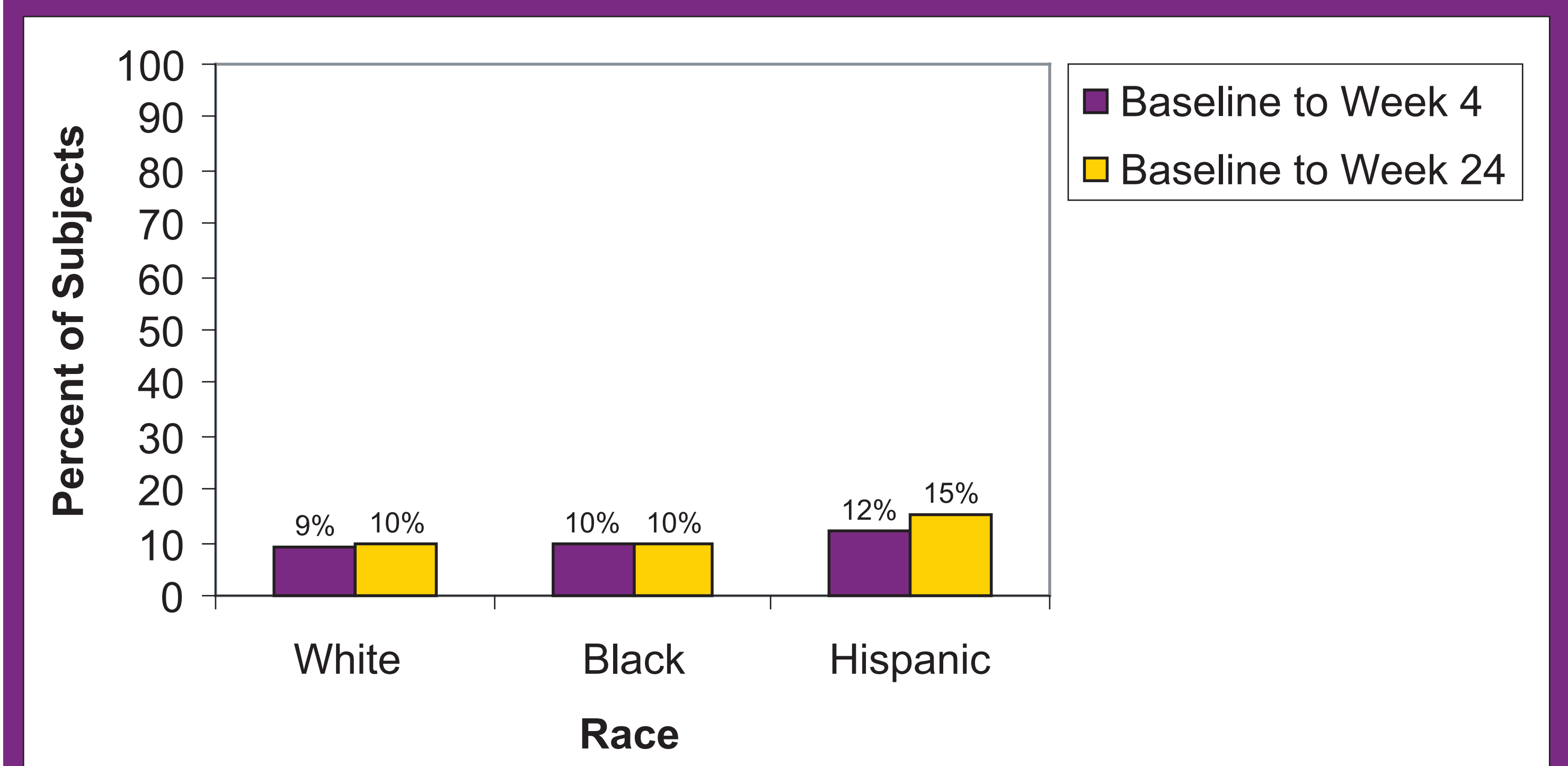
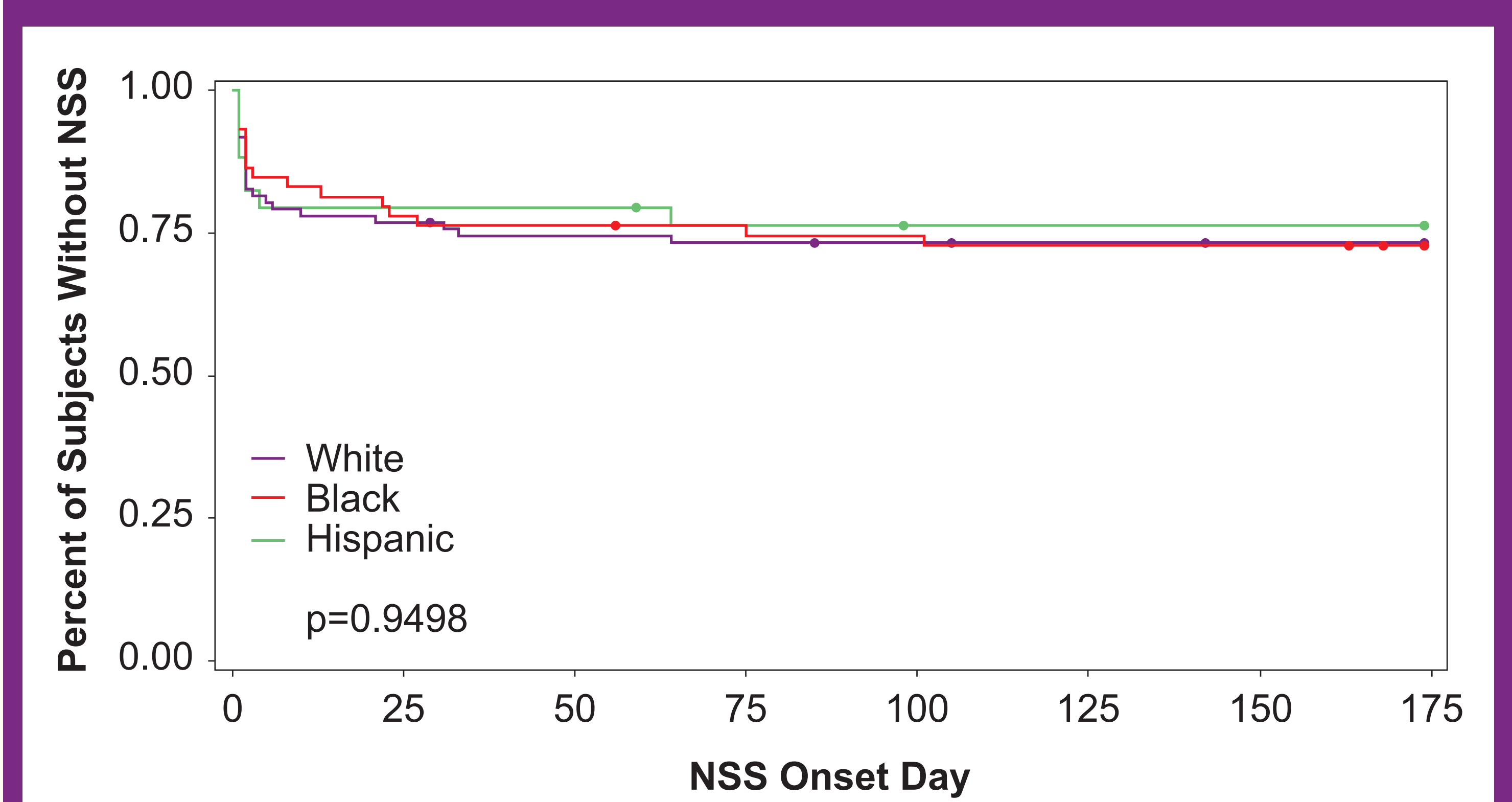


Figure 3: Onset of New NSS (Grades 2-4) Through Week 24



- There are no statistically significant differences ($p>0.05$) between racial groups in the percentage of subjects with new onset NSS (range of subjects by race with NSS AE): all grades through Week 4 (24-27%) and Week 24 (26-27%); Grades 2-4 through Week 4 (9-12%) and Week 24 (10-15%).
- NSS adverse events were mild and occurred principally in the first 4 weeks of therapy.
- There were no Grade 4 NSS adverse events.

Figure 4: Kaplan-Meier Estimates of Onset of NSS Through Week 24



- There were no statistically significant differences ($p=0.9498$) in the time of onset of NSS between race.

Table 3: Frequency of All Grade NSS by Race Through Week 24

	White (n=86) n (%)	Black (n=59) n (%)	Hispanic (n=34) n (%)
Dizziness	13 (15%)	9 (15%)	4 (12%)
Abnormal Dreams	7 (8%)	5 (8%)	3 (9%)
Insomnia	6 (7%)	4 (7%)	2 (6%)
Somnolence	0 (0%)	4 (7%)	0 (0%)
Depressed Levels of Consciousness	0 (0%)	2 (3%)	0 (0%)
Agitation	1 (1%)	0 (0%)	0 (0%)
Disturbance in Attention	1 (1%)	0 (0%)	0 (0%)
Confusion	0 (0%)	0 (0%)	1 (3%)
Disorientation	0 (0%)	1 (2%)	0 (0%)
Euphoria	1 (1%)	0 (0%)	0 (0%)
Amnesia	0 (0%)	1 (2%)	0 (0%)
Sleep Disorder (unspecified)	0 (0%)	0 (0%)	1 (3%)
Stupor	0 (0%)	0 (0%)	1 (3%)

- Similar types and frequencies of new onset NSS were reported in each racial group.

Table 4: Reasons for Treatment Discontinuation Through Week 24

	White (n=86)	Black (n=59)	Hispanic (n=34)
Total Discontinuations, n (%)	5 (6%)	5 (8%)	4 (12%)
Reasons for Discontinuation (d/c)			
NSS Adverse Event, n (%)	0 (0%)	2 (3%)	1 (3%)
Total Non-NSS d/c, n (%)	5 (6%)	3 (5%)	3 (9%)
Non-NSS Adverse Event	1	0	1
Protocol Violation	1	0	0
Withdrew Consent	2	2	1
Virologic Failure	0	1	0
Other	1	0	1

- There were no statistically significant differences ($p>0.05$) in NSS and Non-NSS discontinuation rates between races.

Conclusions

- Continued viral suppression following a switch from a PI to an EFV-based regimen through Week 24 did not differ between White, Black, and Hispanic subjects.
- Most new onset NSS were mild (Grade 1) and occurred during the first four weeks, regardless of race.
- There were no racial differences in treatment discontinuation rates or in those with new onset NSS.

Reference

¹Cohen C, Schneider S, Dretler R et al. Efficacy and Safety of Switching HIV-1 Infected Subjects from a Protease Inhibitor to an Efavirenz-Based Regimen: VEST-QD Week 24 Interim Results. Poster H-577, 44th Interscience Conference on Antimicrobial Agents and Chemotherapy (ICAAC), Washington DC, USA, October-November 2004.