

# Abacavir Compared to Protease Inhibitors as Part of HAART Regimens for Treatment of HIV Infection: Patient Satisfaction and Implications for Adherence

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## ABSTRACT

The purpose of this study was to compare treatment satisfaction with triple nucleoside reverse transcriptase inhibitor (NRTI) highly active antiretroviral treatment (HAART) regimens including abacavir (ABC) to HAART regimens that include protease inhibitors (PIs) and to estimate the relationship between patient satisfaction and adherence to HAART. Three open-label clinical trials comparing ABC-including HAART regimens with PI-including HAART regimens were completed, two with patients previously untreated with antiretroviral therapy and one with patients successfully treated with PI-including HAART regimens. The HIV Treatment Satisfaction Questionnaire (HIVTSQ) was completed at several time points during each trial. Levels of patient satisfaction with the ABC and PI regimens were compared for all three trials. The correlation between adherence and patient satisfaction scores was measured using data from an adherence questionnaire in one of the studies. In all three clinical trials, patient satisfaction scores were significantly higher with an ABC-including triple NRTI HAART regimen than with a PI-including HAART regimen. The difference was apparent by week 4 of the trial and was maintained throughout the trial time period. Inspection of the item responses in the patient satisfaction questionnaire indicated that treatment convenience, flexibility, impact on lifestyle, and side effects were key factors in the difference in satisfaction between the treatment groups. In addition, patient satisfaction was shown to be significantly correlated with adherence defined as taking 95% or more of prescribed doses. Greater satisfaction was reported by patients given an ABC-including HAART regimen than those given a PI-including HAART regimen. Patient satisfaction may be an indicator for better treatment adherence.

## INTRODUCTION

SINCE THE INTRODUCTION OF highly active antiretroviral therapy (HAART), life expectancy after diagnosis with human immunodeficiency virus (HIV) infection has increased

from 10–12 years to 17 years or more.<sup>1</sup> However, HAART regimens, especially those that include protease inhibitors (PIs), require the intake of many pills at specific time intervals with different requirements for food and liquid intake.<sup>2</sup> In addition, HAART regimens are asso-

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ciated with serious side effects including dyslipidemia and lipodystrophy.<sup>2</sup>

Several factors have been correlated with adherence to HAART regimens, including patient, illness, and treatment attributes. Patient attributes include age, mental state, and patient belief or trust in the medication and medical care.<sup>3,4</sup> Illness attributes include whether or not the HIV infection is symptomatic and the severity of those symptoms. Treatment attributes include both perceived and actual efficacy of the treatment, quality of the physician/patient relationship, pill burden, side effects, and dietary restrictions.

Several studies have shown a negative correlation between regimen complexity or pill burden and adherence.<sup>5-10</sup> Increased adherence has also been associated with better quality physician/patient relationships.<sup>11</sup> Patient satisfaction with a HAART regimen is one measure of patients' views of these treatment attributes.

Patient satisfaction can be measured with a single general question about overall satisfaction or using a multi-item measure, including satisfaction with aspects of treatment known to be relevant for HIV treatment regimens.<sup>12</sup> Measurement of satisfaction using a multi-item measure rather than a single score indicates more specifically where problems lie and where solutions are needed.<sup>13</sup>

The primary objective of this paper is to present patient satisfaction measures reported during three clinical trials comparing the use of abacavir (ABC), a nucleoside reverse transcriptase inhibitor (NRTI), with the use of PIs as part of a HAART regimen. One clinical trial randomized patients who had responded to a PI-including HAART regimen, predominantly indinavir (IDV) or nelfinavir (NFV), either to continue the PI-including regimen or to switch the PI to ABC. The other two clinical trials compared ABC-including HAART regimens to IDV or NFV including HAART regimens for previously untreated patients. Patient satisfaction was measured using a validated measure, the nine-item HIV Treatment Satisfaction Questionnaire (HIVTSQ).<sup>12</sup>

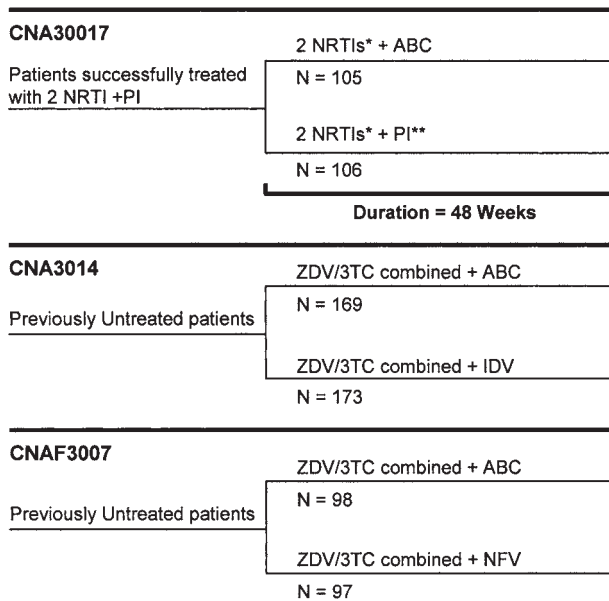
The secondary objective of this paper is to present the results of an analysis of the correlation between adherence and patient satisfaction using data from one international study of previously untreated patients.

## MATERIALS AND METHODS

Data on patient satisfaction and adherence with different HAART regimens were collected over 48 weeks in three clinical trials, each comparing a combination of three NRTIs with a combination of a PI and two NRTIs. These trials were all randomized open-label studies conducted at multiple sites for patients who were either successfully treated with their first antiretroviral therapy (ART) regimen or previously untreated with ART. The primary and secondary clinical endpoints included the proportion of study participants with viral load less than 400 copies per milliliter at 48 weeks and the change in CD4<sup>+</sup> cell count from baseline to 48 weeks. The designs of these studies are illustrated in Figure 1 and summarized below.

- In trial CNA30017, virologically suppressed patients from 29 sites in Europe and Canada ( $n = 211$ ) were randomized to continue their current two NRTIs plus PI regimen or to switch from the PI to ABC. Patient satisfaction was measured at study weeks 4, 8, 12, 16, 24, 32, 40, and 48.
- In trial CNA3014, previously untreated patients from 19 sites in Argentina, Brazil, Mexico, Italy, and Thailand ( $n = 329$ ) were randomized to receive zidovudine/lamivudine combined (ZDV 300 mg/3TC 150 mg) (Combivir<sup>®</sup>, GlaxoSmithKline Research Triangle Park, NC) twice per day plus ABC 300 mg twice per day or ZDV/3TC plus IDV 800 mg three times per day. Approximately 25% of patients had an initial viral load of more than 100,000 copies per milliliter. Patient satisfaction and adherence were measured at study weeks 4, 8, 12, 16, 24, 36, and 48.
- In trial CNAF3007, previously untreated patients from 61 sites in France ( $n = 195$ ) were randomized to receive ZDV 300 mg/3TC 150 mg twice per day plus ABC 300 mg twice per day or ZDV/3TC plus NFV 750 mg three times per day. Approximately 6% of patients had an initial viral load of more than 100,000 copies per milliliter. Patient satisfaction was measured at study weeks 4, 8, 12, 16, 24, 36 and 48.

Regimen-dosing requirements (number of pills, dosing regimen, and dosing conditions



**FIG. 1.** Trial design. \*Nucleoside reverse transcriptase inhibitor (NRTI) combinations used most frequently in the clinical trial were ZDV/3TC, either combined in a single pill or as separate components, and d4T/3TC. Of the 167 patients in whom NRTI identity was known (16 patients had missing values) ZDV/3TC combined = 63 (37.5%), ZDV/3TC separately = 50 (30%), 3TC/d4T = 41 (24.4%), ddI/d4T = 9 (5.4%), ZDV/ddI = 3 (1.8%), ZDV/ddC = 1 (0.6%). \*\*NFV and IDV comprised the majority of PI use, while RTV and SQV were used to a lesser extent. Of the 80 patients in whom PI identity was known (11 patients had missing values) IDV = 39 (48.8%), NFV = 18 (22.5%), SQV = 7 (8.8%), SQV/RTV = 12 (15%), RTV = 4 (5%). 3TC, lamivudine; ABC, abacavir; d4T, stavudine; ddC, zalcitabine, ddI, didanosine; IDV, indinavir; NFV, nelfinavir; RTV, ritonavir; SQV, saquinavir; ZDV, zidovudine; ZDV/3TC combined, Combivir®, PI, protease inhibitor.

such as timing and amounts of food and water consumption) for the two studies of previously untreated patients, CNA3014 and CNAF3007, are shown in Table 1. The dosing requirements for the third study, CNA30017, are not presented in Table 1 because the study included a wide variety of NRTIs and PIs with a variety of regimen-dosing requirements, although the majority of the patients in the trial received ZDV and 3TC and IDV or NFV.

In all three clinical trials, participants completed the nine-item HIVTSQ. This measure has been shown to be valid, reliable, and sensitive to differences between treatment groups in a study comparing satisfaction with two PIs.<sup>12</sup> The nine aspects of satisfaction included in the measure are shown in Table 2. Likert-scale response options for each item range from 0 to 6, with zero indicating the least favorable option (e.g., very dissatisfied) and 6 the most favorable (e.g., very satisfied). Principal components analyses suggested that patients' ratings of the nine items could be summed to compute a total satisfaction score. This sum was then converted from a 0–54 range to a 0–100 range for presentation of the results.

The HIVTSQ was originally validated in English for the United States and Canada by the questionnaire developers.<sup>12</sup> The questionnaire was then translated by a translation agency (without the knowledge or involvement of the developers) into English for the United King-

**TABLE 1.** REGIMEN COMPARISON FROM CNA3014 AND CNAF3007

Regimen	Application study	# Separate meds	# Pills per day	Dosing frequency	Food/Fluid requirements
ZDV 300 mg and 3TC 150 mg combined/ ABC 300 mg	CNA3014,CNAF3007	2	2 + 2 = 4	BID/BID	None
ZDV 300 mg and 3TC 150 mg combined/ NFV 750 mg	CNAF3007	2	2 + 9 = 11	BID/TID	With food
ZDV 300 mg and 3TC 150 mg combined/ IDV 800 mg	CNA3014	2	2 + 6 = 8	BID/TID	Empty stomach, with water 1.5qt/d

ZDV, zidovudine; 3TC, lamivudine; ABC, abacavir; NFV, nelfinavir; IDV, indinavir; BID, twice per day; TID, three times per day.

TABLE 2. HIV TREATMENT SATISFACTION QUESTIONNAIRE ITEMS<sup>a</sup>

<i>Items</i>
How satisfied are you with your current treatment?
How well controlled do you feel your HIV has been recently?
How satisfied are you with the nature and extent of any unwanted side effects involved with your present form of treatment?
How convenient have you been finding your treatment to be recently?
How flexible have you been finding your treatment to be recently?
How satisfied are you with your understanding of your HIV?
How satisfied are you with the extent to which the treatment fits in with your lifestyle?
Would you recommend this combination of treatment to someone else with HIV?
How satisfied would you be to continue with your present form of treatment?

<sup>a</sup>Response options are scored on a Likert scale between 0 (least favorable option) and 6 (most favorable option)

dom, French (for France, Belgium, and Canada), Spanish (for Argentina and Mexico), Italian, Portuguese (for Brazil), and Thai, to be used in the multinational clinical trials. Once the clinical trials were completed, a separate psychometric and linguistic validation was conducted by the developers for each questionnaire translation. Three translations—Italian, Portuguese for Brazil, and French for Canada—were found to be inadequate based on psychometric validation techniques, including principal components analysis of factor loadings and Cronbach  $\alpha$  coefficients of internal consistency reliability. The data from these three translations were excluded from the analyses presented in this paper. For the translations retained in the analysis (English for the United Kingdom; French for France and Belgium, Spanish for Argentina and Mexico, and Thai), statistical validation supported computation of the nine-item total satisfaction scale. In each language, the principal components analysis factor loadings for the nine HIVTSQ items all exceeded 0.4. Cronbach  $\alpha$  coefficient of internal consistency and reliability ranged from 0.85 (English for the United Kingdom) to 0.90 (Spanish for Argentina).

Medication adherence data in trial CNA3014 were obtained by completion of a seven-item adherence questionnaire by the study participants.<sup>10</sup> The questionnaire included two questions about the number of missed doses per week and the number of delayed doses (longer than 2 hours) per week over the past 4 weeks, as well as questions about the longest period of consecutive missed doses, difficulty in taking the drugs,

and reasons for nonadherence. The study participant's adherence measure used in this study, 95% or more adherence or less than 95% adherence to prescribed doses, was determined from his or her response to the question, "On average over the past 4 weeks, please estimate how often per week you have *missed* taking doses of your anti-HIV medicines." Response options ranged from, "I have not missed a dose in the last 4 weeks" and "I have missed less than one dose a week in the last 4 weeks," to "I have missed more than 7 doses a week in the last 4 weeks." Those whose response to this question indicated that they had missed less than one dose per week in the last 4 weeks were judged to be 95% or more adherent. The 95% adherence cutoff was selected based on previous studies evaluating the minimum adherence threshold required to adequately suppress HIV.<sup>14,15</sup>

#### *Statistical analysis*

In all three studies, the mean total satisfaction scores at each visit were compared across the treatment regimens.

In the switch study (CNA30017), treatment groups were also compared based on changes in mean total satisfaction scores between baseline and last time point on randomized therapy (LTORT) by analysis of variance (ANOVA) adjusting for age, gender, and country.

In the two studies of previously untreated patients (CNA3014 and CNAF3007), treatment groups were compared based on LTORT total satisfaction scores using ANOVA adjusting for

age, gender, and country. Responses to individual items on the treatment satisfaction questionnaire were also compared across treatment regimens in all three studies using the proportion of patients with scores of 5 or 6 on each item to reflect a high level of satisfaction.

Multiple logistic regression analysis was conducted with data collected in CNA3014 to determine the relationship between self-reported adherence to 95% or more of prescribed doses and a set of explanatory variables, treatment group, total satisfaction score, age, gender, baseline HIV-1 RNA, and CD4<sup>+</sup> cell count.

## RESULTS

The demographic and baseline disease characteristics of the study participants providing treatment satisfaction data are presented in Table 3. With the exception of CD4<sup>+</sup> cell count in the CNAF3007 trial, there were no differences between the treatment arms in demographic and baseline disease characteristics within each trial. Comparing across trials, the previously treated group in trial CNA30017 was older and had a higher CD4<sup>+</sup> cell count than the previously untreated patients in trials CNA3014 and CNAF3007.

The clinical results from these three trials indicated that, at 48 weeks, the ABC-including regimen had similar or better efficacy mea-

sured both in terms of viral load reduction and CD4<sup>+</sup> cell count increase compared to the PI-including regimens.<sup>16-18</sup>

Figure 2 presents the total satisfaction scores from the three clinical trials over the full trial time period. In the switch trial (CNA30017), those who remained on PI therapy reported total satisfaction scores that stayed relatively constant over the full trial time period. Those who were switched to ABC reported a rapid increase in satisfaction, apparent when measured at week 4 after start of treatment, and this gain was maintained for the remaining study period. In the trials including only previously untreated patients (CNA3014 and CNAF3007), higher satisfaction for those on ABC-including regimens compared to those on PI-including regimens was observed at 4 weeks and remained relatively stable for the full 48-week trial time period.

Figure 3 presents data comparing the change in total satisfaction scores in patients receiving ABC and PI-including regimens between baseline and LTORT in the switch study (CNA30017). These results show that, while satisfaction decreased slightly for those who remained on the PI-including regimens, those who were switched to the ABC-including regimen reported a significant increase in satisfaction ( $p < 0.001$ ) compared to those remaining on the PI-including regimen. Subgroup analysis of the CNA30017 data shows a trend toward higher patient satisfaction for those who were given

TABLE 3. PATIENTS' DEMOGRAPHIC AND DISEASE CHARACTERISTICS<sup>a</sup>

Baseline characteristic	CNA30017		CNA3014		CNAF3007	
	ABC n = 89	PI n = 86	ABC n = 121	IDV n = 122	ABC n = 86	NFV n = 84
Median age (years)	38	39	31	32	34	34
Males n (%)	78(85)	70(77)	66(55)	77(63)	60(70)	53(63)
Race n (%)						
Asian	2(2)	0(0)	58(48)	58(48)	N/A	N/A
Black	6(7)	12(13)	0(0)	1(<1)		
Hispanic	5(5)	3(3)	29(24)	32(26)		
Caucasian	78(85)	76(84)	32(26)	27(22)		
Other	1(1)	0(0)	2(2)	4(3)		
HIV-1 RNA log <sub>10</sub> copies per milliliter (median)	N/A	N/A	4.77	4.80	4.21	4.19
CD4 <sup>+</sup> cell count cells/mm <sup>3</sup> (median)	498	502	311	308	391 <sup>b</sup>	439 <sup>b</sup>

<sup>a</sup>n's refer to trial patients providing satisfaction data.

<sup>b</sup>p Value for difference between treatment groups <0.05.

ABC, abacavir; IDV, indinavir; NFV, nelfinavir; PI, protease inhibitor; N/A, not available.

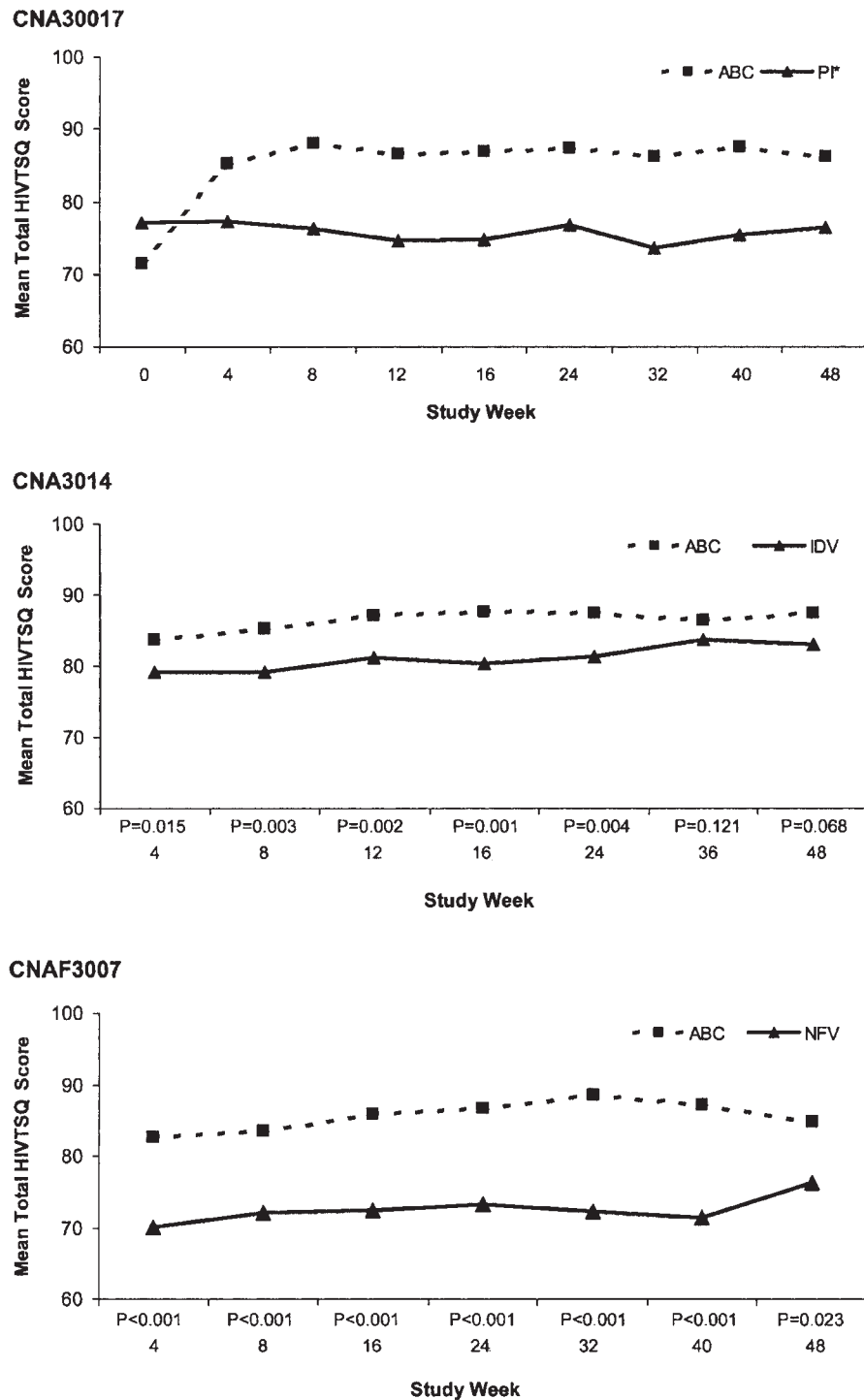


FIG. 2. HIV Treatment Satisfaction Questionnaire (HIVTSQ) total satisfaction scores over time. The protease inhibitor (PI) group included patients taking indinavir, nelfinavir, saquinavir, ritonavir, or saquinavir/ritonavir.

ZDV/3TC as a fixed-dose combination tablet plus ABC than for other NRTI plus ABC regimens [mean total satisfaction score at LTORT of 90.1 versus 84.2 ( $p = 0.039$ )].

Figure 4 presents the LTORT total satisfaction scores from the two trials with previously

untreated patients. In both trials, a total satisfaction score of 86 was achieved for the ABC-including arms. In the IDV-including arm, a total satisfaction score of 80 was achieved, whereas in the NFV-including arm a total satisfaction score of 71 was achieved at LTORT.

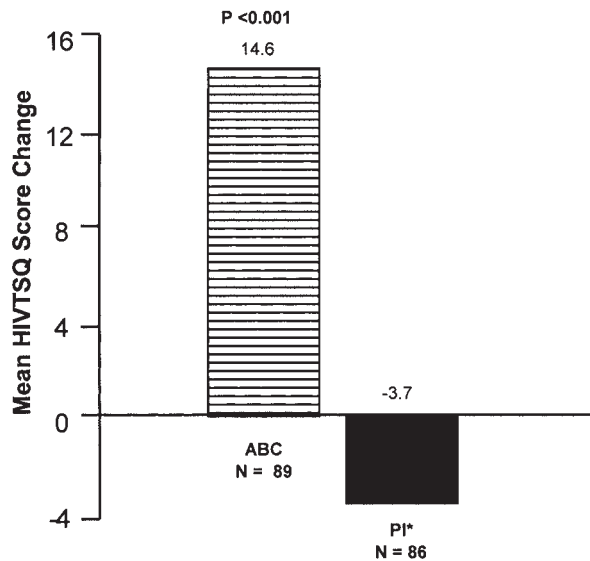


FIG. 3. Change in total satisfaction scores from baseline to last time point on randomized therapy (LTORT) (CNA30017). The protease inhibitor (PI) group included patients taking indinavir, nelfinavir, saquinavir, ritonavir, or saquinovir/ritonavir.

The difference in patient satisfaction between the ABC and the PI regimen was statistically significant ( $p < 0.001$ ) in both trials.

A comparison of the responses to the individual items in the patient satisfaction questionnaire for all three clinical trials is shown in Figure 5. A greater proportion of patients were satisfied with the ABC-including regimen than with the PI-including regimen for each of the scale items. In all three studies, inspection of Figure 5 shows that the largest differences were

seen between regimens in favor of ABC-including regimens for treatment convenience, flexibility, impact on lifestyle, and side effects.

Table 4 presents the results of the multiple logistic regression analysis performed using data from the CNA3014 study to estimate the correlation of self-reported adherence to 95% or more of prescribed doses with a set of explanatory variables. The two explanatory variables that were significantly correlated with high adherence are treatment group and patient satisfaction (HIVTSQ total satisfaction score). This demonstrates an independent effect on adherence of patient satisfaction when controlling for treatment group.

### DISCUSSION

The main strength of the data presented in this paper is the consistency of the findings. Patient satisfaction scores were higher with an ABC-including regimen than with a PI-including regimen. These results were seen in all three clinical trials, which encompassed both previously treated and previously untreated patients from many different countries.

When specific answers on the patient satisfaction questionnaire were examined across the three clinical trials, it appeared that the difference in total patient satisfaction between the ABC- and PI-including regimens was strongly influenced by the magnitude of difference seen

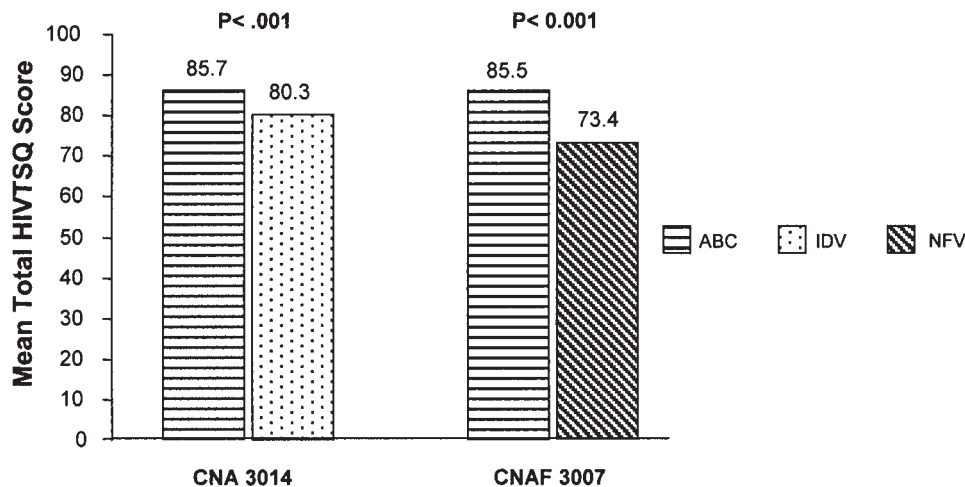


FIG. 4. HIV Total Satisfaction Questionnaire (HIVTSQ) total satisfaction scores at last time point on randomized therapy (LTORT) (CNA3014 and CNAF3007). \*The protease inhibitor (PI) group included patients taking indinavir, nelfinavir, saquinavir, or saquinovir/ritonavir.

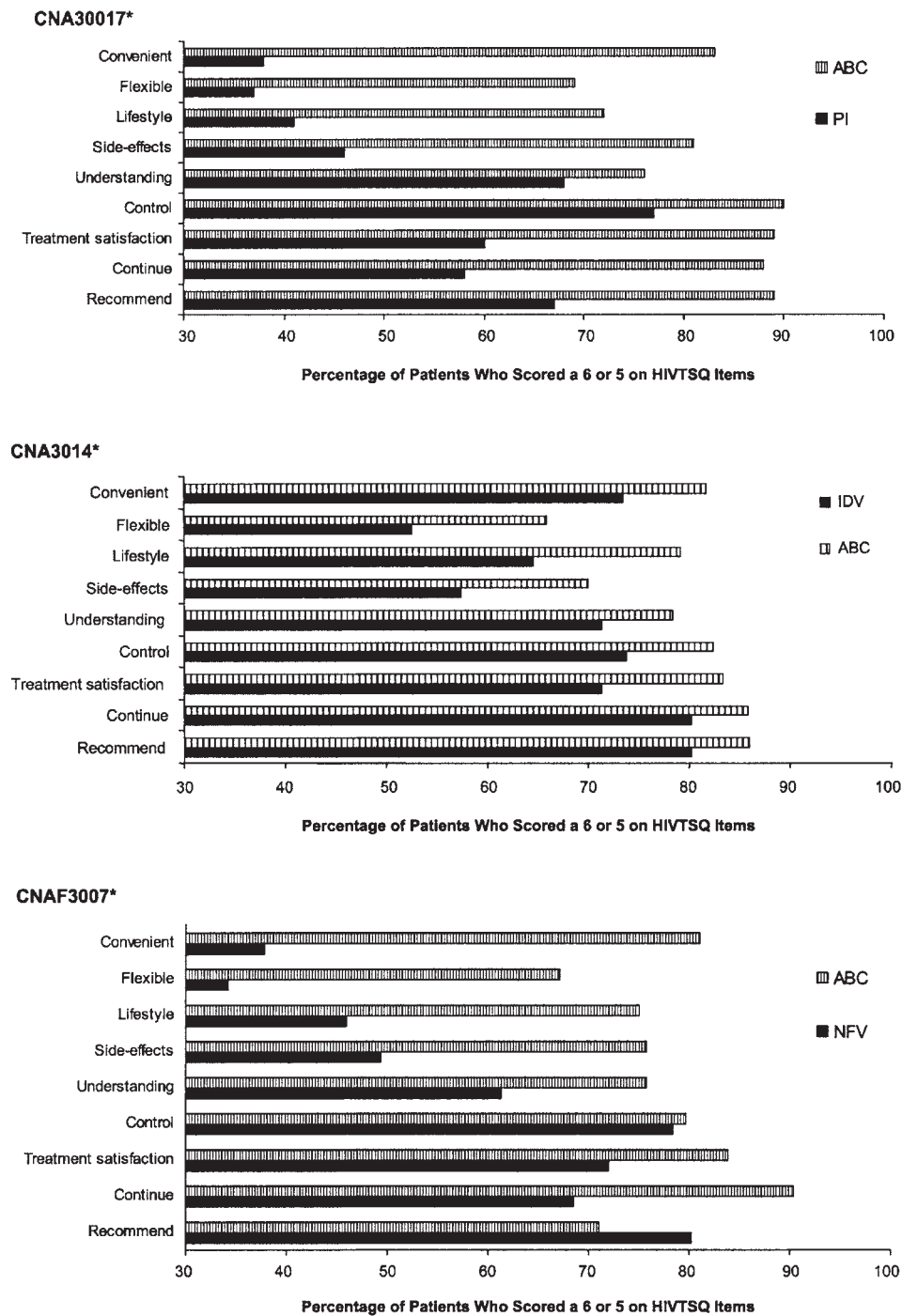


FIG. 5. Comparison of responses to specific HIV Total Satisfaction Questionnaire (HIVTSQ) Items at last time point on randomized therapy (LTORT). \*Results only for patients providing satisfaction data.

in single-item responses for regimen convenience, flexibility, and impact on lifestyle.

The regression results using the data from CNA3014 showed that patient satisfaction was highly correlated with self-reported adherence to 95% or more of prescribed doses. This result was found when controlling for other factors

that are correlated with adherence such as age, gender, disease stage, and treatment. Thus, patient satisfaction may be a valuable predictor of adherence.<sup>19</sup>

Several studies have shown a relationship between adherence and disease outcomes, indicating that better and more durable efficacy



TABLE 4. MULTIVARIATE LOGISTIC REGRESSION ANALYSIS OF ADHERENCE TO 95% OR MORE OF PRESCRIBED DOSES IN CNA3014

<i>Predictor</i>	<i>Odds ratio</i>	<i>95% Confidence interval</i>	<i>p Value</i>
Total satisfaction score (per each 5-point increase)	1.14	1.04, 1.25	0.006
Treatment group (ABC vs. IDV)	3.55	2.01, 6.27	<0.0001
Age	1.02	0.98, 1.06	0.304
Gender (male vs. female)	1.33	0.74, 2.41	0.339
Baseline HIV-1 RNA (per each log <sub>10</sub> increased)	1.12	0.68, 1.83	0.666
Baseline CD4 <sup>+</sup> cells	1.00	0.99, 1.00	0.225

ABC, abacavir; IDV, indinavir.

is achieved when patients are adherent to their HAART regimen.<sup>14,20–24</sup> However, it should be noted that adherence measured by patient self-report probably overestimates actual adherence although the two measures are highly correlated.<sup>25,26</sup>

There are some limitations to the data presented. First, the translation methods used initially by the translation agency (without consultation with the developers) were not sufficiently rigorous to ensure good quality translations and satisfactory psychometric properties in all languages. This meant that the satisfaction data from some of the countries in the trial could not be included in the final analysis. The quality of the Italian, Brazilian Portuguese and Canadian French translations have now been improved in work conducted by specialists in linguistic validation of questionnaires in collaboration with the author (C.B.).

Other limitations include the fact that these studies were not designed in a manner that permits pooling of the data across studies; more detailed analyses would have been possible with pooled data. Another limitation was the statistically significant difference between baseline CD4<sup>+</sup> cell counts in the two treatment groups in trial CNAF3007, with a higher baseline CD4<sup>+</sup> cell count in the NFV group, which might bias the results from that study. Finally, these studies primarily compared ABC-including regimens with two PI-including regimens (NFV, IDV) given three times per day. Currently, PI-including regimens are more frequently given twice per day or daily. The ability to generalize these findings to similar regimens where NFV or IDV are given twice per day or to other HAART regimens with or without PIs is not known. To date, no open-

label trials have been published measuring patient satisfaction with other HAART regimens.

Clinicians and patients must make their treatment choices based on both regimen efficacy as well as the factors that contribute to patient satisfaction and adherence, including regimen complexity and tolerability. While we have presented patient satisfaction data comparing abacavir used in place of a protease inhibitor, there are other alternatives for treatment, including non-nucleoside reverse transcriptase inhibitors (NNRTI). Although no comparative patient satisfaction data have been published for NNRTIs, there are data from blinded studies suggesting that regimens that include an NNRTI may provide a superior virologic response compared to other alternatives, including triple nucleoside regimens that contain abacavir.<sup>27</sup>

It is important to recognize that all three clinical trials described in this paper utilized an open-label design that allowed patients to experience the full benefits of a more convenient regimen. The effectiveness of a drug regimen in real-world practice or in unblinded trials may differ from the efficacy observed in blinded clinical trials because of reduced adherence or persistence for the less convenient or flexible drug regimen.

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## REFERENCES

1. CASCADE Collaboration. Survival after introduction of HAART in people with known duration of HIV-1 infection. *Lancet* 2000;355:1158–1159.
2. AIDSinfo. Antiretroviral drugs: Overview of drugs. US Department of Health and Human Services. [aidsinfo.nih.gov/drugs](http://aidsinfo.nih.gov/drugs). (Last accessed April 2003).
3. Eraker S, Kirscht J, Becker M. Understanding and improving patient compliance. *Ann Intern Med* 1984; 100:258–268.
4. Ickovics J, Meisler A. Adherence to AIDS clinical trials: A framework for clinical research and clinical care. *J Clin Epidemiol* 1997;50:385–391.
5. Stone VE, Hogan JW, Schuman P, et al. Antiretroviral regimen complexity, self-reported adherence, and HIV patients' understanding of their regimens: Survey of women in the HER study. *J Acquir Immune Defic Syndr* 2001;28:124–131.
6. Bartlett JA, DeMasi R, Quinn J, Moxham C, Rousseau F. Overview of the effectiveness of triple combination therapy in antiretroviral-naïve HIV-1 infected adults. *AIDS* 2001;15:1369–1377.
7. Bartlett J, DeMasi R, Quinn J, et al. Correlation between antiretroviral pill burden and durability of virologic response: a systemic overview [Abstract ThPeB44998]. Presented at XIII International Conference on AIDS; Durban, South Africa: 2000.
8. Brook MG, Dale A, Tomlinson D, Waterworth C, Daniels D, Forster G. Adherence to highly active antiretroviral therapy in the real world: Experience of twelve English HIV units. *AIDS Patient Care STDS* 2001;15:491–494.
9. Golin CE, Liu H, Hays RD, et al. A prospective study of predictors of adherence to combination antiretroviral medication. *J Gen Intern Med* 2002;17:756–765.
10. Jordan J, Cahn P, Vibhagool A. Predictors of adherence and efficacy in HIV-1 infected patients treated with abacavir plus Combivir or indinavir plus Combivir: Final 48-week data from CNA3014. Presented at 9th Conference on Retroviruses and Opportunistic Infections. Seattle, WA; 2002; February 24–28, 2002; 543T.
11. Roberts KJ. Physician-patient relationships, patient satisfaction, and antiretroviral medication adherence among HIV-infected adults attending a public health clinic. *AIDS Patient Care STDS* 2002;16:43–50.
12. Woodcock A, Bradley C. Validation of the HIV treatment satisfaction questionnaire (HIVTSQ). *Qual Life Res* 2001;10:517–531.
13. Hudak PL, Wright JG. The characteristics of patient satisfaction measures. *Spine* 2000;25:3167–3177.
14. Paterson DL, Swindells S, Mohr J, et al. Adherence to protease inhibitor therapy and outcomes in patients with HIV infection. *Ann Intern Med* 2000;133:21–30.
15. Low-Beer S, Yip B, O'Shaughnessy MV, Hogg RS, Montaner JSG. Adherence to triple therapy and viral load response [letter]. *J Acquire Immune Defic Syndr* 2000;23:360–361.
16. Vibhagool A. Abacavir/Combivir is comparable to indinavir/Combivir in HIV-1 infected antiretroviral therapy naïve adults: results of a 48-week open label study [Abstract 063]. Presented at 1st IAS Conference of HIV Pathogenesis and Treatment, Buenos Aires, Argentina: July 8–11, 2001.
17. Clumeck N, Goebel F, Rozenbaum W, et al. Simplification with abacavir-based triple nucleoside therapy versus continued protease inhibitor-based highly active antiretroviral therapy in HIV-1-infected patients with undetectable plasma HIV-1 RNA. *AIDS* 2001; 15:1517–1526.
18. Matheron S, Descamps D, Boue F, et al. Triple nucleoside combination zidovudine/lamivudine/abacavir versus zidovudine/lamivudine/nelfinavir as first-line therapy in HIV-1-infected adults: a randomized trial. *Antiviral Ther* 2003;8:73–81.
19. Ley P. Satisfaction, compliance, and communication. *Br J Clin Psych* 1982;21:241–254.
20. Katzenstein DA. Adherence as a particular issue with protease inhibitors. *J Assoc Nurses AIDS Care* 1997; (Suppl 8):10–17.
21. Casado JL, Sabido R, Perez-Elias MJ, et al. Percentage of adherence correlates with the risk of protease inhibitor (PI) treatment failure in HIV-infected patients. *Antivir Ther* 1999;4:157–161.
22. Friedland GH, Williams A. Attaining higher goals in HIV treatment: the central importance of adherence. *AIDS* 1999;13(Suppl 1):S61–72.
23. Pradier C, Carrieri P, Bentz L, et al. Impact of short-term adherence on virological and immunological success of HAART: A case study among French HIV-infected IDUs. *Int J STD AIDS* 2001;12:324–328.
24. Le Moing V, Chene G, Carrieri MP, et al. Predictors of virological rebound in HIV-1 infected patients initiating a protease inhibitor-containing regimen. *AIDS* 2002;16:21–29.
25. Arnsten JH, Demas PA, Farzadegan H, et al. Antiretroviral therapy adherence and viral suppression in HIV-infected drug users: Comparison of self-report and electronic monitoring. *Clin Infect Dis* 2001; 33:1417–1423.
26. Melbourne KM, Geletko SM, Brown SL, et al. Medication adherence in patients with HIV infection: a comparison of two measurement methods. *AIDS Reader* 1999;9:329–338.
27. Gulick RM, Ribaldo HJ, Shikuma CM, et al. ACTG 5095: A comparative study of three protease inhibitor sparing antiretroviral regimens for the initial treatment of HIV infection. *N Engl J Med* 2004;350:1850.

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