

# Predictors of optimal viral suppression in patients switched to abacavir, lamivudine, and zidovudine: the Swiss HIV Cohort Study

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**Objective:** To investigate predictors of continued HIV RNA viral load suppression in individuals switched to abacavir (ABC), lamivudine (3TC) and zidovudine (ZDV) after successful previous treatment with a protease inhibitor or non-nucleoside reverse transcriptase inhibitor-based combination antiretroviral therapy.

**Design and methods:** An observational cohort study, which included individuals in the Swiss HIV Cohort Study switching to ABC/3TC/ZDV following successful suppression of viral load. The primary endpoint was time to treatment failure defined as the first of the following events: two consecutive viral load measurements > 400 copies/ml under ABC/3TC/ZDV, one viral load measurement > 400 copies/ml and subsequent discontinuation of ABC/3TC/ZDV within 3 months, AIDS or death.

**Results:** We included 495 individuals; 47 experienced treatment failure in 1459 person-years of follow-up [rate = 3.22 events/100 person-years; 95% confidence interval (95% CI), 2.30–4.14]. Of all failures, 62% occurred in the first year after switching to ABC/3TC/ZDV. In a Cox regression analysis, treatment failure was independently associated with earlier exposure to nucleoside reverse transcriptase inhibitor (NRTI) mono or dual therapy [hazard ratio (HR), 8.02; 95% CI, 4.19–15.35] and low CD4 cell count at the time of the switch (HR, 0.66; 95% CI, 0.51–0.87 by +100 cells/ $\mu$ l up to 500 cells/ $\mu$ l). In patients without earlier exposure to mono or dual therapy, AIDS prior to switch to simplified maintenance therapy was an additional risk factor.

**Conclusions:** The failure rate was low in patients with suppressed viral load and switch to ABC/3TC/ZDV treatment. Patients with earlier exposure to mono or dual NRTI therapy, low CD4 cell count at time of switch, or AIDS are at increased risk of treatment failure, limiting the use of ABC/3TC/ZDV in these patient groups.

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**Keywords:** abacavir, cohort study, treatment failure, viral rebound, viral suppression

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## Introduction

Triple nucleoside reverse transcriptase inhibitor (NRTI) therapy with abacavir (ABC), lamivudine (3TC) and zidovudine (ZDV) accounts for approximately 10% of all combination antiretroviral therapy (cART) prescriptions in the Swiss HIV Cohort Study (SHCS) since the introduction of the fixed-dose formulation in Switzerland. The main advantages of ABC/3TC/ZDV are a very low pill burden (two pills per day), the association with favourable total cholesterol and triglyceride levels [1–5], and few drug interactions. Although clinical trials have established similar efficacy of ABC/3TC/ZDV as initial therapy compared to two class regimens with indinavir or nelfinavir [6–8], it was inferior to efavirenz-containing regimens [9]; in consequence, current treatment guidelines do not recommend the use of first-line therapy with ABC/3TC/ZDV [10,11].

Evidence from clinical trials indicates that ABC/3TC/ZDV as simplified maintenance therapy may be a valid option in patients after previous successful protease inhibitor (PI) or non-nucleoside reverse transcriptase inhibitor (NNRTI)-based combination antiretroviral therapy (cART) [1–4,12,13]. The likelihood of treatment failure in individuals who harbour resistance due to prior suboptimal antiretroviral therapy with NRTI mono or dual therapy is, however, increased [1,3,4]. There is only limited evidence from observational data on the effectiveness of ABC/3TC/ZDV as maintenance therapy. In two studies [14,15], a slightly higher rate of viral rebound compared to efavirenz-based regimens has been found.

The purpose of the present study was to describe the characteristics of patients being switched to ABC/3TC/ZDV after previous successful treatment with PI or NNRTI-based cART in a large cohort, to identify predictors for continued successful viral suppression and to characterize multi-NRTI or ABC/3TC/ZDV resistance mutations after treatment failure.

## Methods

The Swiss HIV Cohort Study (SHCS, [www.shcs.ch](http://www.shcs.ch)) is a prospective cohort study with continuing enrollment of HIV-infected individuals and biannual follow-up visits in seven centers and specialized private practices in Switzerland. Antiretroviral treatment is documented in detail within the SHCS. RNA viral load (VL) and CD4 cell counts from registered individuals are electronically transferred from the center laboratories at follow-up or routine visits to the SHCS data center. HIV genotypic drug resistance testing is performed within the SHCS by the four laboratories in Switzerland authorized by the Federal Office of Public Health. All laboratories perform population-based sequencing of the full protease gene and in minimum codons 28 to 225 of the reverse transcriptase

gene using a variety of commercial assays (Viroseq Vs.1 PE Biosystems, Rotkreuz, Switzerland; Virsoeq Vs. 2, Abbott AG, Baar, Switzerland; vircoTYPE HIV-1 Assay, Virco Lab, Mechelen, Belgium) and in-house methods [16]. Genotypic resistance data from routine clinical testing and from studies is stored in the SHCS resistance database using SmartGene's Integrated Database Network System (IDNS Version 3.3.0; SmartGene, Zug, Switzerland). Available drug resistance tests collected until October 2006 were considered for this analysis.

We included patients who received a PI or NNRTI-based regimen for at least 3 months prior to switching to ABC/3TC/ZDV as a single triple NRTI therapy, had a viral load < 400 copies/ml at the time of the switch and at least two subsequent viral load measurements under ABC/3TC/ZDV or reached the primary endpoint.

The primary endpoint was time to treatment failure defined as the occurrence of the first of the following events: two consecutive viral load measurements > 400 copies/ml, one viral load measurement > 400 copies/ml and subsequent discontinuation of ABC/3TC/ZDV within 3 months, AIDS or death under ABC/3TC/ZDV. Patients without an event were censored at their last viral load measurement under ABC/3TC/ZDV. The secondary endpoint was based on a stricter definition of treatment failure according to an intention-to-treat approach and included all of the events above plus discontinuation of ABC/3TC/ZDV for any reason.

The primary and the secondary endpoint were analyzed with a multiple Cox regression analysis with the following covariates: age, gender, risk category for HIV transmission [injection drug user (IDU) versus other], basic education (completed 9 years of mandatory schooling or less versus higher), prior AIDS or hepatitis C, earlier exposure to NRTI mono or dual therapy for  $\geq 30$  days, type of previous cART, and CD4 cell count at the time of the switch. CD4 cell count was modeled as a linear spline with one knot at 500 cells/ $\mu$ l.

We also described mutations associated with multi-NRTI or ABC/3TC/ZDV resistance [17] based on available resistance tests prior to start of ABC/3TC/ZDV and after treatment failure. PI-relevant mutations were not evaluated in the present study.

All reported confidence intervals are two-sided 95% confidence intervals (CI). Analyses were performed with SAS 9.1 (SAS Institute, Cary, North Carolina, USA) and R version 2.3.1 [18].

## Results

In the SHCS database, a total of 1187 treatment episodes with ABC/3TC/ZDV from 998 patients are recorded

between July 1997 and September 2006. Single ABC/3TC/ZDV has been the second most used cART in the SHCS since the introduction of the fixed-dose trizivir formulation in Switzerland in July 2001: ABC/3TC/ZDV accounts for 10.6% of the observed exposure to cART; an additional 3.2% of the observed exposure is ABC/3TC/ZDV in combination with PI, NNRTI or additional NRTI; the most used cART in the SHCS is efavirenz+3TC/ZDV with 11.4%. The inclusion criteria of this study were fulfilled by 495 patients. Patients were excluded because they started on ABC/3TC/ZDV as first-line therapy ( $n=106$ ), after a treatment interruption ( $n=105$ ) or after a regimen other than PI or NNRTI-based cART ( $n=103$ ). An additional 65 patients were excluded because they were switched from a PI or NNRTI-based regimen and had stayed less than 3 months on that regimen, 49 individuals had no viral load measurement or a measurement  $\geq 400$  copies/ml at the time of the treatment switch and 75 individuals had less than two follow-up RNA measurements under ABC/3TC/ZDV without reaching the primary endpoint.

Baseline characteristics of the 495 included patients are displayed in Table 1. The majority of patients were male (72%), median age was 40 years and median time from first prescription of any antiretroviral therapy until ABC/3TC/ZDV start was 2.86 years; 20% had earlier exposure to NRTI mono or dual therapy. Forty-two patients had two consecutive viral load measurements  $> 400$  copies/ml under earlier antiretroviral therapy (ART) sampled at least 6 months after ART start and any ART interruption (but, as required by our inclusion criteria, their viral load at the time of the switch to ABC/3TC/ZDV was  $< 400$  copies/ml); 37 of these 42 patients had earlier exposure to NRTI mono or dual therapy. This may, however, underestimate the number of patients with nonsuppressed viral load under ART as 26 patients initiated first ART prior to July 1995 (when viral load collection was introduced into the SHCS) and a further 135 patients started ART prior to registration into the SHCS.

Median duration of follow-up from ABC/3TC/ZDV start to the last available viral load measurement under ABC/3TC/ZDV was 3.26 years. Eighty-two percent of the observed exposure to ABC/3TC/ZDV was after the fixed-dose formulation was introduced in Switzerland in July 2001. Discontinuation of ABC/3TC/ZDV was documented in 227 (46%) patients; the median length of a treatment episode was 4.37 years [Kaplan-Meier estimate, 95% CI: 3.76–5.38 years]. Toxicity was the reason for 20 (9%) of the ABC/3TC/ZDV stops (three stopped due to a hypersensitivity reaction) and the major reason for stopping was unspecified for 126 (56%) of the patients. Subsequent treatment was PI or NNRTI-based cART for 55 patients; 31 patients switched to another ART regimen; 111 patients interrupted treatment, 36 of them were on an ongoing treatment interruption, the others

**Table 1. Baseline characteristics of 495 subjects switched to abacavir/lamivudine/zidovudine (ABC/3TC/ZDV) after being successfully treated with a protease inhibitor (PI) or non-nucleoside reverse transcriptase inhibitor (NNRTI)-based combination antiretroviral therapy (cART) for at least 3 months.**

Characteristic	Summary statistic: <i>n</i> (%) or median (IQR)	
Gender: female	137	(28%)
Age at first cART (years)	40	35 to 49
Most likely source of infection		
Heterosexual	196	(40%)
Homosexual	221	(45%)
IDU	64	(13%)
Other	14	(3%)
Basic education	104	(21%)
Prior AIDS	91	(18%)
Hepatitis C	78	(16%)
Year of ABC/3TC/ZDV begin	2001	2000 to 2002
Time from first ART to ABC/3TC/ZDV begin (years)	2.86	1.44 to 4.33
Earlier exposure to NRTI mono or dual therapy for $\geq 30$ days	98	(20%)
Type of previous cart		
Boosted PI	95	(19%)
Single PI	252	(51%)
NNRTI	148	(30%)
CD4 cell count (cells/ $\mu$ l) at start of ART <sup>a</sup>	262	142 to 378
CD4 cell count (cells/ $\mu$ l) at start of ABC/3TC/ZDV	521	370 to 738
Viral load at start of ART (log <sub>10</sub> copies/ml) <sup>a</sup>	4.92	4.29 to 5.36
Nonsuppressed viral load on earlier ART <sup>b</sup>	42	(8%)

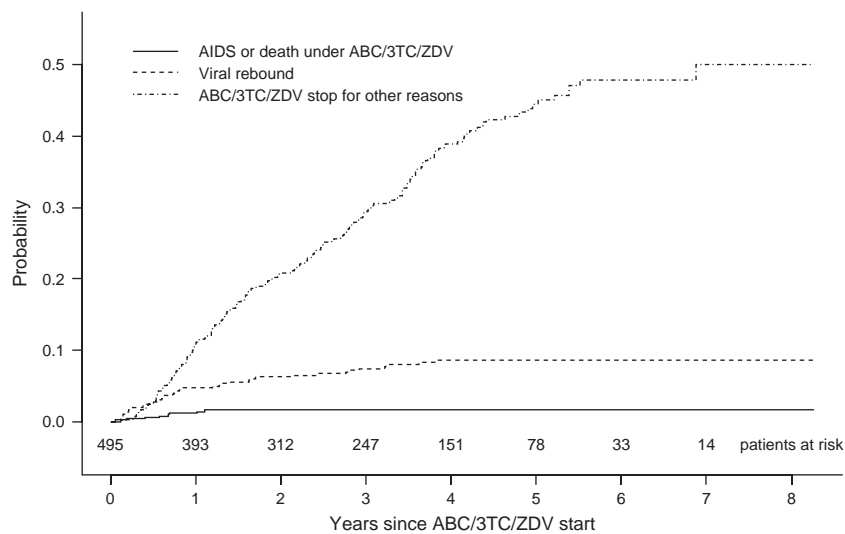
ART, antiretroviral therapy; IDU, injection drug use; IQR, interquartile range; NRTI, nucleoside reverse transcriptase inhibitor.

<sup>a</sup>Start of ART refers to the first prescription of any antiretroviral therapy. CD4 cell count and viral load at start of ART were missing for 112 and 141 subjects, respectively.

<sup>b</sup>Refers to patients with two consecutive viral load measurements  $> 400$  copies/ml under earlier ART sampled at least 6 months after ART start and any ART interruption.

restarted treatment after a median of 96 days; six patients died and 24 were lost to follow-up.

Forty-seven of the 495 subjects experienced treatment failure (39 viral load failures, two AIDS cases, six deaths) in 1459 person-years of follow-up (rate = 3.22 events/100 person-years; 95% CI, 2.30–4.14); failure rates in patients with and without earlier exposure to NRTI mono or dual therapy were 10.80/100 person-years (95% CI, 7.00–14.61) and 1.36/100 person-years (95% CI, 0.70–2.03), respectively. The treatment failure rate strongly decreased over time: the rate was of 6.46/100 person years (95% CI, 4.11–8.81) in the first year of ABC/3TC/ZDV administration and 2.22/100 person years (95% CI, 1.19–3.24) in years 2–4; 29 (62%) of the events occurred in the first year of treatment and no events later than 4 years were observed. Similar decreases were observed in the subgroups of patients with and without earlier exposure to NRTI mono or dual therapy. An additional 185 patients discontinued ABC/3TC/ZDV before reaching the primary endpoint. The cumulative incidence functions of events constituting



**Fig. 1. Cumulative incidence functions of events constituting the primary and the secondary endpoint.** Viral rebound refers to two consecutive viral load measurements > 400 copies/ml or one viral load > 400 copies/ml and subsequent discontinuation of abacavir/lamivudine/zidovudine (ABC/3TC/ZDV) within 3 months.

the primary and secondary endpoint are displayed in Fig. 1.

Results from the multiple Cox regression analysis of time to treatment failure are shown in Table 2. Treatment failure was independently associated with earlier exposure to NRTI mono or dual therapy [hazard ratio (HR) 8.02; 95% CI, 4.19–15.35;  $P < 0.001$ ] and low CD4 cell count at the time of the switch (HR 0.66; 95% CI, 0.51–0.87 by 100 cells/ $\mu\text{l}$  higher up to 500 cells/ $\mu\text{l}$ ,  $P = 0.003$ ) whereas CD4 cell count values above 500 cells/ $\mu\text{l}$  and other covariates including type of previous cART, a basic education and IDU HIV transmission were not significant. In the subset of patients without earlier exposure to NRTI mono or dual therapy, low CD4 cell count (HR 0.48; 95% CI, 0.31–0.75 by 100 cells/ $\mu\text{l}$  higher up to 500 cells/ $\mu\text{l}$ ,

$P = 0.001$ ) and prior AIDS (HR 3.78; 95% CI, 1.32–10.81;  $P = 0.01$ ) were independent predictors of treatment failure. In 185 patients without earlier exposure to NRTI mono or dual therapy, without AIDS and with a CD4 cell count at the time of the switch  $\geq 500$  cells/ $\mu\text{l}$  only one viral load failure and three deaths occurred in 550 person-years of follow-up.

Modelling the influence of CD4 cell count with a more flexible natural cubic spline with five degrees of freedom instead confirmed the effect of CD4 cell count on treatment failure (data not shown). Viral load at first prescription of any antiretroviral therapy was not included in the multiple regression analysis because it was measured a median time of 2.86 years prior to the switch to ABC/3TC/ZDV, not available for 141 (28%) of the patients and

**Table 2. Results of multiple Cox regression for time to treatment failure and time to treatment failure or abacavir/lamivudine/zidovudine (ABC/3TC/ZDV) stop.**

Parameter	Time to treatment failure			Time to treatment failure or ABC/3TC/ZDV stop		
	HR	95% CI	<i>P</i>	HR	95% CI	<i>P</i>
Age: by +10 years	1.33	0.98–1.79	0.07	0.95	0.83–1.09	0.46
Female gender	1.33	0.64–2.79	0.45	1.44	1.07–1.94	0.02
Transmission: IDU	1.18	0.40–3.50	0.76	1.03	0.62–1.71	0.92
Basic education	1.11	0.57–2.17	0.76	1.06	0.77–1.46	0.70
Prior AIDS	1.66	0.84–3.27	0.15	1.22	0.88–1.71	0.23
Prior hepatitis C	1.68	0.61–4.65	0.32	1.51	0.95–2.40	0.09
Earlier exposure to NRTI mono or dual therapy for $\geq 30$ days	8.02	4.19–15.35	$< 0.001$	1.58	1.17–2.12	0.003
Previous cART: NNRTI	1.33	0.67–2.63	0.41	0.96	0.70–1.31	0.80
CD4 cell count at ABC/3TC/ZDV start						
by +100 (up to 500 cells/ $\mu\text{l}$ )	0.66	0.51–0.87	0.003	1.03	0.89–1.19	0.73
by +100 ( $> 500$ cells/ $\mu\text{l}$ )	1.06	0.90–1.25	0.47	0.96	0.90–1.03	0.25

cART, combination antiretroviral therapy; CI, confidence interval; HR, hazard ratio; IDU, injection drug use; NNRTI, non-nucleoside reverse transcriptase inhibitor; NRTI, nucleoside reverse transcriptase inhibitor.

not significant in univariate and multivariate complete-case analyses ( $P=0.75$  and  $0.85$ , respectively). Including current intravenous drug use as a covariate also did not significantly improve the fit (data not shown). In an exploratory analysis, nonsuppressed viral load under earlier ART was included as an additional covariate and it was highly statistically significant (HR 3.88; 95% CI, 1.91–7.88;  $P<0.001$ ); the covariates earlier exposure to NRTI mono or dual therapy and low CD4 cell count at the time of the switch remained significant in this extended model. The effect of earlier nonsuppressed viral load under ART was constrained to patients with prior exposure to mono or dual NRTI therapy as only five other patients were previously nonsuppressed under ART and none of them experienced treatment failure.

Sensitivity analyses which slightly varied the primary endpoint (either counting any increase in viral load to levels  $>400$  copies/ml as an event or censoring AIDS and death cases instead of counting them as events) or which included patients with a documented viral load  $<50$  copies/ml at the time of the switch only lead to highly consistent results with similar effect sizes. Earlier exposure to mono or dual therapy remained an independent predictor for time to treatment failure or stopping ABC/3TC/ZDV for any reason (HR 1.58, 95% CI, 1.17–2.12;  $P=0.003$ ) and female patients were more likely to have an event (HR 1.44; 95% CI, 1.07–1.94;  $P=0.02$ ).

Prior to start of ABC/3TC/ZDV, 107 resistance tests from 98 (20%) patients were documented: 56 were taken while the patient was treatment naive, five while on a treatment interruption, 36 while on cART, nine while on NRTI mono or dual therapy and one while on PI-monotherapy. Mutations associated with multi-NRTI or ABC/3TC/ZDV resistance were detected in 16 of these resistance tests (nine while on single PI cART, six while on NRTI mono or dual therapy, one while on PI-monotherapy): 6·M41L, 7·D67N, 7·K70R, 6·M184V, 1·L210W, 7·T215Y, 1·T215E, 4·K219Q, 2·K219E. Nine of the 98 patients (six of them with prior mutations) subsequently experienced treatment failure.

Resistance tests after viral rebound but prior to stopping ABC/3TC/ZDV were available for 27 (69%) of the 39 patients – 18 of these 27 patients had earlier exposure to NRTI mono or dual therapy for  $\geq 30$  days and 11 had documented nonsuppressed viral load on earlier ART (nine of them under earlier NRTI mono or dual therapy). Only three patients had no documented multi-NRTI or ABC/3TC/ZDV mutations; the most frequent mutations were 24·M184V, 15·M41L, 14·D67N, 13·T215Y, 12·K70R and 10·L210W (Table 3). In five patients with prior mono- or dual-NRTI having resistance tests performed before ABC/3TC/ZDV initiation and after viral rebound, both earlier mutations and newly emergent mutations after treatment failure were detected in all subjects.

**Table 3. Genotypic resistance after treatment failure and before abacavir/lamivudine/zidovudine (ABC/3TC/ZDV) discontinuation, available in 27 (69%) of the 39 patients experiencing viral rebound.**

	Frequency	(%)
Mutations associated with multi-NRTI or ABC/3TC/ZDV resistance		
M41L, M184V, L210W, T125Y	4	15
M184V	3	11
M41L, D67N, M184V, L210W, T125Y	3	11
D67N, K70R, M184V, K219Q	2	7
M41L, D67N, K70R, M184V, L210W, T125Y	2	7
D67N, K70R, M184V, K219E	1	4
D67N, K70R, M184V, T125F	1	4
D67N, K70R, Y115F, M184V, K219Q	1	4
K70R, M184V, K219E	1	4
M41L, D67N, K70R, M184V, T125F, K219E	1	4
M41L, D67N, K70R, M184V, T125F, K219Q	1	4
M41L, D67N, K70R, M184V, T125Y, T125F, K219E	1	4
M41L, D67N, M184V, T125Y	1	4
M41L, K70R, M184V, L210W, T125Y	1	4
M41L, M184V, T125Y	1	4
Wild-type virus	3	11

NRTI, nucleoside reverse transcriptase inhibitor.

## Discussion

In this analysis of the SHCS we investigated 495 patients with successful suppression of viral load who switched to ABC/3TC/ZDV. We confirmed a higher failure rate of ABC/3TC/ZDV in patients with earlier exposure to NRTI mono or dual therapy in comparison with patients without [1,3,4,15,19]. Failure rates decreased with increasing exposure to ABC/3TC/ZDV and 62% of the observed events occurred in the first year of therapy. In a multiple Cox regression analysis low CD4 cell count and in the subset of patients without earlier exposure to mono or dual NRTI therapy prior AIDS were additional risk factors for treatment failure. In exploratory analyses, earlier nonsuppressed viral load under ART was an additional risk factor for patients with prior NRTI mono or dual therapy.

We confirmed that failure rates under ABC/3TC/ZDV were low; indeed, our observed failure rates were rather lower in comparison with other publications where the rate of viral rebound rate per 100 person-years under ABC as the 'third' drug ranged from 3.4 to 7.9 in pre-cART naive and 9.9 to 18.6 in pre-cART NRTI experienced patients [14,15,19]. One possible explanation for our findings is the longer follow-up period of patients in our study with decreasing failure rates over increasing exposure time to ABC/3TC/ZDV. Another explanation may be that patients in our study were more conservatively selected as evidenced by the high median CD4 cell count of 521 cells/ $\mu\text{l}$  at the time of the switch to ABC/3TC/ZDV.

Data from this analysis indicate that CD4 cell count below 500 cells/ $\mu\text{l}$  at the time of switching to ABC/3TC/ZDV was predictive for treatment failure even when AIDS

cases and deaths were censored in sensitivity analyses. This important finding has not been previously documented and if confirmed in other cohort studies should guide clinicians to carefully consider whether to switch patients with lower CD4 cell counts to ABC/3TC/ZDV.

Independent predictors for the secondary endpoint (time to treatment failure or stop of ABC/3TC/ZDV for any reason) were earlier exposure to NRTI mono or dual therapy and female gender. Females had similar rates of treatment failure but stopped ABC/3TC/ZDV therapy more frequently.

Resistance testing among ABC/3TC/ZDV patients with viral rebound showed mutations associated with NRTI resistance in 89% of available sequences. The observed resistance pattern consisted almost exclusively of thymidine analogue mutations (TAM) in combination with the M184V mutation and it is known that such resistance mutations can be present in archived form in patients who were previously on incompletely suppressive cART and may re-emerge during a subsequent virologic failure on ABC/3TC/ZDV [1]. As has previously been shown, neither the ABC-associated K65R mutation nor the L74V mutation were selected in the presence of ABC/3TC/ZDV [20,21]. The lack of selection of these mutations in the presence of ZDV is due to a bidirectional antagonism between K65R and TAMs [22].

The strength of our analysis is the inclusion of a well defined patient population with suppressed viral load at baseline and then being switched to ABC/3TC/ZDV therapy. We excluded patients with initial triple nucleoside therapy with ABC/3TC/ZDV because it has been shown to be inferior to NNRTI regimens in randomized, clinical trials [9]. Our long-term follow-up data with a median follow-up of over 3 years further support the continued virologic efficacy of ABC/3TC/ZDV in patients who switch to this regimen without a history of prior NRTI mono or dual therapy and are in agreement with other published long-term data [23,24].

Finally, there are several important limitations of the present study. While adherence information is known to be associated with optimal viral suppression [25], this information has only been collected within the SHCS since 2003 and could thus not be included in our analysis. We did however include education and current intravenous drug use, which were correlated with nonadherence (defined as taking < 95% of doses) [25] in the primary or sensitivity analyses. Second, viral load measurements at start of first ART were missing for 141 patients mainly due to registration into the SHCS after ART initiation or initiation of ART prior to July 1995. In addition, results from resistance tests prior to the start of ABC/3TC/ZDV were only available in a subset of 98 patients and the available resistance data does not allow the rigorous determination of whether resistance was

acquired previously or under ABC/3TC/ZDV. Third, the rate of patients stopping ABC/3TC/ZDV without prior treatment failure was relatively high. We censored these patients for our primary analysis and used standard survival analysis which requires non-informative censoring, that is the assumption that censored patients would have had the same failure rate if they had stayed on ABC/3TC/ZDV as those remaining at risk. This assumption may, however, only be approximately true. Fourth, we decided not to define a comparator regimen in our study. Although our study population was based on individuals with suppressed viral load at baseline indicating sufficient drug adherence, the characteristics determining the choice of different simplification regimens may be related to the subsequent propensity to experience viral rebound. For example, only five out of 397 patients without prior exposure to NRTI mono or dual therapy experienced earlier nonsuppressed viral load under cART in our study population. On the other hand, intravenous drug users with higher adherence problems in methadone substitution programs may be more likely switched to a triple nucleoside regimen due to drug-drug interactions from NNRTI-based regimens and methadone and thus experience higher failure rates. Such bias can only be controlled by a randomized controlled trial design. Given the observational nature of the present dataset we therefore abstained from choosing a comparison group. Finally, other criteria than treatment failure should also be considered when deciding whether a patient can be switched to ABC/3TC/ZDV. We did not look into metabolic changes associated with switches to triple nucleoside therapy with ABC/3TC/ZDV but previous studies have shown that triple nucleoside therapy with ABC/3TC/ZDV is associated with more favorable lipid profiles [1–5]. On the other hand, extended exposure to zidovudine may contribute to lipodystrophy although the risk is lower compared to patients on stavudine [26].

In conclusion, observed treatment failure rates on ABC/3TC/ZDV were low. In patients with suppressed viral load and normalized CD4 cell counts and without earlier exposure to NRTI mono or dual therapy or prior AIDS, the combination ABC/3TC/ZDV remains an effective maintenance regimen.

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