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Predictors of Late Virologic Failure After Initial Successful Suppression of HIV Replication on Efavirenz-based Antiretroviral Therapy

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Abstract

Background—Practical issues, including cost, hinder implementing virologic monitoring of patients on antiretroviral therapy (ART) in resource-limited settings. We evaluated factors that might guide monitoring frequency and efforts to prevent treatment failure after initial virologic suppression.

Methods—Participants were the 911 HIV-infected antiretroviral-naïve adults with CD4 count <300 cells/μL who started efavirenz-based ART in the international A5175/PEARLS trial and achieved HIV-1 RNA <1,000 copies/mL at 24 weeks. Participant report of ART adherence was evaluated using a structured questionnaire in monthly interviews. Adherence and readily available clinical and laboratory measures were evaluated as predictors of late virologic failure (late VF: confirmed HIV-1 RNA ≥1,000 copies/mL after 24 weeks).

Results—During median follow-up of 3.5 years, 82/911 participants (9%) experienced late VF. Of 516 participants reporting missed doses during the first 24 weeks of ART, 55 (11%) experienced late VF, compared with 27 (7%) of 395 participants reporting no missed doses (hazard ratio: 1.73; 95% CI: 1.08, 2.73). This difference persisted in multivariable analysis, in which lower pre-ART hemoglobin and absence of Grade 3 laboratory results prior to week 24 were also associated with higher risk of late VF.

Discussion—In this clinical trial, the late VF rate after successful suppression was very low. If achievable in routine clinical practice, virologic monitoring involving infrequent (e.g. annual)

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Adherence to ethics: Written informed consent was obtained from all participants, and the human experimentation guidelines of the United States Department of Health and Human Services were followed. The study was approved by local Ethics Committees at each participating institution in the A5175/PEARLS study.

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measurements might be considered; the implications of this for development of resistance need evaluating. Patients reporting missed doses early after ART initiation, despite achieving initial suppression, might require more frequent measurement and/or strategies for promoting adherence.

Keywords

Antiretroviral therapy; adherence; viral load monitoring; resource-limited settings; virologic suppression; virologic failure

INTRODUCTION

Guidelines for antiretroviral treatment (ART) for HIV-infected patients recommend monitoring response to ART and the diagnosis of treatment failure using measurements of viral load.^{1–3} Current United States guidelines recommend frequent monitoring first to establish an initial virologic response after starting or changing ART, and then every 3 to 4 months to confirm continuous suppression, with possible reduction to every 6 months for adherent stable patients whose viral load has been suppressed for more than two years.³ In contrast, current World Health Organization (WHO) guidelines recommend viral load measurements at 6 months after starting ART and then at least every 12 months as the monitoring approach to detect virologic failure (defined as two consecutive HIV-1 RNA measurements greater than 1,000 copies/mL).^{1,2} Even with the reduced frequency in WHO guidelines, practical issues including high cost have resulted in variable implementation of virologic monitoring in many resource-limited settings.

Virologic suppression is achieved in the large majority of patients within 6 months of first starting ART. Virologic monitoring after initial suppression aims at detecting virologic failure prior to accumulation of multiple resistance mutations that may compromise future treatment options, and prior to progression of HIV disease. Allocation of resources could be optimized if monitoring after initial suppression could be effectively targeted to patients at greater risk for virologic failure. A systematic review concluded that WHO clinical and immunologic criteria were insensitive for this purpose.⁴ Other studies have evaluated scoring systems based on more extensive immunologic, clinical, laboratory and adherence evaluations with modest improvements.^{5–8}

In this study, we use data from participants in a large clinical trial conducted in diverse geographical locations (ACTG A5175/PEARLS⁹) in a post hoc analysis to evaluate factors during the first 6 months of ART, particularly a participant's self-reported adherence to ART, that might predict treatment failure during three or more years after initial successful virologic suppression on efavirenz(EFV)-based ART. Such factors might then help identify patient subgroups at higher risk for treatment failure subsequent to initial suppression in which more frequent viral load monitoring and/or efforts to prevent treatment failure might be best used. This extends previous evaluation of adherence in the PEARLS study which focused on predicting virologic failure early during ART, so predominantly reflecting failure to achieve initial virologic suppression.¹⁰

METHODS

The AIDS Clinical Trials Group (ACTG) Prospective Evaluation of Antiretrovirals in Resource-Limited Settings (PEARLS; ClinicalTrials.gov NCT00084136) study was a phase IV, prospective, randomized, open-label evaluation of the efficacy of two once-daily EFV-based antiretroviral regimens and an atazanavir-based regimen for the initial treatment of HIV-1-infected individuals from nine countries: Brazil, Haiti, India, Malawi, Peru, South Africa, Thailand, United States, and Zimbabwe. The study design and primary outcomes have been previously reported.⁹ In brief, participants were 18 years old, had documented HIV-1 infection, had received no more than 7 days of cumulative prior ART (prior use of single-dose nevirapine or zidovudine for any duration to prevent mother-to-child transmission of HIV was allowed), and had a CD4 cell count <300 cells/ μ L within 90 days prior to entry into the study. The eligibility criteria also included hemoglobin ≥ 7.5 g/dL. Written informed consent was obtained from all participants, and the human experimentation guidelines of the United States Department of Health and Human Services were followed. The study was approved by local Ethics Committees at each participating institution.

The results presented here are restricted to participants who were randomized to receive one of the two EFV-based regimens: lamivudine and zidovudine with EFV (3TC/ZDV+EFV), or emtricitabine and tenofovir with EFV (FTC/TDF+EFV). This was because the Data and Safety Monitoring Board recommended stopping treatment with the atazanavir-based regimen due to inferiority and this regimen is not recommended for use in clinical practice. As the focus of our study was to evaluate treatment failure following initial response to ART, we further restricted the study population to participants who had a plasma HIV-1 RNA measurement <1,000 copies/mL at 24 weeks after starting ART with no virologic failure or AIDS-defining event during the first 24 weeks of ART. Changes in one or more drugs at or prior to week 24 did not lead to exclusion from the study population.

Plasma HIV-1 RNA was measured prior to starting ART, and then at weeks 4 and 8 and every 8 weeks thereafter through the end of study follow-up. A standard questionnaire^{10,11} was used to obtain a participant's self-report of adherence to ART at weeks 2 and 4 and then every 4 weeks through to week 24 after starting ART, and every 8 weeks thereafter. This questionnaire included multiple questions about whether any dose of each drug was missed on each of the prior three days, during the past weekend, or during the previous two weeks. In addition participants were asked when they last missed taking any of their anti-HIV medications, if at all. Adherence counseling by trained site personnel was conducted prior to starting ART using a checklist of discussion points, and as needed at follow-up visits at the discretion of the site investigator.

For this report, the outcome of interest is "late" virologic failure, defined as two successive measurements of plasma HIV-1 RNA $\geq 1,000$ copies/mL, with the first measurement more than 24 weeks after starting ART, so following the week 24 HIV-1 RNA measurement which had to be <1,000 copies/mL. As possible predictors of late virologic failure, we considered variables which would often be routinely available in clinical practice prior to starting ART or obtained during the first 24 weeks of ART: demographic (age, sex, country); pre-ART

disease status (CD4 count, log₁₀ HIV-1 RNA and clinical status including prior or active AIDS or tuberculosis [TB], hepatitis B infection, Karnofsky Score, weight, and body mass index [BMI]); pre-ART laboratory test results (creatinine clearance, albumin, hemoglobin; and platelet, absolute neutrophil, absolute lymphocyte and white blood cell counts); changes in disease status from pre-ART to week 24 (change in CD4 count, HIV-1 RNA at week 24 classified as 400 versus 401 to 999 copies/mL, change in weight, and change in BMI); initial ART regimen (TDF/FTC+EFV or ZDV/3TC+EFV); ART changes, Grade 3 or 4 laboratory test results and Grade 3 or 4 signs and symptoms during the first 24 weeks of treatment (graded according to the DAIDS Toxicity Tables¹²); and participant's self-reported adherence to ART (categorized as report of missed versus no missed doses at any of the evaluations through to 24 weeks after starting ART).

Statistical analysis used proportional hazards models to evaluate possible predictors of late virologic failure. Censoring of follow-up was at the last available HIV-1 RNA measurement. Age and laboratory measurements were included as continuous variables; linearity assumptions appeared reasonable based on standard graphical and residual plots. Variables that achieved $p < 0.10$ in univariable analysis were considered for inclusion in multivariable analysis using stepwise variable selection with $p < 0.10$ required for variable retention in the model and $p > 0.10$ for removal. The models were extended to check for effect modification (interaction) between included variables and randomized treatment.

RESULTS

Of the 1045 participants randomized to receive TDF/FTC+EFV or ZDV/3TC+EFV, 911 (87%) had plasma HIV-1 RNA $< 1,000$ copies/mL at week 24 and were included in our study population. The reasons for excluding the other 134 participants were: virologic failure at or prior to week 24 ($n = 64$ participants), plasma HIV-1 RNA $> 1,000$ copies at week 24 ($n = 18$), new AIDS-defining event prior to week 24 ($n = 3$), death prior to week 24 ($n = 11$), loss to follow-up at or before week 24 ($n = 28$), and no plasma HIV-1 RNA measurement at week 24 ($n = 10$). Table 1 summarizes characteristics of the 911 participants prior to starting ART and after 24 weeks of ART.

At the time of closure of follow-up of the randomized trial, participants had been followed for a median of 184 weeks (3.5 years) from starting ART. During this time, 82 (9%) of the 911 participants experienced late virologic failure. Among the remaining 829 participants, 7% were lost to follow-up and 3% died without experiencing late virologic failure. Figure 1, panel A, shows the cumulative incidence of late virologic failure. The late virologic failure rate appeared slightly higher (3%) during the period from 24 to 48 weeks after starting ART, but was reasonably constant thereafter (about 3% per year).

Participants who reported missing doses during the first 24 weeks of ART had significantly higher risk of late virologic failure compared to participants who reported no missed doses ($p = 0.023$; Figure 1, panel B). Specifically, 55 (10.7%) of the 516 participants reporting missed doses experienced late virologic failure compared with 27 (6.8%) of the 395 participants reporting no missed doses. The absolute difference between participants

reporting missed versus no missed doses appeared to increase during the four years of follow-up after starting ART.

Among the other possible predictors of late virologic failure evaluated (see Methods), lower pre-ART hemoglobin ($p=0.025$), lower pre-ART absolute neutrophil count ($p=0.044$) and higher pre-ART white blood cell count ($p=0.026$) were also significantly associated with higher risk of late virologic failure. Associations for higher risk with older age and with higher pre-ART albumin level, and for lower risk among participants with a Grade 3 laboratory test result during the first 24 weeks of ART also met the statistical criterion ($p<0.10$) for consideration for inclusion in the multivariable analysis. There were no significant associations with demographic variables (age, sex, country) or disease status variables including plasma HIV-1 RNA at baseline or week 24 (the latter categorized as 400 versus 401–999 copies/mL) and CD4 count at baseline or week 24. In addition, the proportion of participants experiencing late virologic failure was not significantly different between the two randomized regimens (42 of 417 [9.2%] for 3TC/ZDV+EFV versus 40 of 412 [8.9%] for FTC/TDF+EFV; hazard ratio: 1.05, 95% confidence interval: 0.68 to 1.62).

In multivariable analysis, participant report of missed doses and lower pre-ART hemoglobin were significantly associated with increased risk of late virologic failure, while a grade 3 laboratory test result during the first 24 weeks of ART was significantly associated with lower risk (Table 2). For each of these three factors, the unadjusted hazard ratios (from univariable analysis) and the adjusted hazard ratios (from multivariable analysis) were very similar suggesting minimal confounding of these associations. In particular, participant report of missed versus no missed doses was associated with 72% and 73% increases in risk of late virologic failure in unadjusted and adjusted analysis. Panels B, C and D of Figure 1 show the cumulative incidence of late virologic failure by time for these three factors (categorizing, for illustration, pre-ART hemoglobin level as above or below the median level of 12.4 g/dL). There was no significant evidence that these associations varied between the two EFV-based randomized treatments. Very similar results were obtained in a sensitivity analysis which was restricted to participants who remained on their randomized ART at week 24. In addition, the associations with self-reported adherence and with pre-ART hemoglobin were very similar in an analysis restricted to participants who did not have a grade 3 laboratory test result during the first 24 weeks of ART.

Table 3 provides a summary of how the model results might be used to suggest a range of simple decision rules for identifying a subgroup of participants at higher risk of late virologic failure in which more frequent monitoring and/or efforts to prevent failure might be best used. Again, for simplicity of illustration, pre-ART hemoglobin level is categorized as above or below the median level of 12.4 g/dL. For example, the multivariable model might suggest the subgroup of participants who reported missed doses, had a pre-ART hemoglobin (less than the median of 12.4 mg/dL is used in the table), and did not have a Grade 3+ laboratory result during the first 24 weeks of ART. For this subgroup, shown in the first row of the table, 195 (21%) of the 911 participants met all three criteria including 30 (37%) of the 82 participants who experienced late virologic failure during follow-up (the 37% is equivalent to the sensitivity of the decision criterion). In this subgroup, 30 (15.4%) of

the 195 participants experienced late virologic failure. As would be expected, as the criteria are relaxed so increasing the size of the subgroup identified, the sensitivity increases.

DISCUSSION

In this multinational clinical trial setting, the rate of late virologic failure after successful virologic suppression on EFV-containing ART was low, about 3% per year. A similarly low rate has been reported among patients initiated on public sector EFV- or nevirapine-based ART in South Africa.¹³ If such low rates are achievable more generally in clinical practice and for other regimens, then less frequent virologic monitoring such as annual monitoring (as suggested in current WHO guidelines) might be reasonable. For example, if the rate of late virologic failure is 3% per year, then annual monitoring would delay detection of virologic failure by 6 months for 1.5% of patients each year but at the expense of twice as much virologic monitoring. The major downside of less frequent monitoring is the increased risk of viral resistance mutations leading to decreased future treatment options and increased risks of disease progression and transmission of resistant virus.^{14,15} The risks associated with cost savings in less frequent virologic monitoring then need balancing against the potential benefits of having more resources available to increase drug availability, adherence to treatment, and retention in care. Further exploration of these competing issues is needed, building on cost effectiveness modelling of ART monitoring strategies in the resource limited setting.¹⁶

Motivated by the idea that more intensive virologic monitoring might be best used among patients at increased risk of late virologic failure, we evaluated a variety of possible predictors of late virologic failure that are routinely available in clinical practice. However, we found few variables that were statistically significant predictors in multivariable analysis. Of note, despite achieving plasma HIV-1 RNA <1,000 copies/mL after 24 weeks of ART, study participants who reported missed doses during the first 24 weeks appeared to have an ongoing increased risk of late virologic failure over several years (Figure 1, panel B). This confirms findings from a smaller study undertaken in South Africa using a similar questionnaire to obtain patient-reported adherence.¹⁷ Having increased frequency of virologic monitoring for those that report missed doses might therefore be reasonable. In addition, this finding emphasizes the need for ongoing adherence support systems for patients who report missed doses despite achieving initial virologic suppression as a possible approach for reducing late virologic failure rates.

Lower pre-ART hemoglobin level was associated with higher risk of late virologic failure despite the fact that the large majority of study participants had normal levels (median: 12.4 g/dL; inter-quartile range: 11.2 to 13.8 g/dL). The mechanism for this is unclear. While it could reflect increased risk for ART- and/or disease-related adverse events leading to poorer adherence or treatment interruptions around ART changes, the effect persisted in multivariable analysis adjusted for adherence and persisted in analysis restricted to participants who did not change ART. Other studies suggest associations of hemoglobin with virologic failure: greater decreases in hemoglobin, though not pre-ART hemoglobin levels, were predictive of late virologic failure in a case-control study of patients initiating ART in South Africa;⁷ and hemoglobin decreases were associated with virologic failure in a cross-

sectional study among Cambodian patients on first-line ART.⁵ In addition, lower pre-ART hemoglobin levels have been associated with increased mortality among patients starting ART in sub-Saharan Africa.¹⁸ Hemoglobin levels were not collected in the database during follow-up in the A5175 trial (except in the presence of Grade 3 levels) so we are not able to explore further the importance of changes in hemoglobin for predicting late virologic failure.

Our study also found that participants who experienced a grade 3 or higher laboratory test result during the first 24 weeks of ART were at lower risk of late virologic failure. This finding persisted in a sensitivity analysis restricted to participants who did not have a change in their ART during the first 24 weeks and so the association is not explained by ART change. This finding was not expected and might reflect chance given the large number of associations evaluated. Alternatively, laboratory test abnormalities might reflect higher drug concentrations within study participants for pharmacokinetic reasons or better adherence not captured by a participant's self-report, which might also then be associated with more potent virologic suppression.

Based on the three variables included in the multivariable model, we evaluated simple criteria for identifying a subgroup of study participants at higher risk of late virologic failure (Table 3). In clinical practice, such a subgroup might be identified for more frequent virologic monitoring or adherence-based intervention. A key finding, also apparent in other studies,^{5–8} is that to achieve high sensitivity, that is to identify a subgroup which included the large majority of participants who experienced late virologic failure, the subgroup also included a large majority of participants. For example, the subgroup of participants who reported missed doses or who had a pre-ART hemoglobin <12.4 mg/dL included 82% of participants who experienced late virologic failure (sensitivity of 82%) but also included 78% of participants. Of note in this example, the observed sensitivity was also little different from what would be achieved by taking a random sample of 78% of participants. These findings provide support for a strategy of virologic monitoring for all patients rather than restricting monitoring to a particular subgroup. The risk factors for late virologic failure that were identified might, however, be used to identify a smaller subgroup for more frequent virologic monitoring. For example, 39% of participants who experienced late virologic failure had lower pre-ART hemoglobin levels and reported missed doses during the first 24 weeks of ART (Table 3) suggesting that more frequent monitoring in this subgroup might be useful. The cost effectiveness of increased monitoring in selected patient subgroups needs exploration.¹⁶

Our study has some strengths and limitations. Strengths include the prospective follow-up with real-time measurement of plasma HIV-1 RNA at 2 month intervals over a median 3.5 year period, low rate of loss to follow-up,⁹ and diverse geographical settings which may increase the generalizability of results. Provision of adherence counselling at study entry using an evidence based approach,^{19,20} and as needed during follow-up (at the discretion of the site investigator), was intended to mimic how adherence counselling is often provided during routine care in antiretroviral treatment programs. However, the study used data from a clinical trial with clinical and laboratory assessments at more frequent intervals than in usual practice, as well as completion of a questionnaire by study participants about missed doses which might itself reinforce adherence. It is possible that the rate of late virologic

failure may be higher in routine clinical practice when clinic visits may be less frequent and so provide fewer opportunities to identify and resolve adherence issues. It is also possible that participants in a clinical trial differ from the general patient population and may be retained in care more readily. In addition, even though 82 participants experienced late virologic failure, the precision to estimate associations is somewhat limited. For example, the confidence interval for the hazard ratio comparing late virologic failure for 3TC/ZDV +EFV versus FTC/TDF+EFV was from 0.68 to 1.62, so modest true differences between regimens, for example due to twice- versus once-daily dosing, cannot be ruled out despite the fact that the observed rates were very similar. Finally, while we identified factors that were associated with increased risk of late virologic failure, it would be important to confirm these findings in general patient populations and to validate any algorithm for selecting a subgroup for increased frequency of monitoring also in general clinical practice.

CONCLUSIONS

In conclusion, our study showed an ongoing but low rate of late virologic failure over several years of follow-up (about 3% per year) among HIV-infected adults in diverse geographical locations who achieved plasma HIV-1 RNA <1,000 copies/mL at 24 weeks after starting EFV-based ART. For patients achieving initial virologic suppression, if such a low rate is achievable in general clinical practice, then less frequent virologic monitoring might be reasonable; however the implications of this for the accumulation of resistance mutations and cost effectiveness of ART programs should be evaluated further in clinical practice. Patients reporting missed doses early after ART initiation despite achieving virologic suppression were at increased risk of virologic failure over several years and so might be targeted for more frequent measurement and/or more intensive strategies for promoting adherence.

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Figure 1.

Cumulative percentage of participants experiencing late virologic failure by time from start of antiretroviral therapy (ART): all participants (A); by participant report of missed versus no missed doses during first 24 weeks of ART (B); by per-ART hemoglobin level (C); and by whether or not participant had a grade 3 or 4 laboratory abnormality during the first 24 weeks of ART.

Table 1

Characteristics of the study population (participants achieving plasma HIV-1 RNA <1,000 copies/mL at 24 weeks after starting efavirenz-based antiretroviral therapy)

Characteristic	Summary statistic (n=911)
Male sex, n (%)	491 (54)
Age, years, median (quartiles)	34 (29, 41)
Country, n (%)	
India	152 (17)
Brazil	145 (16)
South Africa	121 (13)
United States	114 (13)
Malawi	111 (12)
Peru	79 (9)
Zimbabwe	66 (7)
Thailand	65 (7)
Haiti	58 (6)
Pre-ART HIV-1 RNA, copies/mL, median (quartiles)	105,000 (38,480, 261,330)
Pre-ART CD4 count, cells/ μ L, median (quartiles)	168 (89, 232)
Pre-ART hemoglobin, g/dL, median (quartiles)	12.4 (11.2, 13.8)
Pre-ART history of AIDS, n (%)	102 (11)
Initial ART, n (%)	
TDF/FTC+EFV	452 (50)
ZDV/3TC+EFV	459 (50)
Participant-report of missed ART doses during first 24 weeks of ART, n (%)	516 (57)
Week 24 HIV-1 RNA, n (%)	
400 copies/mL	896 (98)
401–<1,000 copies/mL	15 (2)
Week 24 CD4 count, cells/ μ L, median (quartiles)	284 (200, 380)
Change in CD4 count from pre-ART to week 24, cells/ μ L, median (quartiles)	118 (66, 185)
Grade 3 or 4 laboratory abnormality during first 24 weeks of ART, n (%)	111 (12)

Note: ART=antiretroviral therapy; TDF=tenofovir; FTC=emtricitabine; EFV=efavirenz; ZDV=zidovudine; 3TC=lamivudine.

Table 2

Results from univariable and multivariable analyses for participant characteristics predicting late virologic failure that were included in the multivariable model (n=911, including 82 with late virologic failure).

Characteristic	Category	Number	Number (%) with late virologic failure	Unadjusted ^b hazard ratio (95% CI) p-value	Adjusted ^b hazard ratio (95% CI) p-value
Participant-reported ART adherence during first 24 weeks of ART	Missed doses	516	55 (10.7)	1.73 (1.08, 2.73) p=0.023	1.72 (1.08, 2.72) p=0.022
	No missed doses ^a	395	27 (6.8)		
Grade 3 or 4 laboratory abnormality during first 24 weeks of ART	Yes ^c	111	5 (4.5)	0.45 (0.18, 1.12) p=0.085	0.40 (0.16, 0.98) p=0.046
	No ^d	800	77 (9.6)		
Pre-ART hemoglobin	per 1 g/dL lower			1.14 (1.02, 1.29) p=0.025	1.18 (1.04, 1.33) p=0.008

Note: ART=antiretroviral therapy; CI=confidence interval.

^aReference category for hazard ratio.

^bUnadjusted hazard ratio is from univariable analysis; adjusted hazard ratio is from multivariable analysis including all three characteristics as predictor variables.

^cAmong the 111 participants with Grade 3 or 4 laboratory abnormalities, 57% had Grade 3 or 4 absolute neutrophil counts, 14% had Grade 3 or 4 hemoglobin values, and 13% had Grade 3 or 4 alanine transaminase (ALT) and/or aspartate aminotransferase (AST) levels; other abnormalities occurred in fewer than 10% of these participants.

Table 3

Performance of simple algorithms for identifying participants at risk of late virologic failure based on information available at 24 weeks

Criterion for selecting subgroup of participants for VL testing after 24 weeks of ART	Number (%) of the 911 participants meeting criterion	Number (%) of the 82 participants with late VF meeting criterion (sensitivity)	Percentage of participants meeting the criterion who experienced late VF
Reported missed doses AND per-ART hemoglobin <12.4 mg/dL AND no Grade 3+ lab abnormality	195 (21)	30 (37)	15.4
Reported missed doses AND pre-ART hemoglobin <12.4 mg/dL	237 (26)	32 (39)	13.5
Pre-ART hemoglobin <12.4 mg/dL AND no Grade 3+ lab abnormality	366 (40)	41 (50)	11.2
Pre-ART hemoglobin <12.4 mg/dL	434 (48)	44 (54)	10.1
Reported missed doses AND no Grade 3+ lab abnormality	452 (50)	53 (65)	11.7
Reported missed doses	516 (57)	55 (67)	10.7
Reported missed doses OR pre-ART hemoglobin <12.4 mg/dL	713 (78)	67 (82)	9.4
No Grade 3+ lab abnormality	800 (88)	77 (94)	9.6
All participants	911 (100)	82 (100)	9.0

Note: VF=virologic failure.