Published in final edited form as:

J Clin Virol. 2018 August ; 105: 11–17. doi:10.1016/j.jcv.2018.05.008.

Accumulated Pre-Switch Resistance to More Recently Introduced One-Pill-Once-a-Day Antiretroviral Regimens Impacts HIV-1 Virologic Outcome

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Abstract

Background—One-pill-once-a-day regimens (OPODs) appeal to providers and patients. The impact of resistance to OPODs in routine clinical care is important yet unclear, particularly in treatment-experienced patients.

Objectives—We hypothesized that resistance to any OPOD component impacts treatment success and that historical, vs. most recent, resistance better predicts it.

Study Design—In the largest RI HIV Center, we identified all patients starting/switching to Complera/Stribild, evaluated their 12-month viral load (VL) suppression, and examined the impact of demographic, clinical and laboratory data on it, focusing on recent-only vs. accumulated significant resistance, defined as low-, intermediate- or high-level predicted resistance to any OPOD component. Associations with outcomes were evaluated using Fisher exact and Wilcoxon rank sum tests. Hypotheses were tested using logistic regression.

Results—Of 1,624 patients, 224 started/switched to Complera or Stribild, mean age 44 years, 8 years post-diagnosis, CD4 468 cells/μL; 183 treatment-experienced (140 with genotypes; 61% suppressed at switch). Significant OPOD-associated resistance was in 30% by recent-only genotypes, and 38% by all genotypes. 12-month VL suppression was in 83% of treatment-experienced participants: 96% of suppressed at switch, associated with older age, higher CD4, fewer prior genotypes, less accumulated resistance, and better adherence; and 61% of unsuppressed at switch, associated with better adherence. Accumulated resistance independently predicted 12-month failure, better than most-recent resistance only.

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Competing interests: the authors have none to declare.

Ethics approval: Ethics approval was granted by the Institutional Review Board of The Miriam Hospital, Lifespan.

Conclusion—12-month VL suppression to Complera/Stribild was high, suggesting that OPODs remain options even for experienced patients. Clinicians should consider resistance history before switching to OPODs and continue to focus on improving adherence.

Keywords

accumulated drug resistance; HIV-1; anti-retroviral therapy

Background

Antiretroviral therapy (ART) adherence is a major challenge to sustained virologic suppression[1]. Atripla (tenofovir disoproxil fumarate (TDF), emtricitabine, efavirenz), the first one-pill-once-a-day (OPOD) regimen, has appealed to providers and patients since 2006, with improved ease of use and virologic suppression compared to multi-pill regimens[2–8]. Complera (rilpivirine, TDF, emtricitabine) and Stribild (elvitegravir, cobicistat, TDF, emtricitabine) became additional OPOD options in 2011 and 2012[9,10], addressing Atripla's limitations, mostly side-effects, teratogenicity concerns, and low genetic resistance barrier[11]. Recently, Triumeq, Genvoya and Odefsey became additional options, extending the OPOD armamentarium.

Transmitted and acquired resistance are potential consequences of poor adherence and causes of ART failure[12]. Current guidelines recommend resistance testing at diagnosis/ART start and upon failure to guide regimen design[13], and inclusion of three active drugs from two or more classes[14–18]. With ART development, patients were exposed to multiple drugs to decrease toxicity and improve adherence. Indeed, OPOD use increased from 7% in 2006 to 27% in 2013, with high efficacy and tolerability[3,7,19–22]. However, data on impact of resistance to any regimen component before start of/switch to OPODs, particularly newer ones, are limited, mostly due to inclusion criteria of no resistance in non-inferiority switch studies[23–26].

Objectives

To address this gap and evaluate resistance impact on treatment outcomes of newer OPODs, we investigated patients at the largest HIV Center in RI who started/were switched to Complera/Stribild and examined their baseline (pre-start/switch) resistance, 12-month viral suppression and their associations. We hypothesized that resistance to any OPOD component impacts 12-month outcomes; and that consideration of historical, not only most-recent, resistance better predicts suppression.

Study Design

Study Setting; Data Collection

The Immunology Center cares for >1,600 patients, ~70% of RI's HIV infections. We reviewed charts of all adults starting/switching to Complera/Stribild between 10/1/2011 and 4/30/2014 and collected demographic (age, gender), clinical (ART history, switch reasons to OPODs, genotype history, post start/switch clinic and medication adherence) and laboratory (VL, CD4, resistance) data. Suppression was defined as VL < 200 copies/mL. Clinic non-

adherence was defined as missing 50% of appointments in 12-month post OPOD initiation. Medication non-adherence was defined as lack of complete adherence in 1 clinic note post OPOD start. If such documentation was not found patients were considered adherent. The primary outcome was suppressed VL at 12+/- 4.5 months following OPOD initiation.

Data Analysis

All available protease, reverse transcriptase (RT) and integrase sequences before OPOD initiation were reviewed for presence of resistance. Sequence quality control was done with SQUAT[27]. Mutations and predicted susceptibility were derived from the Stanford Database[28]. The primary binary exposure was presence of low-, intermediate- or high-level predicted resistance to any OPOD medication in any genotype (termed significant accumulated resistance). Exposures examined in secondary analyses included intermediate (vs. low-level) resistance or higher and additional resistance measures: predictability of only most-recent genotypes before switch (vs. all prior genotypes), presence of M184I/V, and resistance to each OPOD-specific drug.

Associations between 12-month failure and clinical characteristics were evaluated using Fisher exact and Wilcoxon rank-sum tests, separately for three groups: ART-naïve, ART-experienced suppressed at OPOD initiation, and ART-experienced unsuppressed at OPOD initiation, due to expected fundamental differences between these populations. Since this study is observational, the outcome (12-month failure) and exposures (various resistance measures) for primary hypotheses evaluation are subject to confounding. Measures considered accountable for much of the confounding included: age, gender, OPOD initiation reason, VL at initiation, time on ART before initiation, number of prior regimens/year of ART, and number of prior genotypes/year of ART. For participants with <1 year documentation, values for number of regimens and genotypes/year were set to total numbers observed.

Hypotheses were tested using logistic regression with covariates for exposure and confounders as separate terms. As preliminary analyses, linearity of continuous terms was examined using generalized additive models with smoothed terms. Plots showing estimated relationships between values of covariates and log-odds of outcomes with standard errors were constructed for each term. If a straight line could easily fit, a linear relationship was assumed. Otherwise an appropriate transformation was considered. An attempt was made to fit three models to examine primary exposure on outcome: all participants; only treated participants; and only naive participants. For analyses of secondary exposures, only experienced participants were included; for rilpivirine, only switches to Complera were included.

As an additional secondary analysis, logistic regression was used to explore whether the effect of resistance on 12-month failure differed among those with/without medication non-adherence after OPOD initiation. This was evaluated using likelihood ratio tests to determine significance between the interaction between resistance and adherence.

Results

Patient Characteristics

Of 1,624 patients, 224 (14%; 40% female) started Complera (n=101) or Stribild (n=123), and formed the study population (Figure 1). Of these, 41 (18%) were ART-naïve (18 started Complera, 23 Stribild) and 183 (82%) were ART-experienced (83 switched to Complera, 100 Stribild). At OPOD initiation/switch, median age of the total population (40% female) was 44 years, median 8 years since HIV diagnosis, median 4 years on ART; and median CD4 468 cells/mm³. Of treatment-experienced patients, 61% were virologically suppressed at initiation. Reasons for switching to OPOD included adherence (31%), side-effects (31%), simplification (30%), and resistance (7%). Table 1 provides breakdown of participants' characteristics according to treatment status and resistance.

Pre-OPOD Initiation Resistance

Of 41 ART-naïve patients, prior protease-RT genotypes were available for 38. Of those, one had relevant OPOD resistance: a 42-year-old male with CD4 ~590 cells/mm³, VL ~165,000 copies/mL and NRTI mutations D67N, T215S and K219Q before Stribild; low-level predicted TDF resistance.

Of 183 ART-experienced patients switched to Complera/Stribild, prior protease-RT genotypes were available for 140; 68/140 had one genotype, median 3 years before OPOD initiation; and 72/140 had >1 genotype (median 3; range 2–16), median 4 years before OPOD initiation. There were few significant differences between the 43 without and 140 with genotypes, although a higher percentage of the former were suppressed at switch (81%-35/43 vs 55%-77/140).

When reviewing all prior genotypes from these 140 ART-experienced patients, 82 (59%) had resistance: 56 (40%) 1 OPOD-associated mutation, and 53 (38%) at least low-level resistance to 1 OPOD drug (considered “significant” here; 50 (94%) high-level; 1 (2%) intermediate-level; 2 (4%) low-level resistance; Figure 2). Thirty percent (16/53) had high-level resistance to 2 OPOD components.

When reviewing the most recent genotype only, 77 (55%) had resistance: 46 (33%) 1 OPOD-associated mutation, and 42 (30%) significant resistance to 1 OPOD drug (Figure 2). Compared to those starting Complera, significantly more patients starting Stribild had 1 mutation (p<0.01), but significant resistance to 1 drug in prescribed regimens was not significantly different (p=0.36). Specific mutations are in Figure 3.

Among patients switching to Stribild, 28% were previously exposed to integrase inhibitors; none had integrase genotyping.

12-month Virologic Outcome

Overall, 172/204 (84%) participants with 12-month VLs were suppressed. Participants with 12-month suppression had better medication adherence (91 vs. 33%, p=0.04) and appointment adherence (97 vs. 33%, p=0.01) compared with those not suppressed. Among

37/41 ART-naïve patients with 12-month VLs, 34 (92%) were suppressed, including the one patient with transmitted resistance.

Among 183 ART-experienced, 112 (61%) were suppressed and 67 (37%) had VL>200 at OPOD initiation (four were unknown). Of 163/183 with available 12-month VL, 135 (83%) were suppressed at 12-months (98/102 (96%) who were also suppressed at OPOD initiation; 37/61 (61%) with VL>200 at switch; Table 2). The four suppressed at initiation and failing at 12-months were younger and in care longer, and had lower CD4, more prior genotypes, higher percentages with accumulated resistance, and worse post-switch medication adherence vs. the 98 who remained suppressed ($p<0.05$, Table 2 asterisks). The 24 patients with VL>200 at OPOD initiation and at 12 months had lower post-switch medication adherence vs. the 37 who suppressed at 12-months ($p<0.001$, Table 2 asterisks). There were no significant differences in outcomes between those switched to Complera (64/75, 85% suppressed) and Stribild (71/88, 81%).

Predictors of 12-Month Treatment Failure

The primary hypothesis was that prior resistance to an OPOD component independently predicts 12-month failure. The ART-naïve model could not be fit for small sample size and because only 3 had 12-month failure. Including both naïves and treated in the model showed that accumulated resistance before OPOD initiation independently predicted 12-month failure (OR=5.96, CI=1.57 to 22.6, $p<0.01$). Interestingly, the most informative confounder was number of prior genotypes. There was a non-linear, quadratic shape to the relationship. Therefore, both linear and squared terms were included in the logistic regression analysis.

Table 3 shows relationships between 12-month VL (primary outcome) and both accumulated resistance (primary exposure) and immediate resistance only (secondary exposure) among experienced patients. Except for TDF, all measures of drug-specific accumulated resistance were independent and statistically significant positive predictors of 12-month failure. These results suggest that accumulated genotypes better predict failure vs. most recent genotype only. Some ORs (e.g. RPV resistance) could not be precisely measured as evidenced by very wide confidence-intervals.

Overall, post start/switch medication adherence was associated with 12-month suppression: 25/27 (93%) with prior resistance and adherent, and 91/96 (95%) without prior resistance and adherent; vs. 8/25 (32%) with prior resistance and nonadherence, and 9/16 (56%) without prior resistance and nonadherence. In the logistic regression analysis, those not adherent had 27.6 times the odds of failure vs. those who were adherent (CI=5.57 to 136.9). The interaction between prior resistance and adherence was not statistically significant, indicating that the effect of adherence on failure did not differ among those with/without prior resistance.

Potential drug-drug interactions did not play a role in these results: of 15/101 (15%) participants on Complera who were also on an H2 blocker/Proton Pump Inhibitor, two had 12 month virologic failure, both also were failing prior to switch, with medication non-adherence and one with pre-switch resistance (M184V); and of 6/123 (5%) participants on Stribild who were also on iron or cation containing vitamins, none had virologic failure.

Of the 51/53 treatment-experienced patients with pre-switch resistance and available 12-month VL, 32 (63%) were suppressed. M184I/V, a significant predictor of virologic outcome (Table 3), was the only resistance mutation in 22/51 (43%), of whom 12/22 (54%) were suppressed at 12 months. Suppression rates were not significantly different among those with M184I/V only and those with different resistance patterns ($p=0.38$).

Eleven of 53 (21%) patients with no significant OPOD resistance by most recent genotypes did have significant OPOD resistance per prior genotypes. Of these, six (54%) achieved 12-month viral suppression.

Discussion

OPODs are preferable by patients and providers to simplify ART. In this study of clinical uses of more recently-introduced OPODs, 14% of patients in the largest HIV RI Center started/switched to Complera/Stribild, mostly for pill-burden, side-effects, or adherence concerns. Despite 38% significant accumulated resistance to 1 OPOD component at switch, 83% of treated participants had 12-month suppression, supporting OPODs use, even among treatment-experienced patients, with improved outcomes for patients suppressed at switch and for those with improved medication and clinic attendance adherence. These data should reassure providers regarding OPODs use, and increase awareness to consider all prior genotypes in regimen design.

Data demonstrated here, of lower (63%) 12-month suppression in patients with at-switch resistance versus those without (92%), support our hypothesis that baseline resistance to any OPOD component impacts virologic outcome. These data confirm the benefit of resistance testing to guide regimen choice, demonstrated in several randomized trials[29–33], resulting in guidelines recommendation[13]; and extend them to newer OPOD options. Clinicians should be aware of the need to consider baseline resistance and diverse resistance spectrums in such instances.

Reliance on a single genotype results in underestimation of resistance and combined historical genotypes are more accurate[34]. This study confirms these observations in more current regimens and extends them by demonstrating the 12-month virologic outcomes impact. Accumulated resistance to OPOD components was predictive of failure, more so than the most recent genotype only. Moreover, after resistance, the number of prior genotypes was the most significant predictor of failure in multivariable analyses, suggesting that those with more genotypes may have had more episodes of failure or at least treatment changes. Among 53 treatment-experienced patients with OPOD resistance, 21% had no significant OPOD resistance by most recent genotypes, but did have resistance by accumulated genotypes, with nearly half failing therapy at 12 months. Added to a recent multi-center report from Italy on virologically-suppressed individuals switched to Complera, demonstrating the importance of prior ART regimens to the risk of failure[35], these data provide further guidance on optimization of the use of more recently-introduced OPODs. As HIV-infected patients live longer and are possibly exposed to multiple regimens, pre-switch consideration of full genotype histories to any OPOD component, particularly among

treatment-experienced patients, is important, even if special efforts are required to obtain them, like transferred care or change in medical record systems.

Integrase inhibitors have been introduced into clinical use relatively recently, and integrase resistance is included in guidelines[13]. However, integrase genotyping is often separately-ordered, as recognized in guidelines, and is also the case at the Immunology Center. This extra, separate step may be a barrier to inclusion of routine integrase genotyping. Indeed, here, integrase resistance was not included in analyses, despite Stribild containing elvitegravir, since no patients with integrase inhibitor experience had integrase genotyping before switch to Stribild. It was therefore not possible to evaluate the benefit of pre-switch integrase resistance on outcomes, though it may be assumed to be similar to protease/RT. With expected increased use of integrase inhibitors, clinician's attention to and awareness of integrase inhibitor genotyping should also increase.

In addition to resistance, VL status at switch was also an important predictor of outcome (of 40% not suppressed at switch 39% failed; of 60% suppressed at switch 4% failed). These results support reports that newer OPODs have good outcomes, even among treatment-experienced patients, however, prior studies included only virologically-suppressed patients at time of switch or excluded patient with prior resistance[19,23,24,36,37]. Expanding on this knowledge, the inclusion here of those not virologically-suppressed at switch resulted in 61% suppression at 12 months. These data confirm high benefit of Complera/Stribild in treatment-experienced suppressed individuals, and demonstrate their lower but existing potential benefit even in treatment-experienced failing individuals, while closely addressing resistance and adherence concerns, which may continue even with a simpler regimen. Importantly, proviral genotyping might detect the presence of archived resistance mutations in patients with suppressed HIV RNA before switching or in those with unavailable prior genotypes. The value of this test in clinical practice is still being evaluated[13].

Unsurprisingly, medication adherence was a major predictor, with 94% 12-month VL suppression in adherent vs 41% in non-adherent participants, regardless of pre-switch resistance. Notably, 63% of those with resistance were also successfully suppressed, including 11/14 (79%) with high resistance to 2 OPOD components. Post-switch adherence was clearly an important factor in these outcomes, with 93% suppression in adherent compared with 32% non-adherent individuals, despite pre-switch resistance. There is little literature to explain these observations, though re-suppression without regimen switch despite resistance has been reported[38,39]. OPOD benefit and improved adherence has also been demonstrated[7,20,21]. Additional studies are needed to explore these observations, however based on our findings, clinicians should continue to focus on improving adherence even with less active regimens, while considering full genotypic histories.

Main study limitations include small sample size, short, 12-month, follow up, and lack of a control group, which would have consisted of those starting/switching to non-OPOD regimens. Additionally, clinicians' knowledge of resistance upon switching could not be confirmed, and adherence evaluation was based solely on chart documentation.

In summary, this study provides clinic-level data on the use of Complera and Stribild in HIV care. In addition to OPOD use with no prior ART use, we demonstrate their potential for favorable 12-month virologic outcomes also in treatment-experienced individuals. This study highlights for clinicians the importance of being aware of all prior drug resistance tests as well as continuing the essential focus on adherence to optimize OPOD use.

Acknowledgments

Funding: This work is supported by the National Institutes of Health grants [R01-AI-108441], [P30-AI-042853] (Providence-Boston Center for AIDS Research), [R25MH083620], and [T32DA13911].

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Highlights

- Accumulated resistance mutations impact virologic outcome more than immediate resistance only
- One pill once a day regimens are good options for HIV treatment-experienced patients
- Good adherence to less active regimens associated with virologic suppression

Figure 1.

Study Population Flow Chart and Patient Characteristics at the Time of OPOD Initiation.

Resistance is defined as having low-level or higher predicted resistance to at least one medication in the patient's OPOD regimen over all accumulated genotypes.

Figure 2.

Drug resistance at the time of OPOD switch among 140 patients with prior treatment experience. Bars demonstrate any resistance (left Panel), OPOD-associated mutations (central Panel), and significant (at least low-level) predicted resistance (right Panel). Data are shown for the total population (black bars) and for the specific OPOD regimens (Stribild-dark gray bars; Complera-light gray bars); and stratified by recent genotypes only (solid bars) and all known genotypes (striped bars).

A. NNRTI mutations among the Complera treatment group

B. NRTI mutations among the Complera treatment group

C. NRTI mutations among the Stribild treatment group

Figure 3.

Drug resistance mutations at the time of OPOD switch among 140 patients with prior treatment experience. Bars demonstrate specific NNRTI-associated mutations in Complera recipients (Panel A), NRTI-associated mutations in Complera recipients (Panel B) and NRTI-associated mutations in Stribild recipients (Panel C). Data are stratified by association with (dark bars) or lack of association with (light bars) the specific OPOD patients were receiving

Table 1

Demographic, clinical and laboratory characteristics of participants according to treatment status and drug resistance.

Variable	Value	Total	Naive	Total Treated	Treated-no Resistance	Treated-Resistance	No Genotype Available
N		224	41	183	87	53	43
Regimen	Complera	101, 45%	18, 44%	83, 45%	45, 52%	17, 32%	21, 49%
	Stribild	123, 55%	23, 56%	100, 55%	42, 48%	36, 68%	22, 51%
Gender	Female	90, 40%	11, 27%	79, 43%	34, 39%	30, 57%	15, 35%
Age (years)		44 (18, 72),	37 (18, 61),	45 (20, 72),	42 (21, 65)	48 (20, 66)	48 (23, 72)
	21–34	63, 28%	18, 44%	45, 25%	29, 33%	8, 15%	8, 19%
	35–49	102, 46%	18, 44%	84, 46%	42, 48%	25, 47%	17, 40%
	>=50	59, 26%	5, 12%	54, 30%	16, 18%	20, 38%	18, 42%
Yrs since HIV Diagnosis *		8 (0 – 28)	0.1 (0 – 21)	10 (0 – 28)	6 (0 – 28)	19 (4 – 28)	9 (1 – 24)
Years on ART		4 (0, 21)	0 (0, 0)	5 (0, 21)	3 (0, 17)	9 (0, 13)	5 (0, 21)
CD 4 Count **		468 (4, 1578)	508 (4, 1278)	466 (17, 1578)	493 (55, 1578)	313 (17, 1253)	552 (187, 1260)
VL at 0 months	Undetectable	114, 51%	2, 5%	112, 61%	54, 62%	23, 43%	35, 81%
	Detectable	106, 47%	39, 95%	67, 37%	32, 37%	29, 55%	6, 14%
	Not Available	4, 2%	0, 0%	4, 2%	1, 1%	1, 2%	2, 5%
VL categories	Undetectable	114, 51%	2, 5%	112, 61%	54, 62%	23, 43%	35, 81%
	200–1000	19, 8%	7, 17%	12, 7%	6, 7%	5, 9%	1, 2%
	1000–10,000	19, 8%	4, 10%	15, 8%	7, 8%	5, 9%	3, 7%
	10,000–100,000	45, 20%	21, 51%	24, 13%	15, 17%	7, 13%	2, 5%
	>100,000	23, 10%	7, 17%	16, 9%	4, 5%	12, 23%	0, 0%
	Not Available	4, 2%	0, 0%	4, 2%	1, 1%	1, 2%	2, 5%
Reason for OPOD	Adherence	56, 25%	0, 0%	56, 31%	29, 33%	24, 45%	3, 7%
	Side Effects	56, 25%	0, 0%	56, 31%	29, 33%	6, 11%	21, 49%
	Simplify Regimen	54, 24%	0, 0%	54, 30%	22, 25%	16, 30%	16, 37%
	Resistance	13, 6%	0, 0%	13, 7%	6, 7%	7, 13%	0, 0%
	Not Applicable	41, 18%	41, 100%	0, 0%	NA	NA	NA

Variable	Value	Total	Naïve	Treated			
				Total Treated	Treated-no Resistance	Treated-Resistance	No Genotype Available
				4, 2%	0, 0%	1, 1%	3, 7%
PI Boosted Regimen	Other	10, 4%	0, 0%	10, 5%	0, 0%	9, 17%	1, 2%
Number of Sequences	Yes	1 (0, 14)	1 (0, 2)	1 (0, 14)	1 (0, 7)	2 (1, 14)	0 (0, 0)

Footnote: Categorical variables are presented as n, %; continuous variables are presented as *median (range)*.

* indicating 4 patients with missing years since diagnosis;

** indicating 22 participants with missing CD4 counts within the 4.5 months inclusion criteria window.

12-month viral load outcomes among treatment experienced participants, stratified by viral failure status at switch.

Table 2

	value	Suppressed at OPOD initiation			Virologic Failure at OPOD Initiation		
		Total	Continued Suppression at 12 Mos.	Failure at 12 Mos.	Total	Suppression at 12 Mos.	Continued Failure at 12 Mos.
N		102	98	4	61	37	24
Age (years)		46 (20, 72)	48 (21, 72)	27.5 (20, 32) *	43 (22, 66)	41 (22, 66)	45 (24, 58)
Gender	21-34	21, 21%	17, 17%	4, 100%	14, 23%	11, 30%	3, 12%
	Female	39, 38%	38, 39%	1, 25%	29, 48%	15, 41%	14, 58%
Years since HIV diagnosis		9 (0, 27)	9 (0, 27)	17 (14, 20) *	11 (0, 28)	10 (0, 28)	14 (2, 25)
Regimen	Complera	48, 47%	47, 48%	1, 25%	27, 44%	17, 46%	10, 42%
	Stribild	54, 53%	51, 52%	3, 75%	34, 56%	20, 54%	14, 58%
PI Boosted Regimen	No	100, 98%	97, 99%	3, 75%	54, 89%	32, 86%	22, 92%
	Yes	2, 2%	1, 1%	1, 25%	7, 11%	5, 14%	2, 8%
Reason for OPOD	Adherence	15, 15%	14, 14%	1, 25%	37, 61%	18, 49%	19, 79%
	Side Effects	39, 38%	39, 40%	0, 0%	10, 16%	7, 19%	3, 12%
	Simplify Regimen	40, 39%	39, 40%	1, 25%	5, 8%	5, 14%	0, 0%
	Resistance	4, 4%	2, 2%	2, 50%	9, 15%	7, 19%	2, 8%
	Other	4, 4%	4, 4%	0, 0%			
Number of Sequences		1 (0, 12)	1 (0, 12)	2.5 (2, 5) *	2 (0, 14)	2 (0, 14)	2 (0, 14)
CD4 Count		539 (17, 1578)	540 (128, 1578)	34 (17, 347) *	318 (18, 783)	325 (18, 783)	264 (55, 675)
Medication Adherence	No	12, 12%	9, 9%	3, 75%	29, 48%	10, 27%	19, 79%
	Yes	90, 88%	89, 91%	1, 25% *	32, 52%	27, 73%	5, 21% *
Appointment Adherence	No	20, 20%	18, 18%	2, 50%	28, 46%	14, 38%	14, 58%
	Yes	82, 80%	80, 82%	2, 50%	33, 54%	23, 62%	10, 42%
Accumulated Resistance	No	51, 50%	50, 51%	1, 25%	27, 44%	19, 51%	8, 33%
	No Genotypes	30, 29%	30, 31%	0, 0%	5, 8%	4, 11%	1, 4%
	Yes	21, 21%	18, 18%	3, 75%	29, 48%	14, 38%	15, 62%
Years with ART records		3 (0, 13)	3 (0, 10)	9 (4, 13)	4 (0, 13)	3 (0, 11)	6 (0, 13)

Footnote: Categorical variables are presented as n, %; continuous variables are presented as median (range).
* indicates P<0.05.

Table 3

Relationships between 12-month viral load and at-switch resistance among treatment-experienced patients, considering accumulated and recent-only resistance; low and intermediate predicted resistance; and M184V/I.

Resistance Level	Medications	Sequences	OR (95% CI), p-value
low	Any	Accumulated	7.93 (1.84, 34.22) p=0.005
low	TDF	Accumulated	1.34 (0.35, 5.22) p=0.67
low	FTC	Accumulated	6.46 (1.69, 24.69) p=0.006
low	RPV	Accumulated	40.49 (1.38, 1185.34) p=0.032
M184I/V	FTC	Accumulated	6.46 (1.69, 24.69) p=0.006
Intermediate	Any	Accumulated	8.05 (1.87, 34.7) p=0.005
low	Any	Recent	3.73 (1.1, 12.68) p=0.035
low	TDF	Recent	1.68 (0.34, 8.33) p=0.525
low	FTC	Recent	2.07 (0.6, 7.17) p=0.249
low	RPV	Recent	118.82 (2.15, 6557.24) p=0.02
M184I/V	FTC	Recent	2.07 (0.6, 7.17) p=0.249
Intermediate	Any	Recent	2.79 (0.82, 9.4) p=0.099

Footnote: CI, confidence interval; FTC, emtricitabine; OR, odds ratio; RPV, rilpivirine; TDF, tenofovir disoproxil fumarate.