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Virologic Response using Directly Observed Therapy in Adolescents with HIV: An Adherence Tool

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Abstract

Virologic response to highly active antiretroviral therapy (HAART) treatment of human immunodeficiency virus (HIV) infection depends on viral sensitivity to antiretrovirals (ARV's) and excellent medication adherence. Adolescents with vertically-acquired HIV may require complicated regimens due to significant treatment experience and often have poor medication adherence. A retrospective chart review identified five adolescents with vertically acquired HIV and plasma HIV viral load rebound or nonresponse on a stable HAART regimen followed by a period of directly observed therapy (DOT) in a clinic or hospital setting with serial viral load measurements. Four subjects had a virologic response (mean decline 1.15 log) after DOT. A response to HAART can be seen despite ARV resistance using DOT, and treatment-experienced patients seemingly unresponsive to HAART may be non-adherent even with reassuring adherence measures. A period of clinic-monitored DOT may allow diagnosis of non-adherence, discussion of medication barriers and avoidance of unnecessary medication changes.

Keywords

HIV/AIDS; Directly Observed Therapy; adolescence; adherence; virologic response

Highly active antiretroviral therapy (HAART) is remarkably effective in suppressing HIV replication, preventing opportunistic infections, and prolonging life in children and adults with HIV infection (Gortmaker et al., 2001; Palella et al., 1998). However, the success of HAART

relies on patient adherence. With missed doses, drug resistance may develop; and significant cross-resistance between medications within each class can hinder the efficacy of future regimens (Watson & Farley, 1999).

Adherence to medications is often difficult in the pediatric population for reasons generally related to the developmental stage of the patient. In younger children, poor medication tolerability and palatability, lack of available liquid formulations for some medications, and caregiver non-adherence hinder adherence.

In the adolescent population, psychosocial factors contribute greatly to non-adherence to antiretrovirals (ARVs), and often adolescents are given independence in taking medications despite not fully understanding their regimens (Martin, Elliot, Toledo-Tamula, Wolters, & Wood, 2004; Murphy et al., 2003). However, data on adherence to ARVs in vertically-infected adolescents are limited. In a study by Van Dyke et al., 2002, almost one-third of 125 HIV-infected pediatric subjects, most of whom were not adolescents, reported non-adherence to ARVs over the course of one year. Only 41% of a group of 161 HIV–positive adolescents infected via sexual contact or drug injection reported full ARV adherence (Murphy et al., 2003).

Although adolescents with behaviorally acquired infection are clearly a different cohort in terms of HIV-disease state and ARV experience, they share the same developmental stage as adolescents with vertically-acquired infection. Adolescents with vertically-acquired HIV often have received multiple regimens in the past and have virus with significant resistance to most ARVs, frequently leading to more complex ARV regimens with a greater pill burden, and thus a greater incidence of nonadherence. Unfortunately, for these treatment-experienced adolescents, the options for effective ARV regimens are limited, and frequent ARV changes with poor adherence can lead to further resistance. The great advances that have resulted in the development of simplified regimens that include a regimen of one pill once a day are clearly not an option for these patients. They are highly treatment-experienced patients with multi-drug resistant virus who have difficulty taking and/or tolerating their increasingly complex medication regimens. Hence, adherence is an even more compelling issue for them since options are very limited.

Many of the patients we followed at the pediatric HIV clinic at the National Cancer Institute (NCI) were referred from HIV treatment centers across the United States for salvage therapy and phase I protocols; therefore, we have experience with many vertically-infected, adolescent patients who have significant drug resistance and are placed on difficult treatment regimens. With strict adherence, virologic responses to new regimens are often observed despite significant ARV resistance (Hazra et al., 2005). However, a subsequent increase in HIV viral load sometimes occurs and presents a dilemma for the clinical team.

To evaluate a virologic rebound after initial response or continued nonresponse to a new regimen for patients with self-reported good adherence, it has become our practice to obtain repeated viral loads during a short period of directly observed therapy (DOT) in the clinic setting. By diagnosing non-adherence in several patients, we were able to avoid treatment changes for patients with limited options. Informing our patients and their caregivers that we routinely perform DOT for all patients with nonresponse to ARVs allows for a nonjudgmental approach to accurately document whether virologic response to a regimen was possible.

We report results from 5 patients as illustrative cases of our experience with DOT as a diagnostic tool for adherence, and provide some of the lessons learned about assessing adherence in this challenging patient population.

Methods

Subjects were identified via a retrospective chart review that included records from all patients followed in the pediatric HIV clinic at the National Cancer Institute between 1996 and 2004. Patients were selected if they had undergone DOT by a medical professional; those who had DOT performed at home by a family member (or other non-medical professional) were not included. In addition to a period of medically supervised DOT, we required that patients be on a stable HAART regimen (at least 3 antiretroviral medications, including drugs from at least 2 classes) for at least 8 weeks prior to DOT, and have a viral load done before and after DOT. Using these criteria we identified 5 patients. All of the patients were enrolled on protocols that had been approved by the NCI institutional review board (IRB), and depending on the patient's age, the patient and/or legal guardian had provided informed consent.

Adherence was monitored for each individual as required by his or her protocol. Patients and their caregivers had adherence interviews at clinic visits. Additional measures of adherence included protease inhibitor drug levels (Yasuda et al., 2004), ARV pill counts, and the MEMS™ Medication Event Monitoring System (MEMS™). MEMS™ (MEMS™, AARDEX, Ltd., Zug, Switzerland) involves the use of pill bottle caps that contain a microelectronic circuit that registers the exact dates and times the bottle is opened. Table 1 details each subject's adherence monitoring. The decision to perform DOT was made by the clinical team when the HIV viral load failed to respond to therapy or a virologic rebound was observed. The patient and/or caregiver were told on the telephone prior to the DOT period that we were concerned about the increase in viral load and that we wished to have the patient return to the clinic for a period of DOT to monitor adherence. DOT was performed by medical professionals at the pediatric clinic or by the local healthcare provider(s), and was composed of at least 4 contiguous days of monitored medication administration of at least one dose each day. No patient refused DOT when it was proposed.

Prior to initiation of DOT and after the completion of DOT, viral load was assessed using the Roche (Nutley, NJ) Amplicor polymerase chain reaction assay, with lower limit of detection 50 copies/ml. All of the patients had genotype resistance testing (Virco, Mechelen, Belgium) within the year prior to DOT that confirmed multi- drug resistance in each patient.

Results

Five patients were identified who received DOT in a medical setting for at least 4 contiguous days after at least 8 weeks of a stable HAART regimen. All of these patients had vertically-acquired HIV and ranged in age from 14–19 years old (Table 1). All patients had extensive ARV treatment experience (median of 4 previous HAART regimens) and had significant genotypic evidence of resistance to ARVs as detailed in Table 1. The patients had been treated with their current HAART regimens for a median of 24 weeks (range 10–144 weeks). All of the patients were treated with twice daily regimens containing ritonavir-boosted protease inhibitors, and three of the patients (patients 1, 4, and 5) were treated with more complex regimens with multiple protease inhibitors due to extensive treatment experience and genotypic evidence of antiretroviral resistance. Patients 1 and 4 were prescribed high dosages of saquinavir (2200 mg and 2800 mg twice daily respectively) as specified by their protocols. Patients were seen at the clinic according to protocol, with extra non-protocol visits as required.

Four of the five patients had DOT at the NCI clinic (patients 1–4) with each morning dose observed by one of the clinic care providers. Patient 5 had monitored medication administration during a 2-week hospitalization at his local hospital for a gluteal muscle abscess; a viral load was obtained at the end of the 2-week hospitalization, after the infection had been well

controlled with antibiotics for over a week. The previous viral load was from a clinic visit 1 month prior when the patient had no intercurrent infection.

Information on adherence by interview, pill count, and MEMS™ was available for patients 1 and 4. For patient 1, during the 2 months leading up to DOT, adherence was 100% by patient interview, >90% by pill count, and 91% by MEMS™ (43% for doses within 1 hour of the target time). For patient 4, during the 2 months prior to DOT, adherence was 100% by patient interview, >95% for pill count, and 93% by MEMS™ (37% for doses within 1 hour of the target time). Information for other patients was incomplete; however, on review of the medical records, all patients reported excellent adherence.

Four of the five patients had a decrease in viral load while on DOT (ranging from 0.5–2.46 $\log_{10}$ HIV RNA copies/mL, mean 1.15 $\log_{10}$ HIV RNA copies/mL) (see Table 1). Patient 5 had a decrease of 2.46 $\log_{10}$ HIV RNA copies/mL after a period of more extensive monitoring (2 weeks versus 4–5 days) during his hospitalization. One patient (patient 3) had a decrease in viral load of 0.92$\log_{10}$ HIV RNA copies/mL immediately preceding the DOT and then an increase in viral load of 0.44 during DOT. We postulated that she improved her ARV adherence prior to her return to clinic; however, why her viral load increased with DOT remains unclear. Repeat viral loads 4–8 weeks after the DOT were increased for all the patients studied (ranging from 0.43–1.64 $\log_{10}$ HIV RNA copies/mL, mean 0.86 $\log_{10}$ HIV RNA copies/mL), most likely from continued non-adherence.

Case Presentation

As previously stated, all of the patients included in this study were highly treatment-experienced patients with extensive ARV history and exposure. We present the following case as an example of the challenges inherent in caring for this group of patients and the utilization of DOT. This case was a retrospective chart review of the outpatient medical record. The patient is representative of those seen in our program.

Patient 1 was a 15-year-old female with vertically acquired HIV enrolled in the Therapeutic Drug Monitoring (TDM) Protocol at NCI, a protocol in which the dose of the protease inhibitor of a HAART regimen is adjusted based on serum protease inhibitor levels. The patient was highly treatment-experienced (6 previous HAART regimens) with a viral load >1 million RNA copies/mL and CD4 lymphocyte count (CD4 count) of 50 cells/mm^3 (5%) at the initiation of the protocol. She was placed on saquinavir (SQV), lopinavir/ritonavir (LPV/r), zidovudine (AZT), lamivudine (3TC), abacavir (ABC), and tenofovir (TDF).

The patient responded initially with a 1.7 $\log_{10}$ HIV RNA copies/mL decrease (5.87 to 4.14 $\log_{10}$ HIV RNA copies/mL) in the HIV viral load on day 7 of the new ARV regimen, with protocol-mandated DOT during this first week. At week 12, she had a viral load of <50 copies/mL and a CD4 count of 192 cells/mm^3 (9%). Despite difficulty with pill burden, nausea, and strong dislike of LPV/r the patient reported good medication adherence. At week 16 her viral load had increased to 54,000 copies/mL (4.73 $\log_{10}$ HIV RNA copies/mL) and her symptoms of nausea had diminished significantly. Her MEMS data revealed that the pill bottle was opened twice daily for 95% of the days for the 2 months prior to week 16; when the MEMS was examined for openings during the prescribed target time (+/− 1 hour), the percentage decreased to 75%. Due to our concerns of non-adherence we planned a 5-day period of DOT in our clinic. For the several weeks following the 16-week visit, the MEMS data showed opening of the pill bottle twice daily for 91% of the days, but the percentage decreased to 43% for openings around the target time (+/− 1 hour). During DOT, the patient's nausea returned, and her viral load decreased from 80,700 (4.91 $\log_{10}$ HIV RNA copies/mL) to 25,900 (4.41 $\log_{10}$ HIV RNA copies/mL), providing evidence that she was capable of virologic response when adherent.

After presentation of the MEMS data, pill counts, virologic variability, and response with DOT, she discussed her difficulties with medication adherence. Despite the family-monitored medication administration at home, the level of supervision varied and gave the patient opportunity for deception. Once the patient was able to openly admit to her non-adherence, we discussed the greatest barriers to pill taking and how to work on becoming successful with her ARV regimen. We decreased her SQV dose to decrease both her pill burden and nausea side effects and asked her to eat yogurt when taking LPV/r to mask the taste. We also reviewed closely supervised medication administration with the caregivers. The guardian had been very surprised by the admission of non-adherence, and her relationship with the patient became strained from lack of trust, but with improved adherence the interpersonal problems also improved.

Discussion

The success of HAART is dependent on viral sensitivity to the prescribed medications, tolerable side effects, and excellent patient adherence. Adherence to medication regimens is a significant barrier in the care of children and adolescents with HIV (Matsui, 1997; Murphy et al., 2003; Wiener, Riekert, Ryder & Wood, 2004). In a cohort of 114 adolescents, viral load was significantly correlated with medication adherence self-report (Murphy et al., 2003). Only 28% reported taking all of their prescribed ARVs in the previous month. The two most common barriers to adherence in this group were physical and psychological medication side affects and changes in daily routines. In 2005, 65 patients in this same cohort (ages 12–18 years) had a median time to non-adherence of 12 months (Murphy et al., 2005). Patients who were younger and had depression were more likely to become non-adherent.

Adolescents are often expected to take on additional responsibility with medication taking for which they may not be developmentally ready. Young adolescents are generally still concrete thinkers and not capable of fully understanding the implications of medication non-adherence. Christie and Viner (2005) note that physical and psychological changes interact with external and internal system demands (tasks) during adolescence. When these systems also include the healthcare organization, new challenges arise, especially with risk taking and adherence to medication or treatments.

Recent reports have demonstrated that using medical institution-based DOT can improve adherence and virologic and immunologic responses (Glikman, Walsh, Valkenburg, Mangat, & Marcinak, 2007; Parsons et al., 2006). In these studies, children and adolescents (mean age of 13 years [range, 7–17 years] and 12.6 years [range, 0.8–16 years], respectively) with perinatally-acquired HIV were admitted to the hospital for non-adherence concerns and received DOT for all ARV doses. The subjects had viral load and CD4 counts obtained at admission and discharge. Glikman et al. showed a mean viral load decrease of 0.8 ± 0.55 $\log_{10}$ HIV RNA copies/mL_{10} after a 7-day hospital admission in 8 patients with 11 admissions. Parsons et al. reported that 10 of 19 patients (53%) had a 1 $\log_{10}$ HIV RNA copies/mL_{10} decline in viral load after 8 days (range, 4–22 days) of DOT in a rehabilitation center. Similar to our experience, the decrease in viral load was not sustained in the majority of patients when measured many weeks after discharge. In patients changing their ARV medications, a sustained viral load response was observed 6 months after initiation of the new regimen (Parsons et al.).

Decisions regarding changing medication regimens take on additional importance in adolescents with vertically-acquired infection due to their extensive treatment experience and drug resistance. The use of DOT to assess adherence may be a more effective measurement than serum drug monitoring. While drug level monitoring provides an objective value, it is impractical and potentially quite expensive depending on the number of drugs measured. Additionally, the level probably represents short-term adherence rather than day-to-day

adherence. Actually watching a patient take their medications can identify adherence difficulties, and this additional observation does not occur with drug level measurements. In clinical practice, adherence is typically assessed through interview and pill counts. More intensive measures such as MEMS™ caps or drug level monitoring may be used for more accurate information and in clinical trials (Deschamps et al., 2004; Levy et al., 2004). However, non-adherence can still be very difficult to diagnose, leading to unnecessary ARV changes due to presumed HIV resistance. Without a clear understanding of adherence, changing the regimen can lead to additional resistance, further limiting treatment options.

Our experience shows the potential utility of a brief period of medically monitored DOT to document a virologic response to a treatment regimen, even in patients with extensive ARV resistance. Diagnosing non-adherence in this manner may allow the patient to admit to barriers in medication adherence, such as inability to tolerate a certain medication, and importantly avoids treatment changes in a non-adherent patient. Our patients and caregivers were willing to undergo DOT and to engage in meaningful conversations about the results.

While our results demonstrate the potential ability of DOT to diagnose nonadherence, we did not continue DOT as part of a therapeutic strategy, and all the patients went on to have viral rebound, presumably due to repeated non-adherence. In a study by Roberts et al. (2004), the authors report success with improving adherence through the use of DOT in a group of HIV-infected pediatric patients who were less treatment-experienced and younger than those we studied. This group instituted a step-wise approach to manage non-adherence, first involving, visits by a home health nurse, followed by DOT during a hospitalization and, subsequently, a medical neglect report. That study emphasizes the need for early DOT in patients with ARV sensitivity and high viral load measurements to prevent treatment failure and suggests that fairly drastic measures may be warranted to ensure adherence.

A major limitation of our study was that we did not implement and investigate an ongoing approach of DOT in these treatment-experienced patients. However, we were still able to obtain important information about adherence and the ability to obtain a virologic response in highly treatment-experienced patients with extensive ARV resistance, using clinic-based DOT and administering the same regimen that patients were purportedly failing. Our study was also limited by its retrospective nature and variations of how adherence was assessed for each patient (such as pill count, MEMS™, or interview). There was not a standard time interval between the phone call to inform of the decision to perform DOT and the DOT period, and adherence may have increased after the phone call, as was a possible explanation for patient 3 who had a decrease in viral load immediately preceding the DOT period. In addition, most of the patients had only one dose observed daily.

The lessons learned in our experience with many adolescents and young adults with ARV-resistant HIV and extensive treatment histories has led to insights regarding the extreme difficulty of adherence in this group. Adolescents are often unable to cope with side effects and complexities of regimens that interfere with their active social lives, and as part of their normal developmental stage, they are thinking of immediate consequences and not long-term disadvantages of non-adherence. Therefore, a multidisciplinary approach is necessary to help determine some of the barriers to adherence, and discussions about these barriers need to start prior to new medication regimens and continue at each clinic visit. That our experience documented virologic response to DOT in highly motivated families enrolled on NIH protocols confirms the significance of non-adherence and suggests that even for patients with extensive ARV resistance, nonresponse to medications is often due to non-adherence and not soley ARV resistance. In fact, we have found that it is safer to anticipate non-adherence in patients with increased viral loads and those on salvage regimens (usually receiving two protease inhibitors). In addition, providers should have a certain degree of concern about non-adherence in patients

who do not report ARV drug side effects, especially if they complained of such side effects in the past.

Another important lesson we have learned is that it is often difficult to document non-adherence despite multiple methods of assessment, including interviews by multiple providers patients and their guardians, pill counts, and MEMS™. While MEMS™ potentially can provide the most accurate and detailed information among these methods, a comparison of adherence rates based on the number of days with correct doses versus those taken within one hour of the prescribed target time produce very different pictures of our patients' adherence. Moreover, the fact that you can "fake" a medication dose by opening and closing the pill bottle without actually taking the pill highlights another limitation of the method. In addition to the potential problems with MEMS™, we have found family-monitored medication administration often inaccurate, as adolescents can be quite savvy with quickly disposing of medications even while being observed; for instance, one of our adolescent patients eventually admitted to spitting his protease inhibitor capsules into the can of the drink he used to swallow the medications.

Implications for Clinical Practice and Future Research

Our data, Glikman et al. (2007), and Parsons et al. (2006) demonstrated that measuring viral loads with DOT can provide valuable information about a patient's response to ARV treatment. These results also demonstrate that heavily treatment-experienced patients can experience a virologic response with DOT and without a change in regimen. Roberts et al. (2004) showed that a step-wise approach that emphasized DOT in treatment-naïve patients resulted in improved adherence and clinical responses. A future study should explore whether this step-wise approach can produce persistent improvements and clinical responses in the heavily treatment-experienced patient population that we studied. A policy of DOT prior to treatment changes for medical failure may be beneficial not only for adolescents with HIV but also for adolescents with other chronic illnesses.

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References

Christie D, Viner R. Adolescent development. British Medical Journal 2005;330:301–304. [PubMed: 15695279]

Deschamps AE, Graeve VD, van Wijngaerden E, DeSaar V, Vandamme AM, van Vaerenbergh K, et al. Prevalence and correlates of nonadherence to antiretroviral therapy in a population of HIV patients using Medication Event Monitoring System. AIDS Patient Care and STDs 2004;18(11):644–657. [PubMed: 15633262]

Glikman D, Walsh L, Valkenburg J, Mangat D, Marcinak JF. Hospital-based directly observed therapy for HIV-infected children and adolescents to assess adherence to antiretroviral medications. Pediatrics 2007;119:e1142–e1148. [PubMed: 17452493]

Gortmaker SL, Hughes M, Cervia J, Brady M, Johnson GM, Seage GR 3rd, et al. Effect of combination therapy including protease inhibitors on mortality among children and adolescents infected with HIV-1. New England Journal of Medicine 2001;345(21):1522–1528. [PubMed: 11794218]

Hazra R, Gafni RI, Maldarelli F, Balis FM, Tullio AN, DeCarlo E, et al. Tenofovir disoproxil fumarate and an optimized background regimen of antiretroviral agents as salvage therapy for pediatric HIV infection. Pediatrics 2005;116(6):e846–e854. [PubMed: 16291735]

Levy RW, Rayne CR, Fairley CK, Kong DC, Mijch A, Costello K, et al. Multidisciplinary HIV adherence intervention: A randomized study. AIDS Patient Care and STDs 2004;18(12):728–735. [PubMed: 15659884]

Martin, SC.; Elliott, DK.; Toledo-Tamula, MA.; Wolters, PL.; Wood, LV. Comparison of knowledge and perceptions of responsibility for medication adherence between HIV-positive children and their caregivers; Poster session presented at the annual meeting of the Society of Pediatric Psychology Meeting; Charleston, SC. 2004 Apr.

Matsui DM. Drug compliance in pediatrics: Clinical and research issues. Pediatric Clinics of North America 1997;44(1):1–14. [PubMed: 9057780]

Murphy DA, Sarr M, Durako SJ, Moscicki AB, Wilson CM, Munez LR. Barriers to HAART Adherence among human immunodeficiency virus-infected adolescents. Archives of Pediatrics and Adolescent Medicine 2003;157(3):249–255. [PubMed: 12622674]

Murphy DA, Belzer M, Durako SJ, Sarr M, Wilson CM, Muenz LR. Longitudinal antiretroviral adherence among adolescents infected with human immunodeficiency virus. Archives of Pediatrics and Adolescent Medicine 2005;159(3):764–770. [PubMed: 16061785]

Palella FJ Jr, Delaney KM, Moorman AC, Loveless MO, Fuhrer J, Satten GA, et al. Declining morbidity and mortality among patients with advanced human immunodeficiency virus infection: HIV Outpatient Study Investigators. New England Journal of Medicine 1998;338(13):853–860. [PubMed: 9516219]

Parsons GN, Siberry GK, Parsons JK, Christensen JR, Joyner JL, Lee SL, et al. Multidisciplinary, inpatient directly observed therapy for HIV-1 infected children and adolescents failing HAART: A retrospective study. AIDS Patient Care and STDs 2006;20(4):275–284. [PubMed: 16623626]

Roberts GM, Wheeler JG, Tucker NC, Hackler C, Young K, Maples HD, et al. Nonadherence with pediatric human immunodeficiency virus therapy as medical neglect. Pediatrics 2004;114(3):e346–e353. [PubMed: 15342896]

Van Dyke RB, Lee S, Johnson GM, Wiznia A, Mohan K, Stanley K, et al. Pediatric AIDS Clinical Trials Group Adherence Subcommittee Pediatric AIDS Clinical Trials Group 377 Study Team. Reported adherence as a determinant of response to highly active antiretroviral therapy in children who have human immunodeficiency virus infection. Pediatrics 2002;109(4):e61. [PubMed: 11927734]

Watson DC, Farley JJ. Efficacy of and adherence to highly active antiretroviral therapy in children infected with human immunodeficiency virus type 1. Pediatric Infectious Disease Journal 1999;18 (8):682–689. [PubMed: 10462336]

Wiener L, Riekert K, Ryder C, Wood LV. Assessing medication adherence in adolescents with HIV when electronic monitoring is not feasible. AIDS Patient Care and STDs 2004;18:527–538. [PubMed: 15630773]

Yasuda JM, Miller C, Currier JS, Forthal DN, Kemper CA, Beall GN, et al. The correlation between plasma concentrations of protease inhibitors, medication adherence and virological outcome in HIV-infected patients. Antiviral therapy 2004;9(5):743–761. [PubMed: 15535412]

Table 1

Patient Characteristics

Patient	Age (year/ sex)	Antiretrovira Medications*	CD4 count at start of DOT (cells/m^3)	HIV concentration (viral load) at start of DOT (RNA copies/ml)	HIV concentration (viral load) at end of DOT (RNA copies/ml)	Length of time on Regimen at start of DOT	Adherence Monitoring	Number of NRTI/PI Mutations
1	15/F	AZT/3TC/TDF/SQV/LPV/r	183 (11%)	80,700 (4.91 log)	25, 900 (4.41 log)	24 weeks	Interview, MEMS, Drug levels, Pill count	5/9
2	14/F	AZT/3TC/LPV/r	119 (11%)	43,800 (4.64 log)	25, 900 (4.41 log)	126 weeks	Interview	4/3
3	19/F	TDF/DDI/EFV/LPV/r	400 (29%)	17, 200 (4.23 log)	46,700 (4.67 log)	144 weeks	Interview	6/9
4	17/M	AZT/3TC/ABC/TDF/SQV/ LPV/r	50 (6%)	41,600 (4.62 log)	11,000 (4.04 log)	24 weeks	Interview, MEMS, Drug levels, Pill count	9/10
5	18/M	AZT/3TC/ABC/TDF/APV/ ATV/RTV	5 (1%)	2,400,000 (6.38 log)	8,390 (3.92 log)	10 weeks	Interview Pill count	8/10

Major NRTI mutations:41L,44D, 67N, 215Y, 219Q, 184V, 215F, 69D, 70R, 74I, 75M, 118I, 210W, 184I, 210Y, 219R

Major PI mutations: 10I, 20R, 32I, 33F, 47V, 54V, 71V, 82A, 90M, 10F, 84V, 46I, 73S, 54L,63P, 82T

*Antiretroviral Medications: ABC = Abacavir APV = Amprenavir ATV = Atazanavir AZT = Zidovudine 3TC = Lamivudine TDF = Tenofovir SQV = Saquinavir LPV/r = Lopinavir/ritonavir DDI = Didanosine EFV=Efavirenz