Immunological and Virological Outcomes of Patients Switched from LPV/r to ATV/r-Containing Second- Line Regimens

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Abstract: *Background*: Atazanavir/ritonavir (ATV/r) recently became the preferred protease inhibitor (PI) for use in Nigeria since it is dosed once daily, which may improve treatment adherence and has fewer side effects than lopinavir/ritonavir (LPV/r) - the most widely available PI in resource-limited settings. We, therefore, aimed to evaluate the immunologic and virologic effects of switching patients to an ATV/r-containing regimen.

Methods: In a large antiretroviral treatment programme at the Lagos University Teaching Hospital in Nigeria, 400 patients were switched to ATV/r-based second-line ART. We conducted a retrospective evaluation of immunologic and virologic outcomes following 24 months on the ATV/r regimens.

Results: Of the 400 patients switched to an ATV/r containing regimen, 255 were virologically suppressed on LPV/r prior to switch, 107 were switched due to failure on a first-line regimen, 28 were on saquinavir/ritonavir (SQV/r)-based regimen, while 10 were unintentionally switched while non-suppressed on a LPV/r-based regimen. Demonstrable and sustained immunological responses were documented as the median (IQR) CD4+ cell count increased steadily from 466 (323) cells/mm^3 at the time of switch to 490 (346) cells/mm^3 at 6 months, and 504 (360) cells/mm^3 at 24 months. Of 99 patients evaluated 12 months after ATV/r switch, 2 (2%) had detectable viral load (VL). None of the 26 (0%) in this group evaluated at 24 months had detectable viral load.

In a comparison group of 576 patients who were maintained on LPV/r-based second line regimens, 359 (62.3%) had undetectable viral loads. Of 318 patients with VL data 24 months later, 25 (7.9%) had detectable VL. There was no significant difference between the proportion of patients maintained on LPV/r (7.9%) and those switched to ATV/r (0%) in the development of virologic failure after 24 months of follow-up.

Conclusion: Among patients that were switched to ATV/r-containing regimens, we found improvements in immunological responses and no increase in risk of virologic failure.

Keywords: Africa, antiretroviral therapy, HIV/AIDS, protease-inhibitors.

INTRODUCTION

Atazanavir is a potent inhibitor of HIV-1 protease enzyme [1,2]. This drug was approved by the U.S. FDA for treatment of adults with HIV-1 infection in July 20, 2003 and has been widely used in U.S. and Europe since that time [3]. Until recently, the drug was not available in resource-limited settings. Standard antiretroviral therapy (ART) regimens have evolved over time in Nigeria. First-line ART consists of a non-nucleoside reverse transcriptase inhibitor (NNRTI), either nevirapine or efavirenz, in combination with two nucleoside reverse transcriptase inhibitors (NRTIs). From 2003-2007, the NRTI backbone primarily consisted of lamivudine (3TC) and the thymidine analogue,stavudine (d4T), while zidovudine (AZT) replaced d4T in most patient regimens by 2008. As viral resistance testing is generally not available, switch from first- to second-line regimens after established virologic failure is usually empirical. The standard second-line regimen consists of a protease inhibitor (PI) to replace the NNRTI, as these are known to have a low genetic barrier to resistance. Additionally, among patients who received AZT or d4T as part of the failing first-line regimen, the NRTI, tenofovir disoproxilfumarate (TDF) – a drug that is active against most thymidine analogue and other NRTI drug resistant mutants – is usually started as part of the second-line switch. In many cases, 3TC is retained as part of the empirical second-line regimen in order to conserve M184V mutation, selected by 3TC, which has been shown to impair viral fitness for replication and improves susceptibility of AZT-resistant viruses [4-6]. Over the years, the PI component of the second-line regimen has evolved. Softgel saquinavir boosted with ritonavir was initially used as the PI component of the second-line regimen. This was supplanted with heat labile ritonavir-boosted lopinavir (Kaletra). In 2007, heat stable lopinavir co-formulated with ritonavir became available and has remained the most widely used PI in second-line regimens in most resource-limited settings.

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In the 2010 Update on Treatment of HIV Infection in Adults, the International AIDS Society recommended the use of atazanavir boosted with low dose ritonavir (ATV/r) as the preferred PI-based second-line regimen for adults [7]. This recommendation also appeared in the WHO 2010 revision of antiretroviral therapy for HIV infection in adults and adolescents [8], and was based on the superiority of ATV/r in terms of ease of dosing, virologic potency, and unique and high genetic barrier to resistance when compared with boosted fosamprenavir or LPV/r [9, 10]. It also has less effect on lipid and glucose metabolism, and generally minimal toxicity compared with LPV/r [11]. Except for benign unconjugated hyperbilirubinaemia as a result of azapeptide (ATV belongs to the group of compounds called azapeptides) [12], inhibition of hepatic glucoronic transferase, and risk of nephrolithiasis, the drug is generally considered safe. The ease of once daily dosing improves patient adherence [7,10]. All these factors, coupled with cost considerations, make ATV/r a highly attractive option as the preferred PI for second-line ART, particularly in a large public health programme as we have in Nigeria. Although a pill of ATV/r is costlier ($6.93) than a pill of boosted LPV/r ($3.68), the pill burden (one daily for ATV/r) makes the cost of treatment per month ($208) much cheaper than that of LPV/r ($401) because of higher pill burden (4 tablets daily) [13, 14]. For this reason, in 2011 at the Lagos University Teaching Hospital ART Center, a programme policy change was adopted where adults stable on LPV/r-based second line regimen were switched to ATV/r regimen. This programmatic switch has yet to be evaluated for immunologic and virologic outcomes. We present the findings of this programmatic evaluation of ATV/r treatment after 24 months of follow-up as compared with outcomes of patients maintained on LPV/r over the 24-month period.

METHODS

Setting

The Antiretroviral Treatment Centre at the Lagos University Teaching Hosptial (LUTH) was established in October 2004 with the support of the Harvard/APIN PEPFAR grant. Since that time, over 15,000 adults and 1,200 children had been enrolled into the treatment programme. Approximately 8,000 adult patients are currently receiving ART, of which approximately 10% are confirmed to be in virologic failure. All patients who fail first-line regimens are empirically switched to LPV/r-based second-line regimens, usually consisting of TDF+3TC+AZT+LPV/r. A few patients, however, are on saquinavir/ritonavir (SQV/r) second-line regimens.

The Programmatic Switch

The antiretroviral therapy programme in Nigeria is largely a public health programme guided by the National Antiretroviral Therapy protocol [15]. The national ART guidelines are consistent with the WHO guidelines and recommend LPV/r along with two NRTIs as the empirical second-line regimen. In the later part of 2010, the Clinton Health Foundation in Nigeria brought to the attention of the National Task Team on Antiretroviral Therapy in Nigeria strategies that could be adopted to put thousands of Nigerians that were failing first-line therapy on a more affordable, effective, less toxic, and simpler regimen. Data from antiretroviral programmes in Nigeria showed that less than 50% of subjects who failed first-line ART were promptly switched. Reasons for the delays in switching included: failure to recognize treatment failure in a timely manner, unwillingness of patients to change regimens that consist of one pill a day or one pill twice daily to more complex second-line regimens, as well as cost considerations of the second-line regimen. The Task Team also considered that among adults on LPV/r-based second-line ART, switching to an ATV/r-containing regimen may be beneficial since once daily dosing may improve adherence and side effects such as diarrhea and lipid abnormalities may be reduced. Although there was no theoretical basis to suggest that patients who were virologically suppressed on LPV/r-based regimens would have an increased risk of failure after switch to ATV/r-based regimens, members of National Task team on ART were reluctant to adopt this concept until evidence confirmed the safety of this approach. The Lagos University Teaching Hospital thus chose to evaluate the strategy. Together, with the Clinton Health Foundation, a focus group discussion with over 60 subjects who were on LPV/r-based ART was held in February 2011 to discuss the principles of the proposed programmatic switch. The subjects were eager and enthusiastic to participate in the switch programme. On the 18th of May 2011 the first patient was switched from LPV/r (400mg/100mg (2 tablets of LPV/r 200mg/50mg) twice daily) to ATV/r (300mg/100mg once daily); the NRTI backbone remained unchanged.

Patient Selection Criteria

For the programmatic switch, adult men and women who were virologically suppressed with undetectable viral load (VL) assessments in the last 6 months and beyond and who were on a LPV/r-based second-line regimen were switched to an ATV/r-based second-line regimen. Excluded were: pregnant women, adults and children weighing <39 kilograms (kg), patients on proton pump inhibitors, and patients with renal failure. The patients were counselled on the risks and benefits of the regimen switch. All patients signed an approved informed consent form prior to participation.

Monitoring Schedule

Patients returned for drug refills on a monthly basis. Although routine clinical, virologic and immunologic monitoring occurs every 6 months, for the programmatic switched patients, CD4+ cell counts and VL assessments occurred every 3 months for for the first 12 months and 6 monthly thereafter. The CD4+ cell count was assayed using a semi-automated flow cytometer (Partec, Germany). Before September 2013, VL assessments were performed using Roche Amplicon version 1.5. Virologic failure was defined as a single plasma VL exceeding the limit of detection, 400 copies/mL. Although the lipid profile, direct and indirect serum bilirubin, plasma glucose levels, urea and creatinine changes in the switched patients were not the focus of this report, patients were also monitored for these laboratory parameters. Patients were also asked about adherence during

the last 3 days as part of the clinical adherence assessments. The clinical, pharmacy, virologic, immunology and other laboratory data were routinely captured in the programme's electronic database (FileMaker Pro, Santa Clra, CA) [16].

Control Subjects

To use as comparators, we retrospectively identified subjects who were on LPV/r-based second-line therapy and were virologically suppressed, but did not undergo switch to ATV/r. We queried the database that includes over 8,000 patients to select the subjects who met the criteria of virologic suppression by the end of 2009. The virologic outcome of this group was evaluated 12 months and 24 months later, with results abstracted from the laboratory records in our database.

Outcome Measures

For this evaluation, our main immunologic outcome was the change in CD4+ cell count at 12 months among the switched patients and the secondary outcome was the change in CD4+ cell count at 24 months post switching. Our main virologic outcome was proportion of patients with a detectable viral load among the switched patients at 12 months follow-up and the secondary outcome was proportion of patients with a detectable viral load at 24 months post switching. We also evaluated whether the duration of time from first-line failure ("Time to Failure") to ATV/r switch impacted virologic failure rates. Finally, we compared second-line virologic failure rates among subjects who switched to ATV/r from successful LPV/r regimens to the rate of failure among those retained on LPV/r-based regimens after 12 months, and secondarily, after 24 months of follow-up.

Data Abstraction

The programme's electronic database system has a utility that allows linkage of data from multiple data sources for a given patient in the graphical timeline format [16]. This treatment response utility was used to capture a patient's demographic, laboratory, clinical and pharmacy drug pick up detail in a single summary page with a graph of relevant parameters over time. For each patient switched to ATV/r, demographic information, date of enrolment into the programme, date of initiation of first-line regimen, type of first-line regimen, baseline VL, CD4+ cell count and subsequent values as well as dates of drug pickups, dates of detectable VL measurements, date of switch to second-line regimen, and date of switch to ATV/r-based second-line regimen were extracted.

Data Handling and Analysis

The longer an individual is maintained on a failing ART regimen, the higher the risk of accumulating drug resistance mutations that may compromise future empirical regimens. We calculated the following entities using Microsoft Excel date calculator: (1) "Time to first-line failure" was defined as the difference in weeks between the date of first-line ART initiation and the date of first laboratory evidence of virologic failure; (2) "Time to switch" defined as the difference in weeks between the date of first detectable VL in a patient who had been on first-line regimen and the date the patient was eventually switched to a second-line regimen; (3) "Duration on LPV/r-based second-line ART" defined as the difference in weeks between the date the patient initiated LPV/r-based second-line ART and the date of switch to ATV/r-based second-line regimen. The CD4+ cell count results were presented as median values at 3, 6, 9, 12, 18 and 24 months follow up periods. Kruskal-Wallis one way analysis of variance was used to compare the medians. The Wilcoxon rank sum test was also used to compare medians where appropriate. Viral load results were presented as detectable or undetectable, noting that undetectable results are values below 400 copies/mL.

RESULTS

Between May 27, 2011 and April 14, 2014, a total of 400 patients were switched to ATV/r; of these, 255 were patients who had failed first-line regimen and were stable (virologically suppressed) on a LPV/r-based second-line regimen for a median of 84.4 weeks (19.4 months) before they were switched and represented the programme policy (PP) switches to ATV/r. 107 patients were switched directly from a failing first-line regimen to ATV/r, representing treatment failure (TF) switches. There were 28 patients whose first-line regimen included SQV/r that were switched to ATV/r-based regimen, these being programme policy switches from SQV/r (PPS). Ten patients who failed LPV/r second-line ART were erroneously switched to ATV/r-based second-line therapy, representing an error in program policy switch (PPE). Table **1** shows age and sex distribution of subjects stratified by switch group and control patients (i.e., retained on LPV/r). Overall, 358 (90%) of patients received a NNRTI-based first-line regimen (Table **2**).

Relationship Between "Time to Switch" and Virologic Outcomes at 12 and 24 Months Post ATV/r Switch

The mean time to failure (the length of time between treatment initiation and the first detectable viral load) did not differ among the 4 groups of subjects (Table **3**). Specifically, when compared to programme policy (PP) switch patients, the time to failure was not significantly different from the other groups [programme policy switch in error (PPE), programme policy switch for patients on SQV/r (PPS), and subjects switched directly following first-line treatment failure (TF)], P = 0.32, 0.55 and, 0.58, respectively. The mean duration of time that the TF group remained on a failing regimen before being switched to ATV/r (131.0 weeks) was significantly longer than that for the PP group (91.6 weeks), P = 0.001 (Table **4**). At 12 months after ATV/r switch there were only 99 viral load reports available for the PP group. Of these, 2 (2.0%) subjects had a detectable viral load. There were only 21 viral load reports available for the TF group that included 107 patients. Of these, 2 (9.5%) patients had a detectable viral load. This difference did not reach a level of statistical significance (χ^2, = 3.03; p = 0.14). At 24 months post ATV/r switch, only 26 viral load reports

Table 1. Patient groups included in the evaluations.

Patient Groups	Age Group	Sex		Total
		Female	Male	
Programme Policy Switch (PP) to ATV/r	15-29 yrs	3	0	3
	30-39 yrs	44	15	59
	40-49 yrs	54	50	104
	50-59 yrs	26	40	66
	60-69yrs	4	16	20
	≥70 yrs	1	2	3
	Total	**132**	**123**	**255**
Programme Policy switch in Error (PPE) to ATV/r	30-39 yrs	4	0	4
	40-49 yrs	2	2	4
	50-69 yrs	1	1	2
	Total	**6**	**3**	**10**
Programme policy switch from SQV/r (PPS) to ATV/r	20-29 yrs	2	0	2
	30-39 yrs	15	0	15
	40-49 yrs	8	0	8
	50-59 yrs	0	2	2
	60-69 yrs	1	0	1
	Total	**26**	**2**	**28**
Treatment failure (TF) and switched to ATV/r	20-29 yrs	4	3	7
	30-39 yrs	32	8	40
	40-49 yrs	14	20	34
	50-69 yrs	8	18	26
	Total	**58**	**49**	**107**
Control Group (Retained on LPV/r)	15-29 yrs	4	3	7
	30-39 yrs	50	7	57
	40-49 yrs	105	66	171
	50-59 yrs	32	49	81
	60-69 yrs	12	23	35
	≥70 yrs	4	4	8
	Total	**207**	**152**	**359**

were available for the PP group and none (0.0%) of these had detectable viral loads, while 20 viral load results were available for the TF group and 4 (20%) of these had detectable results. This difference was statistically significant ($\chi^2 = 5.7$; p=0.029).

Immunologic Outcomes 24 Months After Switching to ATV/r

Of the 400 patients that were later switched to ATV/r, 394 had CD4+ cell counts available at initiation of first-line ART, while 358 had CD4+ cell count data reported at the time of first-line virologic failure. As shown in Table **4**, 296 patients had CD4+ cell counts available at the time of switch to ATV/r, while 205 had data available 12 months after switching to ATV/r. The median CD4+ cell count at switch to ATV/r was 466 (IQR, 323) cells/mm^3, which significantly increased to 560 (IQR, 361) cells/mm^3 after 12 months on ATV/r (P = 0.021).

Sub-analysis of the 255 subjects who were previously suppressed on LPV/r (PP), revealed that 248 had CD4+ cells counts available at the time of ATV/r switch with a median of 476 (IQR, 318) cells/mm^3. These values significantly increased to a median of 552 (IQR, 316) cells/mm^3 after 24 months of follow- up (P = 0.03).

For the subjects maintained on LPV/r therapy, modest increase was also demonstrable between baseline CD4+ cell count (403 cells/mm^3; IQR, 273) (the count at the point in time that the subject was entered to be followed for 24 months) and measurements at 12 months (421 cells/mm^3; P = 0.138) and 24 months (461 cells/mm^3; P = 0.005).

Viral Load Outcomes 12 Months After Switch from LPV/r to ATV/r

Of the 255 patients who were switched to an ATV/r-based regimen after achieving virologic suppression on LPV/r (PP), 99 had an available viral load after 12 months follow-up. Of these 99, two (2.0%) had a detectable VL, and by 18 months follow-up one of 56 available viral loads was detectable. None of the 26 patients with an available viral load at 24 months had a detectable viral load (Fig. **1**).

Outcomes After 12 Months Among Patients Maintained on LPV/r

As of December 2009, there were 576 patients that were on LPV/r based second-line regimen. Of these, 217 (37.7%) had a detectable viral load. The data from 379 patients who had undetectable VL measurements was evaluated 12 and 24 months later. At 12 months, 258 of the 379 patients had available viral load measurements. Of the 258 patients with evaluable viral loads, 25 (9.7%) had detectable viral load. In comparison, among the 255 programme policy switch patients (PP), 99 had available viral loads at 12 months, and 2 (2.0%) patients were detectable. The difference between the failure rates was significant (P = 0.014). At 24 months, however, only 26 of 255 subjects on ATV/r had evaluable VL results. Although none (0%) of these patients had detectable viral loads, we consider the number too small to compare with the 318 patients who were maintained on LPV/r that had evaluable VL data at 24 months, among whom 25 (7.9%) had failed therapy.

Outcomes of ATV/r-Based Second-Line ART Among Patients Switched Directly from a Failing First-Line Regimen

Of the 107 subjects who failed first-line regimens and were switched directly to an ATV/r-based regimen, only 21 had viral load results at 12 months and 2 (9.5%) of these had detectable viral load values. At 24 months however, a larger percentage 4 (20.0%) of the 20 that had viral load results remained unsuppressed.

Table 2. Distribution of first- and second-line ART regimens.

First-Line Regimen			Second-Line Regimen		
Regimen	**N**	**Percentage**	**Regimen**	**N**	**Percentage**
d4T/3TC/NVP	230	57.5	CBV/SQV/r	29	7.3
AZT/3TC/NVP	69	17.3	TRUV/SQV/r	18	4.5
AZT/3TC/EFV	12	3.0	AZT/TRUV/ATV/r	92	23.0
TDF/FTC/NVP	22	5.5	AZT/TRUV/LPV/r	193	48.3
TDF/FTC/EFV	22	5.5	ABC/3TC/SQV/r	3	0.8
AZT/3TC + boosted PI	27	6.8	d4T/3TC/SQV/r	4	1.0
TDF/FTC + boosted PI	8	2.0	CBV/LPV/r	4	1.0
3TC/ABC/EFV	3	0.8	TRU/LPV/r	9	2.3
CBV/ABC	1	0.3	AZT/TRUV/SQV/r	1	0.3
OTHERS	6	1.5	ABC/3TC/ATV/r	2	0.5
TOTAL	400		TDF/3tc/ATV/r	10	2.5
			NA	35	8.8
			TOTAL	400	

d4T = stavudine; 3TC = lamivudine, AZT = zidovudine, NVP = nevirapine; TDF= tenofovir disopropylfumarate, FTC= emtrictabine; EFV = efavirenz; PI = protease inhibitor, ABC = abacavir, SQV/r= saquinavir/ritonavir, ATV/r = atazanavir/ritonavir; Truv = Truvada, LPV/r = lopinavir/ritonavir; CBV = Combivir; NA = Number of patients who were enrolled in the programme on a PI-based regimen as first- line therapy.

Table 3. Duration of time patients were on LPV/r before switching to ATV/r.

	Time in Weeks	**Programme Policy (PP)**	**Programme Policy in Error (PPE)**	**Patients who were on SQVr (PPS)**	**Patients that Failed 1st Line (TF)**
Time to failure of 1st line regimen (Date of initiation of ART to date of 1st lab evidence of failure)	Mean	83.40	107.46 (0.32*)	76.93 (0.55*)	88.12 (0.58*)
	SD	63.45	74.86	53.72	78.19
	Median	67.00	89.14	69.93	68.29
Time to switch to 2nd Line (Date of lab failure of first line regimen to date of switch)	Mean	91.56	93.94 (0.93*)	68.39 (0.15*)	131.04 (0.001*)
	SD	75.10	66.26	82.00	114.57
	Median	85.00	89.79	34.90	95.29
Time on LPV/r 2nd line before switch to ATV/r (Date of initiation of 2nd line regimen to date of ATV/r switch)	Mean	204.91	173.93	128.15	0.70
	SD	84.43	104.48	87.16	4.67
	Median	219.36	208.08	130.71	0.00

*p-values when compared with PP.

DISCUSSION

This programmatic evaluation was undertaken to evaluate the policy of switching patients who were virologically suppressed on LPV/r-based second-line ART to ATV/r-based regimens with respect to immunologic and virologic response. From the data presented, only a small proportion (7.9% at 12 months and 0% at 24 months) of patients who were previously suppressed on LPV/r-based regimens eventually failed ATV/r-based ART. Literature is sparse on studies that evaluate outcomes after switching patients who are virologically suppressed on LPV/r to ATV/r-based regimens. This practice theoretically should be safe as ATV/r is said to have a high barrier to genotypic resistance. Indeed when the resistance to ATV/r occurs, this tends to be unique whereby isoleucine replaces leucine at amino acid 50 of the protease peptide, with the I50L mutation being the signature major genotypic resistance mutation associated with this drug [9,10]. The uniqueness of this mutation results in the increased susceptibility of the virus to other protease inhibitors. The mechanism of this unique susceptibility has been proposed whereby the substitution of isoleucine with leucine results in conformational alteration in protease enzyme structure. This structural change is said to make the active sites of the enzyme more accessible to other protease inhibitors [17,18]. Thus, it may be theoretically possible that a patient who failed ATV/r-based ART could be retained on this regimen to encourage persistent selection of I50L mutant, which is susceptible to other PIs, including LPV/r and nelfinavir.

Table 4. 12- and 24-Month Immunological Outcome (CD4+ Count, cells/mm^3) For Patients Switched to ATV/r-Containing Regimen and Those Retained on LPV/r.

Assessment Time Point	Patients Switched to ATV/r			Control (LPV/r)		
	N	Median	IQR	N	Median	IQR
At Initiation of ARV	394	153	194			
At failure of first-line therapy	358	207	220			
Study Baseline	296	466	323	317	403	273
3 months	172	465	364			
6 months	188	490	346			
9 months	149	552	345			
12 months	205	560	361	317	421	262
18 months	123	487	377			
24 months	73	504	360	317	461	(286)

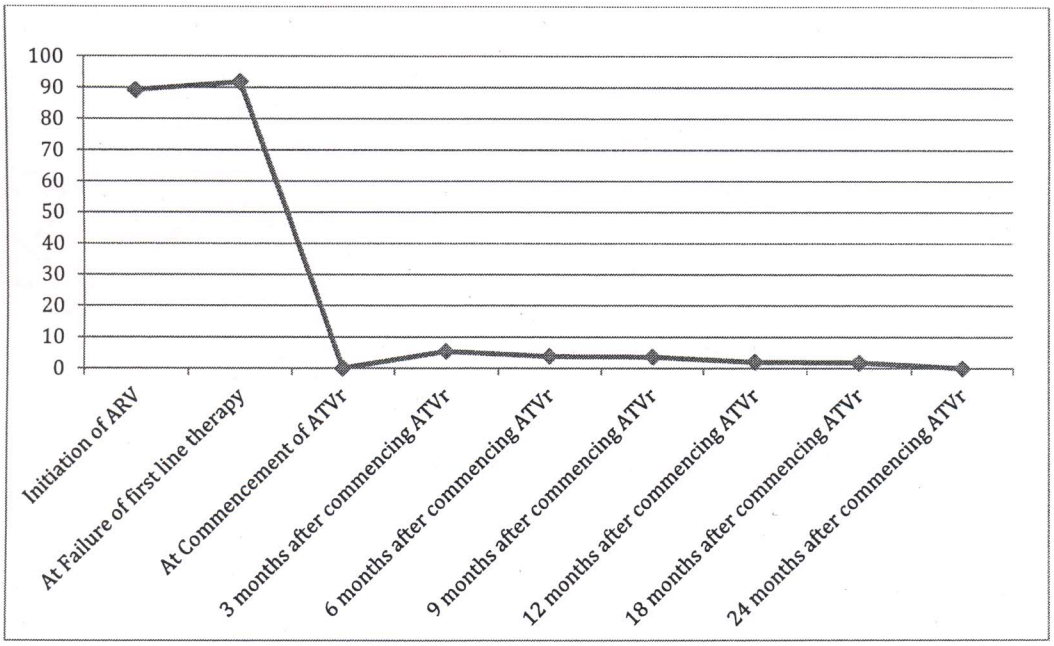

Fig. (1). The Proportion of Subjects with detectable viral Load Over 24 Months Period Post ATVr switch.

Those who failed ATV/r-based regimens in this programmatic switch may still benefit from LPV/r-based ART as it is thought that LPV/r-specific mutations may not have occurred at the time of the programmatic switch.

The finding that 37% of patients on LPV/r were failing this regimen is worrisome. Adherence data and toxicity measures among patients on LPV/r were not collected for this evaluation. We hypothesize that this high rate of failure may not be due to drug resistance but rather poor adherence resulting from complications of LPV/r, particularly diarrhea [19]. Although data is not presented, in a focus group discussion including patients that were programmatically switched in this review, 40% of the patients reported having had diarrhea not easily correctable with loperamide while on LPV/r. For those patients that were initially virologically controlled on LPV/r and who were maintained on LPV/r regimen for an additional 24 months, we found that nearly 8% of them subsequently developed virologic failure. This proportion may reflect true virologic failure due to universal protease inhibitor-associated mutations. The mutations associated with LPV/r use has been extensively reported and include the following protease mutations: 50V, 54VLA, 63P 71V/Y 82A/L, 84V, 90N [20]. Although LPV/r has a high genetic barrier to genotypic resistance, this may be a contributing factor to the enhanced forgiveness of non-adherence for patients on this drug [21]; this claim needs to be further substantiated with HIV genotyping studies.

It is surprising to find that 20% of patients that switched to ATV/r as a result of first-line regimen failure developed virologic failure by 24 months. This may be due to the small number patients available for analysis at 24 months. However, further analysis of the 4 patients who failed

treatment showed that these were patients who had never been suppressed on the first-line regimen and all had been maintained on their failing first-line regimen for over 2 years before ATV/r switch. In the ANRS Puzzle 2 study, ATV/r-based regimens had virtually no virologic activity in patients with multiple PI mutations [22]. In the BMS A1424-045 study, ATV/r was also shown to have very limited utility in achieving virologic suppression among highly treatment-experienced patients with possible multi-drug resistance mutations [23].

CONCLUSION

This evaluation was undertaken to determine if a recommended programmatic policy in second-line ART regimens would prove to be sound in our setting. Despite a significant number of patients on second- line ART in our centre, the evaluation was limited by poor reporting of laboratory data, such as VL measurements. As a result, we are cautious in interpreting our results. Our evaluation does highlight the many real-life circumstances that occur when international guidelines change, including various categories of patients that were placed on ATV/r most of which were not newly initiating second-line ART. While it appears that there is no apparent difference between patients that were switched to ATV/r compared to those maintained on LPV/r, further studies that incorporate analyses of drug resistance mutations are needed to confirm these findings.

CONFLICT OF INTEREST

The authors confirm that this article content has no conflict of interest.

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